

JCTC

Journal of Chemical Theory and Computation

Assessment of Model Chemistries for Noncovalent Interactions

Yan Zhao and Donald G. Truhlar*

*Department of Chemistry and Supercomputing Institute, University of Minnesota,
Minneapolis, Minnesota 55455-0431*

Received February 9, 2006

Abstract: In the present study, we report tests of 57 model chemistry methods for calculating binding energies of 31 diverse van der Waals molecules arranged in five databases of noncovalent interaction energies. The model chemistries studied include wave function theory (WFT), density functional theory (DFT), and combined wave function-density-functional-theory (CWFDFDFT), and they include methods whose computational effort scales (for large systems) as N^7 , N^6 , N^5 , and N^4 , where N is the number of atoms. The model chemistries include 2 CWFDFDFT N^7 models, 4 multilevel WFT N^7 models, 5 single-level WFT N^7 models, 4 CWFDFDFT N^6 models, 3 multilevel WFT N^6 models, 11 single-level WFT N^6 models, 5 CWFDFDFT N^6 models, 10 single-level WFT N^6 models, 4 multilevel WFT N^5 models, 4 single-level DFT N^4 models, and 5 single-level WFT N^4 models. We draw the following conclusions based on the mean absolute errors in 31 noncovalent binding energies: (1) MCG3-MPW gives the best performance for predicting the binding energies of these noncovalent complexes. (2) MCQCISD-MPWB and MCQCISD-MPW are the best two N^6 methods. (3) M05-2X is the best single-level method for these noncovalent complexes. These four methods should facilitate useful calculations on a wide variety of practical applications involving hydrogen bonding, charge-transfer complexes, dipole interactions, weak (dispersion-like) interactions, and $\pi\cdots\pi$ stacking. If a user is interested in only a particular type of noncovalent interactions, though, some other methods, may be recommended for especially favorable performance/cost ratios. For example, BMC-CCSD has an outstanding performance for hydrogen bonding, and PWB6K has an outstanding cost-adjusted performance for dipole interaction calculations on very large systems. We also show that M05-2X performs well for interactions of amino acid pair residues.

1. Introduction

Noncovalent interactions play very important roles in many areas of science such as molecular recognition, protein folding, stacking of nucleobases, crystal packing, vapor–liquid condensation, polymer packing, soft materials design, self-assembly, supramolecular chemistry, solvation, and molecular scattering. It is especially noteworthy that noncovalent interactions underlie many complex biological functions including cell–cell recognition, intracellular signaling, and the regulation of gene expression. Understanding

various noncovalent interactions is a key to unraveling the mysteries of cellular function in health and disease and to developing new drugs as well as being a critical component in nanotechnological uses of soft materials.

Model chemistry is “an approximate but well-defined mathematical procedure of simulation”¹ of chemical phenomena. As pointed out by Pople,¹ there is a wide range of possible empiricism; model chemistry can even be *ab initio* (i.e., without parameters except for fundamental constants of physics). Several multilevel model chemistry methods, such as the Gaussian- n theories and their variants developed by Pople and co-workers,^{2–5} the related Weizmann- n methods,^{6,7}

* Corresponding author e-mail: truhlar@umn.edu.

the complete basis set (CBS) family of methods by Petersson and co-workers,^{8–10} the single-coefficient^{11–15} and multi-coefficient^{14–24} correlation methods (MCCMs) of our group, and the recent multilevel methods of Hu and co-workers,^{25,26} have been developed and validated for covalent interactions as required for application to thermochemistry (heats of formation, atomization energies, etc.) and kinetics (barrier heights). Although some research^{27–30} has employed these multilevel methods for hydrogen bonded clusters and ionic clusters, until now there has been only one systematic validation of multilevel methods for noncovalent interactions, and that study was limited to rare gas interactions.³¹ The lack of broader validation studies is partly due to the lack, until recently,^{32–34} of standard databases (analogous to the G3 database,^{5,35–37} Database/3,¹⁵ or a recent metal–ligand bond energy database³⁸) for nonbonded interactions. In a recent communication,³⁹ we compared several multilevel methods for the calculation of the stacking interaction energies in benzene dimers, and we found that the empirical hybrid of density functional theory (DFT) and wave function theory (WFT), also called multicoefficient extrapolated density functional theory,^{22,23} give the best results for benzene dimers. A key objective of the present article is to assess multilevel model chemistry methods against several recently developed databases^{32,33} for nonbonded interactions. We also present the results for several single-level methods for comparison. Both DFT and WFT are considered.

Section 2 describes the theories and databases used in the present work. Section 3 presents results and discussion, and section 4 has concluding remarks. The Appendix considers interaction energies of amino acid residues.

2. Theory and Databases

2.1. Theory. The levels of electron correlation used in the present paper include Møller–Plesset second-, third-, and fourth-order perturbation theory (MP2,⁴⁰ MP3,⁴¹ MP4⁴¹), Møller–Plesset fourth-order perturbation theory without singles and triples contributions⁴¹ (MP4DQ), Møller–Plesset fourth-order perturbation theory without triples contributions⁴¹ (MP4(SDQ)), quadratic configuration interaction with single and double excitations⁴² (QCISD), QCISD with quasiperturbative connected triples⁴² (QCISD(T)), coupled cluster with single and double excitations (CCSD),⁴³ and CCSD with quasiperturbative connected triples (CCSD(T)).⁴⁴ In general, core orbitals are doubly occupied in all configurations except for some MP2 calculations, and those are denoted MP2(full). We also present results for two hybrid meta-DFT methods, PWB6K³³ and M05-2X.⁴⁵ We note that PWB6K was found in a previous study³³ to perform best out of 25 density functionals tested against the databases employed here, and readers interested in the performance of other density functionals are referred to that study. For example, PWB6K was found to have an error three times lower than the popular B3LYP⁴⁶ functional. PWB6K was also found to have excellent performance for hydrogen bonds to π acceptor,⁴⁷ a type of interaction not present in the database. The M05-2X functional was not available (it had not yet been developed) at the time of those assessments,

but was subsequently shown to be very accurate,³⁴ and so it is included here.

Multicoefficient extrapolated DFT methods^{22,23} include both DFT and WFT components in the same calculation.²³ These calculations may be labeled as combined wave function density functional methods (abbreviated CWFDF or WFT/DFT) or as fifth-rung methods on Jacob's ladder^{48,49} of density functionals. We compare the results obtained by multicoefficient extrapolated DFT methods (MC3BB,²² MC3MPW,²² MC3MPWB,²³ MCCO-MPW, and MPWB,²³ MCUT-MPW and MPWB,²³ MCQCISD-MPW and -MPWB,²³ and MCG3-MPW and -MPWB²³) to those obtained by pure-WFT-based multilevel methods, in particular, G3SX,⁵ CBS-QB3,⁹ G3SX(MP3),⁵ MCCM/3,¹⁵ and BMC-CCSD.²⁴ Within the MCCM/3 suite, we specifically consider MCG3/3, MC-QCISD/3, and MC-UT/3. We note that G3SX(MP3), MCG3/3, and MC-QCISD/3 were selected as particularly efficient methods in a previous systematic study of multilevel methods for thermochemistry.⁵⁰ Since then, though, the multicoefficient extrapolated DFT methods^{22,23} have been developed, and they show an even better performance. We note that the recently developed multilevel method BMC-CCSD²⁴ has similar cost to MC-QCISD/3 but improved performance for atomization energies, barrier heights, ionization potentials, and electron affinities. Thus it will be interesting to test BMC-CCSD for noncovalent interactions. BMC-CCSD and MC-QCISD/3 are considerably less expensive than G3SX and G3SX(MP3).

We also consider some examples of the older scaling-all-correlation (SAC) methods,^{12,14,15} which are single-coefficient correlation methods. Although previous tests of these methods for thermochemistry have shown worthwhile improvement over MP2 at essentially no additional cost, they are not as powerful as MCCMs, and the present tests will show if they are useful for noncovalent interactions. The three scaling-all-correlation (SAC) methods tested in this study use version-3s scaling coefficients.¹⁵

Note that the zero-point corrections were excluded from the G3SX, G3SX(MP3), and CBS-QB3 calculations (and all other methods) in this article since, in the standard spectroscopic notation, we are interested in predicting D_e ,⁵¹ not D_0 .

2.2. Noncovalent Interaction Databases. We tested all 57 considered methods (22 multilevel methods and 35 single-level methods) against five recently developed databases, in particular, HB6/04,³² CT7/04,³² DI6/04,³² WI7/05,³³ and PPS5/05,³³ for various kinds of noncovalent interactions. HB6/04 is a hydrogen bond database that consists of the equilibrium binding energies of six hydrogen bonding dimers, namely (NH₃)₂, (HF)₂, (H₂O)₂, NH₃...H₂O, (HCONH₂)₂, and (HCOOH)₂. The CT7/04 database consists of the binding energies of seven charge-transfer complexes, in particular C₂H₄...F₂, NH₃...F₂, C₂H₂...ClF, HCN...ClF, NH₃...Cl₂, H₂O...ClF, and NH₃...ClF. The DI6/04 database contains the binding energies of six dipole interaction complexes: (H₂S)₂, (HCl)₂, HCl...H₂S, CH₃Cl...HCl, CH₃SH...HCN, and CH₃SH...HCl. The WI7/05 database consists of the binding energies of seven weak interaction complexes, namely HeNe, HeAr, Ne₂, NeAr, CH₄...Ne, C₆H₆...Ne, and (CH₄)₂, all of which are bound by dispersion interactions.

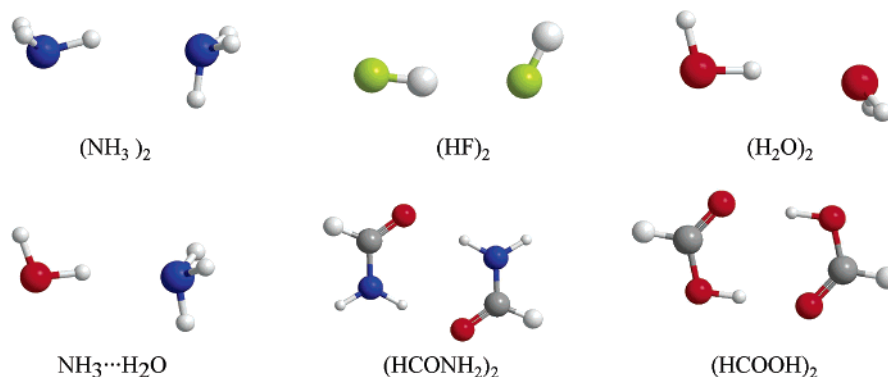


Figure 1. Geometries of the dimers in the HB6/04 database.

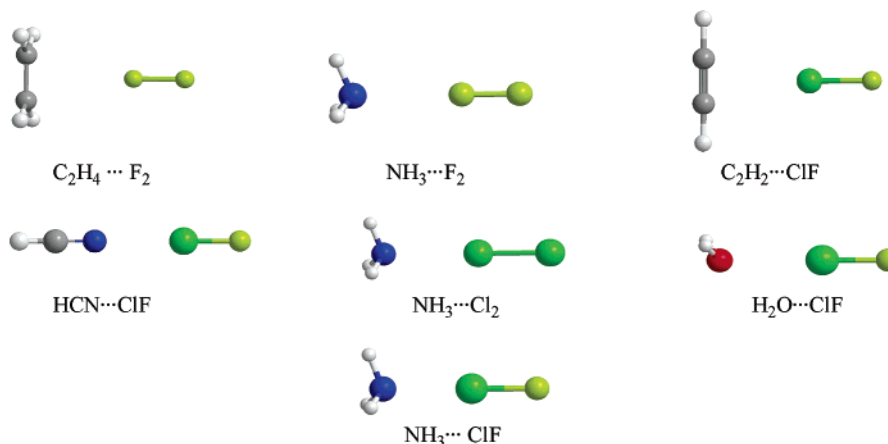


Figure 2. Geometries of the complexes in the CT7/04 database.

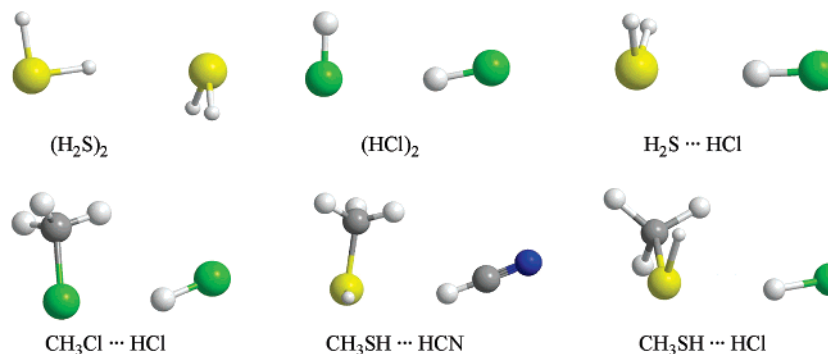


Figure 3. Geometries of the dimers in the DI6/04 database.

The PPS5/05 database consists of binding energies of five π – π stacking complexes, namely (C₂H₂)₂, (C₂H₄)₂, sandwich (C₆H₆)₂, T-shaped (C₆H₆)₂, and parallel-displaced (C₆H₆)₂.

Figures 1–5 depict the geometries of the noncovalent complexes in the present study.

2.3. Computer Programs, Geometries, Basis Sets, Counterpoise Correction, and Full Models. All the calculations in the present study are performed by using the locally developed program *MLGAUSS*⁵² in conjunction with *Gaussian03*.⁵³ The *MLGAUSS* program is available from the Truhlar group's software Web page.⁵⁴

The geometries for the benzene dimers are taken from Sinnokrot and Sherrill.⁵⁵ The geometries of all other complexes are optimized at the MC-QCISD/3¹⁵ level of theory. Note that these same geometries are used for all methods tested. For methods, namely G3SX(MP3), CBS-QB3, and

G3SX, that are ordinarily *defined* to use other geometries, we added the suffix “//Q” to denote this choice of geometries, which is used for *all* methods in this article.

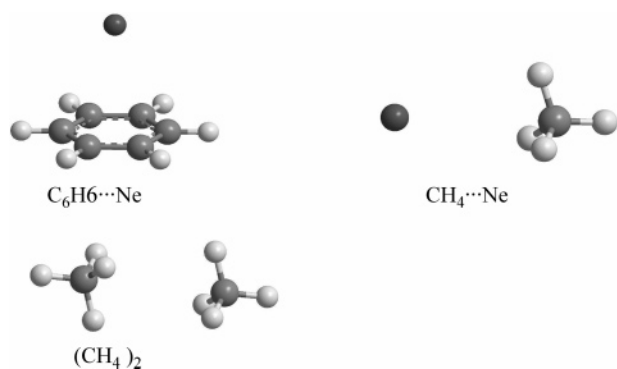
The basis sets used include the 6-31G(d),⁴¹ 6-31+G(d,p),⁴¹ 6-31G(2df,p),⁴¹ 6-31B(d),²⁴ G3Large,³ G3XLarge,⁵ modified Gaussian-3¹⁴ (MG3), and modified Gaussian-3 semidiffuse⁵⁶ (MG3S) basis sets. We note that the MG3 basis¹⁴ is also denoted G3LargeMP2.⁵⁷

For most of the tested methods, we perform calculations without the counterpoise corrections (CP)^{58,59} for basis set superposition error (BSSE). We do present, however, the CP-corrected results for the MP2/MG3S, M05-2X/MG3S, and PWB6K/MG3S levels of theory.

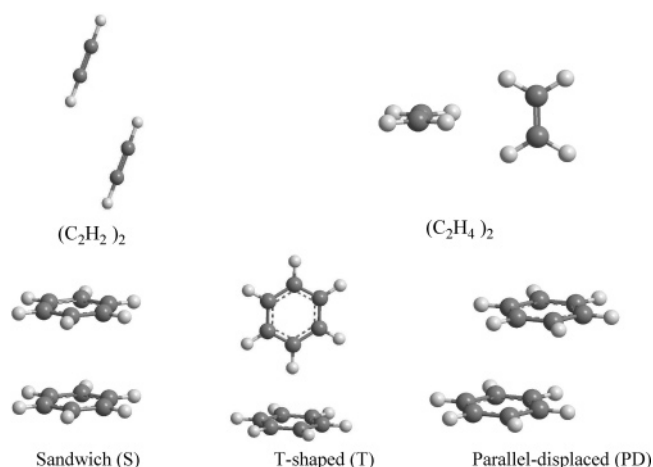
A comment on the distribution between all possible models and a “full theoretical model chemistry” is in order here. When special procedures for particular molecules or par-

Table 1. Binding Energies (kcal/mol) and Mean Errors (kcal/mol) for the HB6/04 Database by Multilevel Methods

| | (NH ₃) ₂ | (HF) ₂ | (H ₂ O) ₂ | NH ₃ ...H ₂ O | (HCONH ₂) ₂ | (HCOOH) ₂ | MSE | MUE |
|-------------------------------|---------------------------------|-------------------|---------------------------------|-------------------------------------|------------------------------------|----------------------|-------|------|
| best estimate | 3.16 | 4.57 | 4.97 | 6.41 | 14.94 | 16.15 | | |
| <i>N</i> ⁷ Methods | | | | | | | | |
| G3SX(MP3)//Q | 3.15 | 4.57 | 5.10 | 6.39 | 14.67 | 15.91 | −0.07 | 0.11 |
| MCG3 | 3.14 | 4.41 | 5.06 | 6.36 | 14.69 | 15.75 | −0.13 | 0.16 |
| CBS-QB3//Q | 3.26 | 4.80 | 5.18 | 6.61 | 15.02 | 16.35 | 0.17 | 0.17 |
| G3SX//Q | 3.23 | 4.84 | 5.26 | 6.52 | 15.10 | 16.52 | 0.21 | 0.21 |
| MCG3-MPW | 2.91 | 4.48 | 4.86 | 6.09 | 14.39 | 15.72 | −0.29 | 0.29 |
| MCG3-MPWB | 2.86 | 4.44 | 4.83 | 6.06 | 14.07 | 15.49 | −0.41 | 0.41 |
| <i>N</i> ⁶ Methods | | | | | | | | |
| BMC-CCSD | 3.25 | 4.87 | 5.22 | 6.43 | 14.94 | 16.08 | 0.10 | 0.12 |
| MC-QCISD/3 | 3.16 | 4.48 | 5.07 | 6.34 | 14.25 | 15.22 | −0.28 | 0.32 |
| MCUT/3 | 3.22 | 4.60 | 5.14 | 6.41 | 14.20 | 15.12 | −0.25 | 0.34 |
| MCQCISD-MPW | 2.87 | 4.45 | 4.83 | 6.07 | 13.98 | 15.35 | −0.44 | 0.44 |
| MCQCISD-MPWB | 2.86 | 4.38 | 4.84 | 6.06 | 13.65 | 15.09 | −0.55 | 0.55 |
| MCUT-MPW | 2.79 | 4.42 | 4.72 | 5.99 | 13.64 | 15.06 | −0.59 | 0.59 |
| MCUT-MPWB | 2.80 | 4.41 | 4.79 | 6.02 | 13.37 | 14.95 | −0.64 | 0.64 |
| <i>N</i> ⁵ Methods | | | | | | | | |
| SAC-MP2/MG3S | 3.38 | 4.93 | 5.51 | 6.85 | 15.01 | 16.39 | 0.31 | 0.31 |
| MC3MPW | 3.26 | 4.76 | 5.52 | 7.04 | 14.17 | 16.21 | 0.13 | 0.39 |
| MCCO/3 | 3.17 | 4.20 | 5.01 | 6.71 | 13.85 | 15.33 | −0.32 | 0.44 |
| MC3MPWB | 3.20 | 4.80 | 5.45 | 6.82 | 13.80 | 15.73 | −0.07 | 0.46 |
| MCCO-MPW | 2.76 | 4.17 | 4.82 | 6.24 | 13.45 | 15.62 | −0.52 | 0.52 |
| MC3BB | 2.77 | 4.38 | 4.97 | 6.32 | 13.05 | 15.00 | −0.62 | 0.62 |
| MCCO-MPWB | 2.69 | 4.24 | 4.77 | 6.06 | 13.03 | 15.19 | −0.70 | 0.70 |
| SAC-MP2/6-31+G(d,p) | 4.28 | 5.02 | 6.61 | 8.25 | 15.00 | 15.97 | 0.82 | 0.88 |
| SAC-MP2/6-31G(d) | 4.83 | 7.76 | 7.54 | 8.93 | 18.85 | 19.28 | 2.83 | 2.83 |
| average | | | | | | | −0.06 | 0.52 |

**Figure 4.** Geometries of selected dimers in the WI7/05 database.

particular symmetries are avoided, and a model is general and continuous, the model may be called a full theoretical model chemistry.¹ For this reason,^{17,18} we prefer SAC-,^{12,13} MCG3-,¹⁸ G3S-,⁴ and G3SX-type⁵ methods to G2-,² G3-,³ and G3X-type⁵ methods because the G2-, G3-, and G3X-type methods involve a discontinuous high-level correction, whereas scaling methods do not. Similarly, the use of CP corrections disqualifies a method as “full” because, for example, one needs special decisions such as whether to apply it only to van der Waals molecules but not (for example) to the O–H bond in water. Similarly, should Ne₂Be be treated as a complex of Ne₂ with Be or NeBe with Ne? Should NH₄Cl be treated as NH₃ complexed to HCl or NH₄⁺ complexed to Cl[−]? Finally, it is essentially impossible to apply CP corrections to amorphous solids and many other cases.

**Figure 5.** Geometries of the dimers in the PPS/05 database.

Nevertheless, CP corrections are often used for calculating van der Waals binding energies, so we do consider some non-“full” models employing CP corrections in this paper.

3. Results and Discussion

Results are given in Tables 1–3 and S1–S8, where tables with an S prefix are found in the Supporting Information. In particular, the binding energies and mean errors of the tested multilevel methods are listed in Tables 1, S1, S3, S5, S7, and 3, and results for the tested single-level methods are presented in Tables 2, S2, S4, S6, S8, S10, and 3. In these tables we classify the methods according to their scaling

Table 2. Binding Energies (kcal/mol) and Mean Errors (kcal/mol) for the HB6/04 Database by Single-Level Methods

| method | (NH ₃) ₂ | (HF) ₂ | (H ₂ O) ₂ | NH ₃ ...H ₂ O | (HCONH ₂) ₂ | (HCOOH) ₂ | MSE | MUE |
|-------------------------------|---------------------------------|-------------------|---------------------------------|-------------------------------------|------------------------------------|----------------------|-------|------|
| best estimate | 3.16 | 4.57 | 4.97 | 6.41 | 14.94 | 16.15 | | |
| <i>N</i> ⁷ Methods | | | | | | | | |
| CCSD(T)/6-311+G(d,p) | 3.66 | 4.66 | 5.91 | 7.17 | 13.48 | 14.51 | −0.13 | 0.90 |
| MP4/6-31G+(d) | 4.25 | 5.51 | 6.90 | 8.31 | 14.89 | 15.80 | 0.91 | 1.05 |
| MP4/6-31G(2df,p) | 3.87 | 7.12 | 6.44 | 6.99 | 17.65 | 18.98 | 1.81 | 1.81 |
| QCISD(T)/6-31G(d) | 4.28 | 7.10 | 6.81 | 8.00 | 17.30 | 17.64 | 1.82 | 1.82 |
| MP4/6-31G(d) | 4.31 | 7.19 | 6.88 | 8.05 | 17.40 | 17.86 | 1.92 | 1.92 |
| <i>N</i> ⁶ Methods | | | | | | | | |
| MP3/6-311+G(d,p) | 3.54 | 4.61 | 5.76 | 6.98 | 13.23 | 14.30 | −0.30 | 0.89 |
| MP3/6-31G+(d) | 4.14 | 5.40 | 6.73 | 8.12 | 14.73 | 15.62 | 0.76 | 1.01 |
| CCSD/6-311+G(d,p) | 3.43 | 4.54 | 5.67 | 6.85 | 12.69 | 13.70 | −0.55 | 1.03 |
| MP4(SDQ)/6-311+G(d,p) | 3.45 | 4.53 | 5.70 | 6.89 | 12.56 | 13.56 | −0.58 | 1.09 |
| MP4(DQ)/6-31B(d) | 4.50 | 6.10 | 6.41 | 8.08 | 15.46 | 15.41 | 0.96 | 1.21 |
| CCSD/6-31B(d) | 4.51 | 6.14 | 6.43 | 8.06 | 15.82 | 15.77 | 1.09 | 1.21 |
| MP4(SDQ)/6-31G(2df,p) | 3.64 | 6.87 | 6.15 | 6.67 | 16.45 | 17.72 | 1.22 | 1.22 |
| MP3/6-31G(2df,p) | 3.74 | 6.83 | 6.20 | 6.82 | 16.85 | 18.09 | 1.39 | 1.39 |
| QCISD/6-31G(d) | 4.11 | 6.99 | 6.65 | 7.77 | 16.51 | 16.91 | 1.46 | 1.46 |
| MP4(SDQ)/6-31G(d) | 4.14 | 7.02 | 6.69 | 7.82 | 16.45 | 16.87 | 1.47 | 1.47 |
| MP3/6-31G(d) | 4.21 | 6.94 | 6.71 | 7.96 | 16.72 | 17.15 | 1.58 | 1.58 |
| <i>N</i> ⁵ Methods | | | | | | | | |
| MP2/MG3 | 3.32 | 4.92 | 5.43 | 6.74 | 14.87 | 16.29 | 0.23 | 0.25 |
| MP2/MG3S | 3.33 | 4.91 | 5.46 | 6.78 | 14.87 | 16.27 | 0.24 | 0.26 |
| MP2(full)/G3Large | 3.34 | 4.99 | 5.48 | 6.80 | 14.97 | 16.46 | 0.31 | 0.31 |
| MP2/6-31+G(d,p) | 4.02 | 4.91 | 6.37 | 7.89 | 14.40 | 15.51 | 0.48 | 0.88 |
| MP2/MG3S-CP | 2.87 | 3.94 | 4.53 | 5.96 | 13.22 | 14.10 | −0.93 | 0.93 |
| MP2/6-311+G(d,p) | 3.73 | 4.66 | 5.99 | 7.35 | 13.31 | 14.45 | −0.12 | 0.99 |
| MP2/6-31G+(d) | 4.27 | 5.51 | 7.00 | 8.49 | 14.87 | 15.96 | 0.98 | 1.07 |
| MP2/6-31B(d) | 4.73 | 6.35 | 6.78 | 8.59 | 16.57 | 16.89 | 1.62 | 1.62 |
| MP2/6-31G(2df,p) | 4.01 | 7.22 | 6.61 | 7.25 | 17.76 | 19.19 | 1.97 | 1.97 |
| MP2/6-31G(d) | 4.40 | 7.34 | 7.08 | 8.35 | 17.48 | 18.19 | 2.11 | 2.11 |
| <i>N</i> ⁴ Methods | | | | | | | | |
| M05-2X/MG3S-CP | 3.01 | 4.78 | 5.13 | 6.40 | 14.33 | 16.22 | −0.05 | 0.20 |
| PWB6K/MG3S-CP | 3.05 | 4.78 | 5.09 | 6.40 | 13.75 | 15.72 | −0.23 | 0.34 |
| M05-2X/MG3S | 3.19 | 5.17 | 5.53 | 6.71 | 14.71 | 16.81 | 0.32 | 0.40 |
| PWB6K/MG3S | 3.23 | 5.19 | 5.51 | 6.73 | 14.13 | 16.43 | 0.17 | 0.44 |
| HF/6-31G(d) | 3.00 | 5.95 | 5.59 | 6.43 | 12.93 | 14.61 | −0.28 | 0.95 |
| HF/6-311+G(d,p) | 2.25 | 4.17 | 4.75 | 5.42 | 10.41 | 12.17 | −1.84 | 1.84 |
| HF/MG3S | 1.71 | 3.99 | 3.97 | 4.54 | 10.22 | 12.30 | −2.24 | 2.24 |
| HF/MG3 | 1.71 | 3.99 | 3.97 | 4.54 | 10.22 | 12.30 | −2.24 | 2.24 |
| HF/G3Large | 1.71 | 3.99 | 3.96 | 4.54 | 10.21 | 12.29 | −2.25 | 2.25 |
| average | | | | | | | 0.37 | 1.21 |

properties⁶⁰ (*N*⁷, *N*⁶, *N*⁵, or *N*⁴), where *N* is the number of atoms. The tables show the mean unsigned error (MUE, also called mean absolute deviation) and mean signed error (MSE). We use “CP” to denote calculations that do include the counterpoise correction for the BSSE.

To put the large number of results in this paper into perspective, we define an overall error quantity in Table 3, namely the mean MUE:

$$\text{MMUE} = [\text{MUE}(\text{HB}) + \text{MUE}(\text{CT}) + \text{MUE}(\text{DI}) + \text{MUE}(\text{WI}) + \text{MUE}(\text{PPS})]/5 \quad (1)$$

Our discussion will focus *mainly* on the highly averaged MUEs and MMUEs because they provide measures of the broad usefulness of the methods tested for various kinds of noncovalent interactions. The tables are arranged in such a

way that users interested in one or another subsets of the results may make their own comparisons and draw their own conclusions.

3.1. Hydrogen Bonding. Tables 1 and 2 summarize the results for hydrogen bonding calculations. Among the tested multilevel methods, G3SX(MP3) gives the lowest MUE for binding energies in the HB6/04 database. BMC-CCSD is the best *N*⁶ multilevel method, and it has an MUE only 10% larger than G3SX(MP3) with a cost more than five times lower, as well as having better scaling to large systems. MC3MPW is the best *N*⁵ multilevel method, with an MUE much larger than BMC-CCSD and a cost only slightly smaller, but better scaling. Table 2 shows that the best of the tested single-level methods for hydrogen bonding calculations are M05-2X/MG3S and MP2/MG3. MP2/MG3S

Table 3. Overall Results

| method | type ^a | HB6/05 MUE | CT7/05 MUE | DI6/05 MUE | WI7/05 MUE | PPS5/05 MUE | MMUE | cost ^b |
|-------------------------------|-------------------|---------------|---------------|---------------|---------------|----------------|------|-------------------|
| <i>N</i> ⁷ Methods | | | | | | | | |
| MCG3-MPW | ML DFT/WFT | 0.29 | 0.13 | 0.15 | 0.06 | 0.18 | 0.16 | 110 |
| MCG3-MPWB | ML DFT/WFT | 0.41 | 0.13 | 0.20 | 0.05 | 0.17 | 0.19 | 111 |
| MCG3 | ML WFT | 0.16 | 0.19 | 0.29 | 0.05 | 0.80 | 0.30 | 104 |
| G3SX(MP3)//Q | ML WFT | 0.11 | 0.18 | 0.35 | 0.08 | 0.80 | 0.31 | 135 |
| CBS-QB3//Q | ML WFT | 0.17 | 0.38 | 0.36 | 0.11 | 0.57 | 0.32 | 204 |
| G3SX//Q | ML WFT | 0.21 | 0.26 | 0.39 | 0.11 | 0.84 | 0.36 | 1116 |
| CCSD(T)/6-311+G(d,p) | SL WFT | 0.90 | 0.62 | 0.47 | 0.07 | 0.95 | 0.60 | 409 |
| MP4/6-31G(2df,p) | SL WFT | 1.81 | 0.71 | 0.31 | 0.25 | 0.58 | 0.73 | 848 |
| MP4/6-31G+(d) | SL WFT | 1.05 | 0.96 | 0.50 | 0.14 | 1.06 | 0.74 | 150 |
| MP4/6-31G(d) | SL WFT | 1.92 | 0.75 | 0.69 | 0.10 | 0.28 | 0.75 | 61 |
| QCISD(T)/6-31G(d) | SL WFT | 1.82 | 0.83 | 0.74 | 0.10 | 0.46 | 0.79 | 71 |
| <i>N</i> ⁶ Methods | | | | | | | | |
| MCQCISD-MPWB | ML DFT/WFT | 0.55 | 0.12 | 0.19 | 0.05 | 0.18 | 0.22 | 29 |
| MCQCISD-MPW | ML DFT/WFT | 0.44 | 0.12 | 0.18 | 0.07 | 0.33 | 0.23 | 29 |
| MCUT-MPWB | ML DFT/WFT | 0.64 | 0.14 | 0.25 | 0.06 | 0.52 | 0.32 | 22 |
| MCUT/3 | ML WFT | 0.34 | 0.25 | 0.35 | 0.07 | 0.74 | 0.35 | 16 |
| MCUT-MPW | ML DFT/WFT | 0.59 | 0.18 | 0.22 | 0.09 | 0.75 | 0.37 | 22 |
| MC-QCISD/3 | ML WFT | 0.32 | 0.23 | 0.37 | 0.07 | 0.85 | 0.37 | 23 |
| BMC-CCSD | ML WFT | 0.12 | 0.31 | 0.58 | 0.14 | 1.17 | 0.46 | 26 |
| MP3/6-31G+(d) | SL WFT | 1.01 | 0.86 | 0.56 | 0.12 | 0.47 | 0.60 | 5 |
| MP3/6-311+G(d,p) | SL WFT | 0.89 | 1.00 | 0.55 | 0.07 | 0.55 | 0.61 | 14 |
| MP4(SDQ)/6-31G(2df,p) | SL WFT | 1.22 | 0.80 | 0.66 | 0.24 | 0.24 | 0.63 | 18 |
| MP4(SDQ)/6-311+G(d,p) | SL WFT | 1.09 | 0.84 | 0.70 | 0.07 | 0.47 | 0.63 | 15 |
| MP3/6-31G(2df,p) | SL WFT | 1.39 | 0.85 | 0.45 | 0.23 | 0.26 | 0.63 | 17 |
| CCSD/6-311+G(d,p) | SL WFT | 1.03 | 0.99 | 0.74 | 0.07 | 0.46 | 0.66 | 68 |
| MP3/6-31G(d) | SL WFT | 1.58 | 0.90 | 0.73 | 0.09 | 0.69 | 0.80 | 2 |
| MP4(SDQ)/6-31G(d) | SL WFT | 1.47 | 0.85 | 0.87 | 0.10 | 0.76 | 0.81 | 1 |
| QCISD/6-31G(d) | SL WFT | 1.46 | 0.89 | 0.93 | 0.10 | 0.81 | 0.84 | 8 |
| MP4(DQ)/6-31B(d) | SL WFT | 1.21 | 1.99 | 0.86 | 0.14 | 0.69 | 0.98 | 1 |
| CCSD/6-31B(d) | SL WFT | 1.21 | 2.19 | 0.86 | 0.13 | 0.73 | 1.03 | 8 |
| <i>N</i> ⁶ Methods | | | | | | | | |
| MC3MPWB | ML DFT/WFT | 0.46 | 0.46 | 0.38 | 0.07 | 0.48 | 0.37 | 7 |
| MCCO-MPWB | ML DFT/WFT | 0.70 | 0.27 | 0.33 | 0.07 | 0.69 | 0.41 | 21 |
| MP2/MG3S-CP | SL WFT | 0.93 | 0.26 | 0.25 | 0.18 | 0.48 | 0.42 | 22 |
| MCCO-MPW | ML DFT/WFT | 0.52 | 0.36 | 0.31 | 0.12 | 0.81 | 0.43 | 20 |
| MC3MPW | ML DFT/WFT | 0.39 | 0.52 | 0.36 | 0.13 | 0.93 | 0.47 | 6 |
| MP2/MG3S | SL WFT | 0.26 | 0.73 | 0.45 | 0.07 | 1.24 | 0.55 | 14 |
| MP2/MG3 | SL WFT | 0.25 | 0.72 | 0.44 | 0.09 | 1.32 | 0.56 | 15 |
| MC3BB | ML DFT/WFT | 0.62 | 0.32 | 0.75 | 0.27 | 1.10 | 0.61 | 7 |
| SAC-MP2/MG3S | ML WFT | 0.31 | 0.86 | 0.53 | 0.08 | 1.38 | 0.63 | 14 |
| MP2(full)/G3Large | SL WFT | 0.31 | 0.80 | 0.57 | 0.10 | 1.40 | 0.63 | 36 |
| MP2/6-31+G(d,p) | SL WFT | 0.88 | 0.71 | 0.23 | 0.13 | 1.40 | 0.67 | 1 |
| MP2/6-311+G(d,p) | SL WFT | 0.99 | 0.47 | 0.29 | 0.08 | 1.69 | 0.70 | 5 |
| MCCO/3 | ML WFT | 0.44 | 0.60 | 0.70 | 0.04 | 1.80 | 0.72 | 15 |
| MP2/6-31G(d) | SL WFT | 2.11 | 0.87 | 0.46 | 0.12 | 0.21 | 0.75 | 1 |
| MP2/6-31G+(d) | SL WFT | 1.07 | 1.01 | 0.29 | 0.14 | 1.37 | 0.78 | 1 |
| SAC-MP2/6-31+G(d,p) | ML WFT | 0.88 | 1.24 | 0.15 | 0.15 | 2.17 | 0.92 | 1 |
| MP2/6-31G(2df,p) | SL WFT | 1.97 | 1.18 | 0.18 | 0.26 | 1.16 | 0.95 | 3 |
| SAC-MP2/6-31G(d) | ML WFT | 2.83 | 1.67 | 0.17 | 0.14 | 1.04 | 1.17 | 1 |
| MP2/6-31B(d) | SL WFT | 1.62 | 3.35 | 1.13 | 0.13 | 0.31 | 1.31 | 1 |
| <i>N</i> ⁶ Methods | | | | | | | | |
| M05-2X/MG3S-CP | SL DFT | 0.20 | 0.30 | 0.32 | 0.03 | 0.71 | 0.31 | 9 |
| M05-2X/MG3S | SL DFT | 0.40 | 0.46 | 0.27 | 0.09 | 0.49 | 0.34 | 6 |
| PWB6K/MG3S | SL DFT | 0.44 | 0.25 | 0.24 | 0.15 | 0.81 | 0.38 | 9 |
| PWB6K/MG3S-CP | SL DFT | 0.34 | 0.16 | 0.32 | 0.07 | 1.02 | 0.38 | 9 |
| HF/6-31G(d) | SL WFT | 0.95 | 2.39 | 2.12 | 0.23 | 2.69 | 1.68 | 0.1 |
| HF/6-311+G(d,p) | SL WFT | 1.84 | 3.09 | 2.17 | 0.31 | 3.42 | 2.17 | 1 |
| HF/MG3S | SL WFT | 2.24 | 3.77 | 2.40 | 0.30 | 3.39 | 2.42 | 5 |
| HF/MG3 | SL WFT | 2.24 | 3.77 | 2.40 | 0.30 | 3.39 | 2.42 | 6 |
| HF/G3Large | SL WFT | 2.25 | 3.77 | 2.41 | 0.30 | 3.39 | 2.42 | 8 |
| average | | 0.95 | 0.93 | 0.62 | 0.13 | 1.01 | 0.73 | |

^a ML denotes multilevel; SL denotes single-level. ^b The cost for each method is measured by the computer time for a single-point energy calculation of the T-shaped benzene dimer (at the fixed geometry of Sinnokrot and Sherrill⁵⁵) divided by the computer time for an MP2/6-31+G(d,p) energy calculation on the same dimer with the same computer program and same computer.

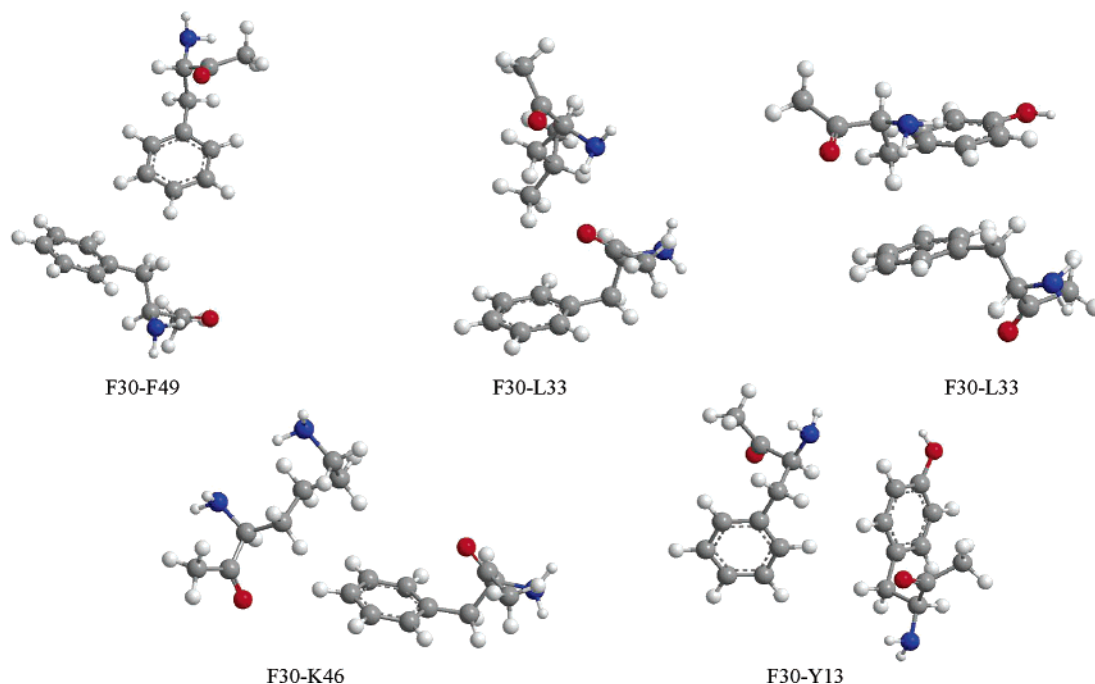


Figure 6. Geometries of the pairs of amino acid residues.

gives almost identical results to those obtained with MP2/MG3. Note that the only difference between MG3 and MG3S is that MG3S does not have diffuse basis functions on hydrogen atoms. The counterpoise correction improves the performance of the M05-2X/MG3S calculations, but it deteriorates the performance of the MP2/MG3S method by a large margin.

Evaluation of energies at a standard geometry to assess hydrogen bonding sometimes may lead to significantly different conclusions than would be obtained if the level of theory used for the energy calculation is also used for geometry optimization. This is especially true for methods that are defined to use inappropriately low levels of geometry. For example G3SX is defined to use B3LYP/6-31G(2df,p) geometries, which are not very good for hydrogen bonding because of the lack of diffuse functions.³⁷ CBS-QB3 suffers in the same way. In the present study, though, we use MC-QCISD/3 geometries, which are quite accurate. We have previously³² validated that mean errors are only slightly changed for hydrogen bonding, dipole interactions, and weak interactions when MC-QCISD/3 geometries instead of using consistently optimized geometries.

3.2. Charge-Transfer Complexes. Tables S1, S2, and 3 present the results for the charge-transfer complexes. Among the multilevel methods, MCQCISD-MPWB and MCQCISD-MPW give the lowest MUE for calculating the binding energies in the CT7/04 database. MCG3-MPW and MCG3-TS are the two best N^7 methods, and MC3MPWB is the best N^5 multilevel method.

Tables S2 and 3 show that the PWB6K/MG3S method is the best single level method for calculating interaction energies in charge-transfer complexes.

3.3. Dipole Interaction. Tables S3, S4, and 3 summarize the results for the dipole interaction complexes. Among the multilevel methods, MCG3-MPW gives the lowest MUE for calculating the binding energies in the DI6/04 database.

MCQCISD-MPW is the best N^6 multilevel method, and SAC-MP2/6-31+G(d,p) is the best N^5 method.

From Tables S4 and 3, we can see that MP2/6-31G(2df,p) is the best single-level method, but this good performance is due to the error cancellation between the BSSE and the incomplete treatment of correlation, as can be ascertained by noticing that the MP2 method with larger basis sets gives worse results. PWB6K is the best N^4 method for dipole interactions.

3.4. Weak Interaction. Tables S5, S6, and 3 present the results for the weak interaction complexes. These complexes are bound by dispersion-like forces. MCCO/3 is the best multilevel method, whereas MCG3-MPWB and MCQCISD-MPWB are the best N^7 and N^6 methods, respectively.

Tables S6 and 3 show that M05-2X/MG3S (with CP correction) is the best single-level method for the calculations of binding energies of these weakly bound van der Waals complexes.

3.5. $\pi\cdots\pi$ Interaction. Tables S7, S8, and 3 summarize the results for the $\pi\cdots\pi$ stacking complexes. Among the multilevel methods, MCG3-MPWB gives the lowest MUE for calculating the binding energies in the PPS5/05 database. MCQCISD-MPWB is the best N^6 multilevel method, and MC3MPWB is the best N^5 multilevel method. Table S8 shows that MP2/6-31G(d) is the best single-level method, but this good performance is again due to error cancellation, since the MP2 method with larger basis sets give worse results. PWB6K was found to be the best density functional for stacking interactions in biological systems⁶¹ and tetramers⁶² of formic acid and formamide. Here we find that the new M05-2X functional is even better for $\pi\cdots\pi$ stacking.

3.6. Overall Results. Table 3 is a summary of the performance of the tested methods for noncovalent interactions. The rank order is according to the MMUE column, which is the average of the five database columns included in this table, as defined by eq 1. Clearly the exact position

Table 4. Binding Energies (kcal/mol) and Mean Errors for Amino Acid Residue Pairs^a

| methods | F30-K46 | F30-L33 | F30-Y13 | F30-F49 | F30-Y4 | MSE | MUE |
|---------------|--------------------|--------------------|--------------------|--------------------|--------------------|-------|------|
| best estimate | 3.10 ^b | 5.00 ^b | 3.90 ^b | 2.70 ^c | 5.30 ^c | | |
| M05-2X | 2.53 | 4.47 | 3.41 | 2.07 | 3.62 | −0.78 | 0.78 |
| PWB6K | 2.20 | 3.87 | 2.87 | 1.49 | 2.80 | −1.35 | 1.35 |
| PW6B95 | 1.82 | 2.91 | 2.36 | 1.04 | 2.03 | −1.97 | 1.97 |
| MPWB1K | 1.55 | 2.76 | 2.05 | 0.85 | 1.81 | −2.20 | 2.20 |
| MPW1B95 | 1.47 | 2.41 | 1.93 | 0.72 | 1.53 | −2.39 | 2.39 |
| B97-1 | 1.69 | 1.65 | 2.17 | 1.08 | 0.72 | −2.54 | 2.54 |
| PBE | 1.47 | 1.17 | 1.87 | 0.83 | 0.22 | −2.89 | 2.89 |
| TPSS | 0.81 | −0.35 ^d | 0.82 | 0.07 | −1.17 ^d | −3.97 | 3.97 |
| B3LYP | 0.42 | −0.66 ^d | 0.49 | −0.24 ^d | −1.81 ^d | −4.36 | 4.36 |
| O3LYP | −0.30 ^d | −4.13 ^d | −1.00 ^d | −1.41 ^d | −4.73 ^d | −6.31 | 6.31 |

^a Basis set: 6-31+G(d,p); geometries from ref 69. No counterpoise correction was made. MSE denotes mean signed error, i.e., mean signed deviation from the best estimate, and MUE denotes mean unsigned error. ^b MP2/CBS + Δ CCSD(T) from ref 69. ^c MP2/CBS + side chain Δ CCSD(T) from ref 69. ^d A negative number denotes that the interaction energy is repulsive at the geometry of ref 69.

in the ranking is not as meaningful as the general trends, but the MMUE provides a way to organize the discussion. In Table 3, we also tabulate the “cost” for each method, which is measured by the computer time for a single-point energy calculation of the T-shaped benzene dimer (at the fixed geometry of Sinnokrot and Sherrill⁵⁵) divided by the computer time for an MP2/6-31+G(d,p) energy calculation on the same dimer with the same computer program and the same computer. Although we are aware of the danger of timing algorithms with specific programs on specific computers, these costs (if not interpreted too finely), nevertheless help place the methods in a perspective of affordability.

From Table 3, we can see that the best performer for these noncovalent databases is MCG3-MPW, and its cost is much less than the G3SX, MP4/6-31(2df,p), and CCSD(T)/6-311+G(d,p) methods. The best N^6 method is MCQCISD-MPWB. Note that three N^6 methods, namely MCQCISD-MPWB, MCQCISD-MPW, and MCQCISD-TS, outperform the CBS-QB3 and G3SX N^7 methods with much less cost. The best N^4 method, M05-2X, outperforms the best N^5 method, MC3MPWB. M05-2X is also the best single-level method. To obtain better performance than M05-2X one must go to a method almost four times as expensive and with much worse scaling.

4. Concluding Remarks

It is clear that even the best single-level WFT methods are not competitive with the single-level DFT methods, multilevel WFT methods, and multilevel DFT/WFT methods, either for the kind of accuracy (MMUE of 0.31 kcal/mol) attainable with the low-cost methods or for the much higher standard of about half that error (MMUE of 0.16 kcal/mol). Although model chemistries were originally developed for covalent interactions and have been widely applied to such interactions, several of the modern model chemistries are sufficiently robust that they also give excellent results for noncovalent interactions, and they should be very useful for many important applications that require accurate models for noncovalent interactions. It is encouraging that the best performing methods in the current tests (MCG3-MPW,²³ MCQCISD-MPWB,²³ MCQCISD-MPW,²³ and M05-2X³⁴) also show excellent performance^{22,23,34} for atomization ener-

gies, bond energies, barrier heights, ionization potentials, and electron affinities.

5. Software

M05-2X has been incorporated in *NWCHEM*⁶³ and *GAUSS-IAN03*⁵³ and will soon be available in release versions of these programs. All multilevel methods tested in this paper except CBS-QB3 are available in *MLGAUSS*,⁵² which requires *GAUSSIAN03* in order to execute. CBS-QB3 is available in *GAUSSIAN03*.⁵³

Acknowledgment. This work was supported by the Office of Naval Research under grant no. N00012-05-01-0538 and the U.S. Department of Energy, Office of Basic Energy Sciences.

Appendix

As an adjunct to this study, as requested by a referee, we calculated the binding energies of five pairs of amino acid residues by 10 different density functionals; the tested DFT methods are B3LYP,⁴⁶ PBE,⁶⁴ B97-1,⁶⁵ O3LYP,⁶⁶ TPSS,⁶⁷ MPW1B95,⁶⁸ MPWB1K,⁶⁸ PW6B95,³³ PWB6K,³³ and M05-2X.³⁴ The amino acid residues and the pair geometries are taken from ref 69, where a pair of residues was cut from a crystal structure, and each residue is modeled by an amino acid in which the $-\text{OH}$ group is replaced by a $-\text{CH}_3$ group; see Figure 6. The results are given in Table 4. It is encouraging that the two best performing functionals are (in order) M05-2X and PWB6K because these two functionals (out of 14 tested) were also found³⁴ to be the two best functionals (in the same order) for both stacking and hydrogen bonding interactions in nucleobase pairs.

Supporting Information Available: Calculated binding energies and mean errors for the CT7/04, DI6/04, WI7/05, and PPS5/05 databases. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (1) Pople, J. A. *Rev. Mod. Phys.* **1999**, *71*, 1267.
- (2) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221.

- (3) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1998**, *109*, 7764.
- (4) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **2000**, *112*, 1125.
- (5) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Pople, J. A. *J. Chem. Phys.* **2001**, *114*, 108.
- (6) Martin, J. M. L.; Oliveira, G. d. *J. Chem. Phys.* **1999**, *111*, 1843.
- (7) Boese, A. D.; Oren, M.; Atasoylu, O.; Martin, J. M. L.; Kállay, M.; Gauss, J. *J. Chem. Phys.* **2004**, *120*, 4129.
- (8) Ochterski, J. W.; Petersson, G. A.; Montgomery, J. A. *J. Chem. Phys.* **1996**, 2598.
- (9) Montgomery, J. A.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **1999**, *110*, 2822.
- (10) Montgomery, J. A.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **2000**, 6532.
- (11) Brown, F. B.; Truhlar, D. G. *Chem. Phys. Lett.* **1985**, *117*, 307.
- (12) Gordon, M. S.; Truhlar, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 2.
- (13) Rossi, I.; Truhlar, D. G. *Chem. Phys. Lett.* **1995**, *234*, 64.
- (14) Fast, P. L.; Corchado, J.; Sanchez, M. L.; Truhlar, D. G. *J. Phys. Chem. A* **1999**, *103*, 3139.
- (15) Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2003**, *107*, 3898.
- (16) Fast, P. L.; Corchado, J.; Sanchez, M. L.; Truhlar, D. G. *J. Phys. Chem. A* **1999**, *103*, 5129.
- (17) Fast, P. L.; Corchado, J.; Sanchez, M. L.; Truhlar, D. G. *J. Chem. Phys.* **1999**, *110*, 11679.
- (18) Fast, P. L.; Sanchez, M. L.; Truhlar, D. G. *Chem. Phys. Lett.* **1999**, *306*, 407.
- (19) Tratz, C. M.; Fast, P. L.; Truhlar, D. G. *PhysChemComm* **1999**, *2*, 14.
- (20) Fast, P. L.; Truhlar, D. G. *J. Phys. Chem. A* **2000**, *104*, 6111.
- (21) Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2002**, *106*, 842.
- (22) Zhao, Y.; Lynch, B. J.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 4786.
- (23) Zhao, Y.; Lynch, B. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2005**, *7*, 43.
- (24) Lynch, B. J.; Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 1643.
- (25) Li, T.-H.; Mou, C.-H.; Hu, W.-P. *Chem. Phys. Lett.* **2004**, *397*, 364.
- (26) Li, T.-H.; Chen, H.-R.; Hu, W.-P. *Chem. Phys. Lett.* **2005**, *412*, 430.
- (27) Dunn, M. E.; Pokon, E. K.; Shields, G. C. *J. Am. Chem. Soc.* **2004**, *126*, 2647.
- (28) Day, M. B.; Kirschner, K. N.; Shields, G. C. *Int. J. Quantum Chem.* **2005**, *102*, 565.
- (29) Pickard, F. C.; Dunn, M. E.; Shields, G. C. *J. Phys. Chem. A* **2005**, *109*, 9183.
- (30) Dunn, M. E.; Pokon, E. K.; Shields, G. C. *Int. J. Quantum Chem.* **2004**, *100*, 1065.
- (31) Giese, T. J.; York, D. M. *Int. J. Quantum Chem.* **2004**, *98*, 388.
- (32) Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2005**, *1*, 415.
- (33) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 5656.
- (34) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *2*, 364.
- (35) Curtiss, L. A.; Redfern, P. C.; Rassolov, V.; Kedziora, G.; Pople, J. A. *J. Chem. Phys.* **2001**, *114*, 9287.
- (36) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Pople, J. A. *Chem. Phys. Lett.* **2002**, *359*, 390.
- (37) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K. *J. Chem. Phys.* **2005**, *123*, 124107.
- (38) Schultz, N.; Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 11127.
- (39) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 4209.
- (40) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.
- (41) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.
- (42) Pople, J. A.; Head-Gordon, M.; Raghavachari, K. *J. Chem. Phys.* **1987**, *87*, 5968.
- (43) Purvis, G. D.; Bartlett, R. J. *J. Chem. Phys.* **1982**, *76*, 1910.
- (44) Raghavachari, K.; Trucks, G. W.; Pople, J. A.; Head-Gordon, M. *Chem. Phys. Lett.* **1989**, *157*, 479.
- (45) Zhao, Y.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, submitted for publication.
- (46) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.
- (47) Zhao, Y.; Tishchenko, O.; Truhlar, D. G. *J. Phys. Chem. B* **2005**, *109*, 19046.
- (48) Perdew, J. P.; Schmidt, K. In *Density Functional Theory and Its Applications to Materials*; Van-Doren, V., Alsenoy, C. V., Geerlings, P., Eds.; American Institute of Physics: New York, 2001; p 1.
- (49) Grimme, S. *J. Chem. Phys.* **2006**, *124*, 034108.
- (50) Lynch, B. J.; Truhlar, D. G. In *Recent Advances in Electron Correlation Methodology*; Wilson, A. K., Peterson, K. A., Eds.; American Chemical Society: Washington, DC, in press.
- (51) Herzberg, G. *Molecular Spectra and Molecular Structure. I. Spectra of Diatomic Molecules*, 2nd ed.; D. Van Nostrand: Princeton, NJ, 1950; p 437.
- (52) Zhao, Y.; Truhlar, D. G. *MLGAUSS-version 1.0*; University of Minnesota: Minneapolis, 2005.
- (53) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.;

- Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, revision C.01*; Gaussian, Inc.: Pittsburgh, PA, 2003.
- (54) Truhlar, D. G. <http://comp.chem.umn.edu/mccdir/software.htm>.
- (55) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2004**, *108*, 10200.
- (56) Corchado, J. C.; Chuang, Y.-Y.; Fast, P. L.; Villa, J.; Hu, W.-P.; Liu, Y.-P.; Lynch, G. C.; Nguyen, K. A.; Jackels, C. F.; Melissas, V. S.; Lynch, B. J.; Rossi, I.; Coitino, E. L.; Fernandez-Ramos, A.; Pu, J.; Albu, T. V.; Steckler, R.; Garrett, B. C.; Isaacson, A. D.; Truhlar, D. G. *POLYRATE, 9.1*; University of Minnesota: Minneapolis, MN, 2002.
- (57) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1999**, *110*, 4703.
- (58) Boys, S. F.; Bernardi, F. *Mol. Phys.* **1970**, *19*, 553.
- (59) Schwenke, D. W.; Truhlar, D. G. *J. Chem. Phys.* **1985**, *82*, 2418. **1987**, *86*, 3760 (E).
- (60) Raghavachari, K.; Anderson, J. B. *J. Phys. Chem.* **1996**, *100*, 12960.
- (61) Zhao, Y.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2005**, *7*, 2701.
- (62) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2005**, *109*, 6624.
- (63) Aprà, E.; Windus, T. L.; Straatsma, T. P.; Bylaska, E. J.; de Jong, W.; Hirata, S.; Valiev, M.; Hackler, M.; Pollack, L.; Kowalski, K.; Harrison, R.; Dupuis, M.; Smith, D. M. A.; Nieplocha, J.; V., T.; Krishnan, M.; Auer, A. A.; Brown, E.; Cisneros, G.; Fann, G.; Früchtl, H.; Garza, J.; Hirao, K.; Kendall, R.; Nichols, J.; Tsemekhman, K.; Wolinski, K.; Anchell, J.; Bernholdt, D.; Borowski, P.; Clark, T.; Clerc, D.; Dachsel, H.; Deegan, M.; Dyall, K.; Elwood, D.; Glendening, E.; Gutowski, M.; Hess, A.; Jaffe, J.; Johnson, B.; Ju, J.; Kobayashi, R.; Kutteh, R.; Lin, Z.; Littlefield, R.; Long, X.; Meng, B.; Nakajima, T.; Niu, S.; Rosing, M.; Sandrone, G.; Stave, M.; Taylor, H.; Thomas, G.; van Lenthe, J.; Wong, A.; Zhang, Z. *NWChem, A Computational Chemistry Package for Parallel Computers, 4.7*; Pacific Northwest National Laboratory: Richland, WA, 2005.
- (64) Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett* **1996**, *77*, 3865.
- (65) Hamprecht, F. A.; Cohen, A. J.; Tozer, D. J.; Handy, N. C. *J. Chem. Phys.* **1998**, *109*, 6264.
- (66) Hoe, W.-M.; Cohen, A. J.; Handy, N. C. *Chem. Phys. Lett.* **2001**, *341*, 319.
- (67) Tao, J.; Perdew, J. P.; Staroverov, V. N.; Scuseria, G. E. *Phys. Rev. Lett.* **2003**, *91*, 146401.
- (68) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908.
- (69) Vondrášek, J.; Bendová, L.; Klusák, V.; Hobza, P. *J. Am. Chem. Soc.* **2005**, *127*, 2615.

CT060044J