The S66 noncovalent interactions benchmark reconsidered using explicitly correlated methods near the basis set limit[1]

Manoj K. Kesharwani,[a] Amir Karton,[b] Nitai Sylvetsky, [a] and Jan M.L. Martin [a,*]

(a) Department of Organic Chemistry, Weizmann Institute of Science, 76100 Reḥovot, Israel. Email: gershom@weizmann.ac.il. FAX: +972 8 934 3029

(b) School of Molecular Sciences, The University of Western Australia, Perth, Western Australia 6009, Australia E-mail: amir.karton@uwa.edu.au

Abstract

The S66 benchmark for noncovalent interactions has been re-evaluated using explicitly correlated methods with basis sets near the one-particle basis set limit. It is found that post-MP2 "high-level corrections" are treated adequately well using a combination of CCSD(F12*) with (aug-)cc-pVTZ-F12 basis sets on the one hand, and (T) extrapolated from conventional CCSD(T)/heavy-aug-cc-pV{D,T}Z on the other hand. Implications for earlier benchmarks on the larger S66x8 problem set in particular, and for accurate calculations on noncovalent interactions in general, are discussed. At a slight cost in accuracy, (T) can be considerably accelerated by using sano-V{D,T}Z+

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[1] Dedicated to Graham S. Chandler on the occasion of his 80th birthday.

18 basis sets, while half-counterpoise CCSD(F12*)(T)/cc-pVDZ-F12 offers the best

19 compromise between accuracy and computational cost.

20

21 **Introduction**

22 Noncovalent interactions (NCIs) play crucial roles in supramolecular chemistry and

23 molecular biology, for they are critical in maintaining the three-dimensional structure of

24 large molecules, such as proteins and nucleic acids, and involved in many biological

25 processes in which large molecules bind specifically but temporarily to one another.[1,2]

26 Significant effort has been devoted to the study and benchmarking of various

27 noncovalently-bonded systems using experimental as well as computational methods

28 (see, e.g., refs[3–10] for recent reviews). However, experimental data are not available in

29 sufficient quantity or in isolation from environmental or dynamical effects, and thus

30 cannot easily be used for the parametrization of approximate methods such as

31 molecular mechanics force fields or semiempirical methods.[11–13] For this reason,

32 wavefunction *ab initio* calculations represent a viable alternative for obtaining highly

33 accurate NCIs.

34 Where it comes to bond dissociation energies or reaction barrier heights, "chemical

35 accuracy" is typically defined somewhat arbitrarily as ±1 kcal/mol, while the goal of

36 "benchmark accuracy" is more ambitiously defined at ±0.24 kcal/mol (1 kJ/mol).[14]

37 These correspond to relative errors of about 1% or less, as typical bond dissociation

38 energies are on the order of 10^2 kcal/mol. Noncovalent interactions, on the other hand,

39 are on a much smaller energy scale (an average of 5.5 kcal/mol for the dimers

40 considered in the present study), and a relative accuracy of 1% thus corresponds to

41 about ±0.05 kcal/mol. Such levels of accuracy are, at present, just barely within the

42 reach of wavefunction ab initio methods.[15–18]

43   Over the past decades, density functional theory (DFT) has become the most widely

44   used electronic structure method in computational quantum chemistry due to its

45   attractive accuracy-to-computational cost ratio. It is well established that the

46   performance of DFT can vary for different types of chemical transformations: generally

47   speaking, the accuracy of a given exchange-correlation (XC) functional should increase

48   as larger molecular fragments are conserved on the two sides of the reaction due to an

49   increasing degree of error cancelation between reactants and products. (For an

50   important caveat, see Ref.[19]) This means that the performance of DFT is better for

51   chemical transformations in which non-covalent interactions are disrupted, compared

52   to transformations in which covalent bonds are broken. That being said, even the best

53   density functional methods are still an order of magnitude less accurate than what is

54   achievable through wavefunction ab initio calculations: two massive survey studies[20,21]

55   on the performance of DFT methods have appeared very recently. As semilocal DFT

56   correlation functionals are intrinsically 'near-sighted', dispersion (which is intrinsically

57   a long-range effect[22]) typically requires either a long-range dispersion correction (see

58   Refs.[23,24] for a review) or a fifth-rung[25] functional[26] such as DSD-PBEP86[27,28] or

59   dRPA75.[29,30] All the most successful functionals for noncovalent interactions require

60   parametrization of either the dispersion correction, or the underlying functional, or

61   both: as a rule of thumb, we advocate that parametrization or validation data should be

62   about an order of magnitude more accurate than the method being parametrized or

63   validated, lest one be merely 'fitting to noise'.

64   It is well known (e.g., [31]) that second order Møller–Plesset perturbation theory (MP2)

65   is an adequate starting approximation for NCIs (the same cannot be said, however, for

66   molecular atomization energies or reaction barrier heights). Hence, a consensus

67   strategy has emerged in which MP2 interaction energies, obtained using relatively large

68   basis sets, are combined with high level corrections [HLCs = CCSD(T) – MP2] calculated

69   using smaller sets.

70   However, for interaction energies between bio-molecules and additional realistic-sized

71   systems of interest, the computational cost of HLCs becomes prohibitive even when

72   relatively modest basis sets are used. Therefore, many studies have been devoted to

73   assessing the performance of less-costly density functional methods (with and without

74   dispersion corrections) and low-cost wavefunction methods for standardized NCI

75   benchmarks.

76   Two popular, and interrelated, such benchmarks are the S66 and S66x8 datasets

77   developed by Hobza and coworkers.[32,33] Both datasets are based around 66 noncovalent

78   dimers, generated from combinations of 14 different monomers, which had been

79   selected based on their frequency as motifs or functional groups in the most commonly

80   found biomolecules. These complexes participate in a wide variety of NCIs, including

81   electrostatic dominated interactions (hydrogen bonding), dispersion dominated

82   interactions (π stacking, aromatic-aliphatic interactions, and aliphatic-aliphatic

83   interactions), and mixed-influence interactions, and are therefore representative of

84   NCIs one might see in biomolecules.

85   The reference geometries for the S66x8 dataset were obtained by first optimizing

86   each dimer structure at the RI-MP2/cc-pVTZ level, [32,33] then multiplying the

87   intermonomer distances by factors of {0.9,0.95,1.0,1.05,1.10,1.25,1.50,2.00} while

88   keeping the intramonomer geometries frozen—thus generating 8-point unrelaxed

89   "dissociation curves" for each of the 66 monomers. The original S66x8 reference data

90   were computed at the MP2/haV{T,Q}Z level plus a HLC correction computed at the

91   CCSD(T)/AVDZ level, with full counterpoise correction. Hobza and coworkers then

92   carried out quartic interpolation to the {0.9,0.95,1.0,1.05,1.10} points of each curve and

93   determined the minimum of each polynomial, then used those as the reference

94   geometries for the S66 set. That is to say, while the intramolecular geometry in S66 is

95   still MP2/haVTZ level, the intermolecular part is approximately CCSD(T)/CBS. While for

96   many systems (e.g., $(H_2O)_2$, system 1) the difference between S66 and S66x8@1.0r_e is

97   very small, there are quite substantial differences for the π stacking systems such as

98   benzene parallel-displaced dimer (system 24) and stacked uracil dimer (system 26).

99   [These reference geometry differences can give rise to confusion during benchmark

100 calculations if one is not careful.]

101   Quite recently, the reference values for S66x8 were revised[17] by our group using

102 explicitly correlated MP2 and coupled cluster methods; the revised data were then used

103 for a comprehensive evaluation of many conventional and double-hybrid density

104 functionals.[17] However, due to the relatively-large size of some of the systems in the

105 above datasets (e.g., the uracil dimer), we were unable to obtain HLCs using basis set

106 larger than cc-pVDZ-F12 for the whole set of 528 dimer structures: this might actually

107 be considered as the Achilles' Heel of our study.

108   Meanwhile, we published a family of diffuse-function augmented basis sets for

109 explicitly correlated calculations, aug-cc-pVnZ-F12 (in short aVnZ-F12).[34] Those were

110 originally developed with anionic systems in mind, but turned out to be beneficial for

111 noncovalent interactions as well, particularly hydrogen bonds.

112   Now, we were finally able to perform for the whole S66 dataset, at great

113 computational expense, full CCSD(T)-F12b and CCSD(T)(F12*) calculations, as well as

114 CCSD(F12*)/aug-cc-pVTZ and conventional CCSD(T)/heavy-aug-cc-pVTZ (haVTZ for

115 short) calculations. In addition, we were able to treat a subset of 18 systems with still

116 larger cc-pVQZ-F12 and haVQZ basis sets. For both sets of calculations, appropriate

117 counterpoise corrections were also obtained. Thus, firm and robust HLCs for this

118   dataset, that allow assessing the performance of lower level HLCs, are finally within our

119   reach; results and conclusions for such an assessment will therefore be reported in the

120   present work.

121

122   **Computational Details**

123   All calculations at the Weizmann Institute of Science were carried out on the Faculty

124   of Chemistry's Linux cluster "chemfarm", while those at UWA were carried out on the

125   Linux cluster of the Karton group and at the National Computational Infrastructure

126   (NCI) National Facility. Most wavefunction-based *ab initio* calculations were carried out

127   using MOLPRO 2015.1,[35] while ORCA[36] was used for CCSD(2)$_{F12}$,[37] calculations and

128   TURBOMOLE[38] for some additional CCSD(F12)[39] and CCSD[F12] [40,41] calculations.

129   Conventional, orbital-based, *ab initio* calculations were performed using correlation-

130   consistent[42–45] basis sets. In general, we used the combination of diffuse-function

131   augmented basis sets aug-cc-pVnZ (where n=D,T,Q,5) on nonhydrogen atoms and the

132   regular cc-pVnZ basis sets on hydrogen. For short, this is denoted as haVnZ. In addition,

133   we considered the augmented ano-pVnZ+ and semi-augmented sano-pVnZ+ atomic

134   natural orbital basis sets of Valeev and Neese[46].

135   For the explicitly correlated MP2-F12, CCSD-F12b,[47,48] and CCSD(F12*)[40,41] (a.k.a.,

136   CCSD-F12c) calculations, the correlation consistent cc-pVnZ-F12 basis sets of Peterson

137   et al.[49] were used in conjunction with the appropriate auxiliary basis sets for JKfit[50]

138   (Coulomb and exchange), MP2fit[51,52] (density fitting in MP2), and OptRI [53,54]

139   (complementary auxiliary basis set, CABS) basis sets. For the largest F12-optimized

140   orbital basis set, cc-pV5Z-F12,[55] Weigend's aug-cc-pV5Z/JKFIT basis set[56] for the

141   Coulomb and exchange elements and Hättig's aug-cc-pwCV5Z/MP2FIT basis set[57] for

142   both the RI- MP2 parts and for the CABS; the latter was recommended in Ref. [55] a brute-

143   force alternative, for want of an optimized OptRI. We also employed the aug-cc-pVnZ-

144   F12 basis sets developed in our group[34]; the issue of the appropriate CABS basis set is

145   investigated in detail in Ref.[58]. (See also Ref. [59])

146   For the purposes of basis set extrapolation, we employed a two-point expression of

147   the form $E(L) = E_{\infty} + [E(L) - E(L-1)] / \left[\left(\frac{L}{L-1} \right)^{a} - 1 \right]$, in which α is taken from Table 2

148   of Ref[17]. The notation MP2-F12/V{T,Q}Z-F12, for instance, indicates a value

149   extrapolated using this expression with the appropriate $\alpha=4.3548$ taken from there. For

150   the aV{T,Q}Z-F12 pair, no exponent is given there, and we optimized $\alpha=4.6324$ by the

151   same procedure as described in Ref.[60]; for aV{D,T}Z-F12, we found $\alpha=3.1458$.

152   As suggested in Ref.[60], geminal exponents $\beta=0.9$ were set for cc-pVDZ-F12 basis set,

153     $\beta=1.0$ were set for cc-pVTZ-F12 and cc-pVQZ-F12 basis sets; for cc-pV5Z-F12, as

154   specified in Ref. [55], $\beta=1.2$ was used. CABS correction was used to improve the SCF

155   component.[47,61] For aug-cc-pVnZ-F12, following Ref.[34], we used the same geminal

156   exponents as for the underlying cc-pVnZ-F12 basis sets.

157   Similar to our previous work[17] three different corrections were considered for the (T)

158   term obtained using explicitly correlated methods:

159   (a) CCSD(T*)-F12b: the Marchetti-Werner approximation,[62,63] in which the (T)

160   contribution is scaled by the E_{corr}[MP2-F12]/E_{corr}[MP2] correlation energy ratio.

161   (b) CCSD(T(b/c))-F12(b/c): (T) is scaled by the respective E_{corr}[CCSD-

162   F12(b/c)]/E_{corr}[CCSD] ratios.

163   (c) CCSD(Ts)-F12b:[55] (T) contributions are multiplied by constant scaling factors of

164   1.1413, 1.0527, and 1.0232 for cc-pVDZ-F12, cc-pVTZ-F12, and cc-pVQZ-F12,

165   respectively (Table 3 in Ref. [55]).

166   Options (a) and (b) are not strictly size-consistent, but can be rendered so by applying

167   the dimer E_{corr}[MP2-F12]/E_{corr}[MP2], E_{corr}[CCSD-F12(b/c)]/E_{corr}[CCSD], ratios also to

168   the monomers: This is indicated by the notation CCSD(T*$_{sc}$) and CCSD(T(b/c)$_{sc}$),

169   respectively.

170   The treatment of basis set superposition error (BSSE), and in particular the balance

171   between the countervailing forces of BSSE and intrinsic basis set insufficiency (IBSI),

172   has been discussed in Ref.[64] and references therein. Unless basis sets are very close to

173   the 1-particle basis set limit, half-counterpoise (i.e. the average of raw and

174   counterpoise-corrected interaction energies) has been found to yield fastest basis set

175   convergence for both conventional and explicitly correlated interaction energy

176   calculations.[64,7]

177   Finally,   reference   geometries   were   downloaded   from   BEGDB

178   (http://www.begdb.com)[65] and used verbatim.

179

180   **Results and Discussion**

181   <u>MP2-F12 limit</u>

182   We were able to perform RI-MP2-F12 calculations with cc-pV5Z-F12 basis set for the

183   entire S66 set, both with and without counterpoise corrections. Unfortunately, the very

184   large auxiliary basis sets that these calculations entail cause a large number of

185   numerical problems due to near-linear dependence: with the aug-cc-pwCV5Z/OptRI

186   CABS basis set, one data point (47, T-shaped benzene dimer) even yielded a plainly

187   absurd result. With the aug-cc-pVQZ/OptRI CABS basis set, we were able to obtain a

188   complete set of data: while of course this CABS basis set does not match the orbital basis

189   set, we recently found[58] (for the S66 dataset at the MP2-F12 level) that CABS basis sets

190   are fairly transferable between similar-sized orbital basis sets.

191   With the aug-cc-pVQZ-F12 basis set, no numerical problems were encountered except

192   for the need[34] to delete the diffuse f function from carbon atoms to avoid near-linear

193   dependence in the benzene-containing systems. The RMS counterpoise correction over

194   the S66 set can be taken as a gauge for remaining basis set incompleteness: for aVQZ-

195   F12, that amounts to 0.014 kcal/mol at the MP2-F12 level, of which 0.011 kcal/mol

196   comes from the correlation contribution. This is considerably better than 0.042 and

197   0.034 kcal/mol, respectively, with the cc-pVQZ-F12 basis set, and actually similar to

198   0.012 kcal/mol (both criteria) obtained with the larger cc-pV5Z-F12 basis set.

199   Another option is cc-pV{T,Q}Z-F12 basis set extrapolation. For this, the RMS

200   difference between raw and counterpoise-corrected extrapolated values is 0.022

201   kcal/mol: this drops to 0.006 kcal/mol for cc-pV{Q,5}Z-F12, with the caveat that cc-

202   pV5Z-F12 was obtained using a aug-cc-pVQZ/OptRI CABS.

203   At any rate, the MP2-F12 component is clearly not the accuracy-limiting factor:

204   indeed, Hobza's[33] best estimated counterpoise corrected MP2 limits differ from

205   counterpoise-corrected RI-MP2-F12/cc-pVQZ-F12 by just 0.009 kcal/mol RMS, which

206   increases to 0.017 kcal/mol relative to aV{T,Q}Z-F12 extrapolation (Table 1).

207

208   <u>HLC part 1: CCSD–MP2 difference</u>

209   The largest basis set for which we were able to perform CCSD(F12*) calculations for

210   the whole set turned out to be aug-cc-pVTZ-F12. The RMS counterpoise correction for

211   that, again used as a gauge for basis set incompleteness, was found to be 0.013

212   kcal/mol, comparable to the remaining amount for MP2-F12/aug-cc-pVQZ-F12.

213   Intriguingly, the regular cc-pVTZ-F12 yields a functionally equivalent RMS CP of 0.012

214   kcal/mol: the improvement from the diffuse functions seems to play out primarily at the

215   MP2-F12 level.

216   For a subset of 18 systems, we were able to perform CCSD(F12*)/cc-pVQZ-F12

217   calculations, and achieved a reduction of the RMS CP to 0.008 kcal/mol. This

218   improvement is clearly not commensurate with the immensely greater computational

219   expense (about an order of magnitude more CPU time, aside from much greater

220   memory and I/O requirements). This holds especially true in view of the residual

221   uncertainty in the MP2 part.

222   The CCSD–MP2 difference appears to have stabilized at the CCSD(F12*)/cc-pVQZ-F12

223   level: the difference between raw and counterpoise-corrected values is just 0.008

224   kcal/mol RMSD. As justified at great length in Ref.[64] for explicitly correlated calculations

225   with medium and larger basis sets, and in Ref.[7] for conventional calculations with

226   sufficiently large basis sets, we have chosen the half-counterpoise values as our 'gold

227   standard' reference — by construction, these are equidistant from raw and

228   counterpoise-corrected cc-pVQZ-F12 values, by 0.004 kcal/mol RMS (Table 2).

229   Obviously, cc-pVQZ-F12 is not a realistic option for the entire S66 set. CCSD-F12b/cc-

230   pVTZ-F12 clocks in at 0.015 kcal/mol raw or half-half, and 0.017 kcal/mol with full

231   counterpoise. That drops insignificantly to 0.010 kcal/mol for CCSD(F12*)/cc-pVTZ-

232   F12. With the small cc-pVDZ-F12 basis set, however, CCSD(F12*) has a definite edge

233   over CCSD-F12b, the RMSDs being 0.014 and 0.043 kcal/mol, respectively. This is

234   consistent with what we found in Ref.[17] and applied there for the revised S66x8 dataset.

235   At the CCSD(F12*)/cc-pVDZ-F12 level, raw results have marginally smaller RMSD than

236   half-counterpoise (0.015) and more noticeably smaller than full counterpoise (0.021

237   kcal/mol;). This is consistent with our findings in Ref.[64], where for small basis sets,

238   uncorrected results consistently agreed better with the basis set limit than

239   counterpoise-corrected ones. (For intermediate basis sets, half-counterpoise works

240 best, while for large basis sets, the choice is largely immaterial as the BSSE corrections

241 are so small.)

242 The CP-corrected [CCSD-MP2]/AVDZ used in the S66x8 paper[32] here has an RMSD of

243 0.096 kcal/mol, compared to 0.066 kcal/mol for the CP-corrected [CCSD-

244 MP2]/haV{D,T}Z used in the S66 paper, and just 0.018 kcal/mol for the corresponding

245 *raw* values.

246 What about the various approximations to CCSD-F12? For the cc-pVDZ-F12 basis set,

247 we were able to obtain full CCSD(F12) values using TURBOMOLE for 64 out of 66

248 systems (the two uracil dimers proved too large to converge). The RMSD from these

249 values at the CCSD(F12*) level is just 0.001 (!) kcal/mol, making it clear that

250 CCSD(F12*) is, at least for this type of problem, as good an approximation as we can

251 hope for. At the CCSD-F12b level, we incur an error of 0.039 kcal/mol RMS, which

252 increases to 0.067 kcal/mol at the CCSD-F12a level (Table S1, ESI). (The often-proffered

253 claims, e.g. Ref.[66], that CCSD-F12a is superior to CCSD-F12b for small basis sets rest on

254 an error compensation between basis set incompleteness and CCSD-F12a's tendency to

255 overbind.[16]) The CCSD[F12] level, which includes all third-order cross terms from

256 CCSD(F12) but omits the fourth-order terms, clocks in at 0.027 kcal/mol. Using the

257 CCSD(2)$_{F12}$ implementation in ORCA 4, we obtain 0.022 kcal/mol.

258 It had earlier been suggested to us by reviewers of Refs.[55,16] that the gap between

259 CCSD-F12b and CCSD(F12*) might be closed by evaluating the CABS terms in the

260 projector, which occurs in the dominant CCSD-F12 coupling terms and are neglected in

261 standard CCSD-F12b. (Their evaluation can be forced by setting IXPROJ=1 in MOLPRO.)

262 With the larger cc-pVTZ-F12 basis set, F12b and F12b(IXPROJ=1) are both about 0.02

263 kcal/mol RMS from CCSD(F12*): In the cc-pVDZ-F12 basis set, however, a larger benefit

264 is observed: RMSD=0.018 kcal/mol from full CCSD(F12) is actually better than

265   CCSD[F12] (see above). We noted previously for the water clusters[16] that the projector

266   terms do converge very rapidly with the basis set.

267
268   <u>HLC part 2: triples (T) term</u>

269   This term does not benefit from F12, although various approximate scaling

270   techniques have been proposed (see below).

271   It was previously found for the water clusters[16] as well as for main-group atomization

272   energies[67] that (T) is best obtained from conventional CCSD(T) calculations. We will

273   attempt to do so here.

274   For a subset of 18 systems, we were able to do CCSD(T)/haV{T,Q}Z extrapolation: the

275   RMS counterpoise correction to (T) is just 0.004 kcal/mol: This suggests the

276   extrapolated value is very close to the 1-particle infinite basis set limit, where said

277   difference should vanish. It also means that these values should be an acceptable

278   benchmark for lower-level approaches.

279   Intriguingly, for CCSD(T)/sano-V{T,Q}Z+ the RMS CP correction increases to 0.010

280   kcal/mol, even though atomic natural orbital basis sets should (in principle) minimize

281   basis set superposition error. Extrapolation of raw and counterpoise-corrected

282   (T)/haV{T,Q}Z contributions to the interaction energy led to nearly identical results, the

283   RMS difference between both sets of results being a negligible 0.007 kcal/mol (Table 3).

284   This suggests the extrapolated value is very close to the 1-particle infinite basis set

285   limit, where said difference should vanish. We have somewhat arbitrarily chosen the

286   average of both values — mathematically equivalent to "half-counterpoise" — as our

287   "gold standard" reference value.

288   The (T)/haV{D,T}Z does remarkably well, at an RMSD relative to half-CP

289   (T)/haV{T,Q}Z of just 0.011 kcal/mol without counterpoise and 0.008 kcal/mol with

290 half counterpoise. The (T) for uracil dimer still takes over a week wall time on 16 cores,

291 though: with the smaller sano-V{D,T}Z+ basis sets, the calculation time can be halved, at

292 the expense of increasing RMSD to 0.022 kcal/mol (raw) and 0.027 kcal/mol (half-CP).

293 Thus, sano-V{D,T}Z may be a viable option where haV{D,T}Z is computationally too

294 expensive and various F12 scaling schemes with (aug-)cc-pVDZ-F12 basis sets too

295 inaccurate.

296   What about the various scaling schemes for the triples? With the cc-pVTZ-F12 basis

297 set, which is similar in cost, RMSDs over the small 18-system set are smallest for (Ts)

298 with half-counterpoise (0.006 kcal/mol), (T*$_{sc}$) with full counterpoise (0.007 kcal/mol),

299 or unscaled (T) without counterpoise correction (0.012 kcal/mol, similar to (Tb$_{sc}$) half-

300 counterpoise) (Table 4). For VQZ-F12, very low RMSDs are obtained for (Ts) with half-

301 counterpoise, (Tb$_{sc}$) or (T*$_{sc}$) with full counterpoise, or unscaled raw (T).

302   We now turn to the cc-pVDZ-F12 basis set, where recovery of the (T) term represents

303 a challenge on account of the small basis set. With either the CCSD(F12*) or the CCSD-

304 F12b ansatz, half-counterpoise is clearly superior over the two other choices,

305 particularly CCSD(Tc$_{sc}$) and CCSD(T*$_{sc}$).

306

307   <u>HLC considered as a whole</u>

308   The best level of HLC we can afford, and that only for a subset of 18 systems, would be

309 what we could term GOLD: [CCSD(F12*)–MP2-F12]/cc-pVQZ-F12 half-counterpoise

310 combined with (T)/haV{T,Q}Z. The next level down we term SILVER: CCSD(F12*)/aug-

311 cc-pVTZ-F12 half-counterpoise combined with (T)/haV{D,T}Z , which we were able to

312 complete for all 66 systems. (By far the most CPU-intensive step was the

313 CCSD(T)/haVTZ calculations, which took over 2 weeks on a 16-CPU machine for uracil

314 dimer.)

315   The RMS difference between GOLD and SILVER for the 18 systems where we have the

316   former available is just 0.006 kcal/mol, hence we are probably justified using SILVER as

317   a standard. For comparison, full-CP [CCSD(T)–MP2]/haV{D,T}Z as used for the Hobza

318   S66 reference values has an RMSD=0.053 kcal/mol from SILVER, and 0.054 kcal/mol

319   from GOLD.

320   As unlike for the MP2-F12 part, there seems to be comparatively little effect of the

321   extra diffuse functions on the [CCSD(F12*)–MP2-F12] part, we also considered a lower-

322   cost STERLING level (i.e., silver-copper alloy) in which [CCSD(F12*)–MP2-F12]/aug-cc-

323   pVTZ-F12 is combined with (T)/sano-V{D,T}Z+. Deviation from GOLD is just 0.022

324   kcal/mol RMS over the 18-system subset, from SILVER it is 0.026 kcal/mol over the

325   whole S66 set. As the most expensive calculation step for the largest systems in S66 has

326   now been reduced to "just" five days on a 16-core machine, this may be a viable option

327   for larger benchmarks if greater accuracy is needed.

328   Can we avoid having to do the (T) in a triple-zeta basis altogether? This pretty much

329   implies using some form of scaling scheme. From Table 5, it would seem that

330   CCSD(F12*)(Tc_{sc})/cc-pVDZ-F12 with half-counterpoise would be the lowest-cost option.

331   According to Table 5, this deviates by just 0.032 kcal/mol RMS from SILVER, and hence

332   becomes our new BRONZE (or BRONZEnew) option.

333   The same level of HLC without counterpoise was used in the S66x8 revision paper,

334   and alas incurs RMS=0.096 kcal/mol, even though the deviation from GOLD for the 18-

335   system subset is just 0.044 kcal/mol. The difference between raw CCSD(F12*)(Tc_{sc})/cc-

336   pVDZ-F12 and its half-CP counterpart can indeed be quite nontrivial, reaching a

337   maximum of 0.2 kcal/mol for system 26 (stacked uracil dimer).

338   <u>Final reference data and overall performance</u>

339   Our final reference data are given in Table 6, while Figure 1 graphically represents the

340   errors for the entire S66 set compared to SILVER references. The Hobza S66 reference

341   values are actually quite close to SILVER : unfortunately, the CCSD(T)/haVTZ step they

342   entail makes them essentially as expensive as SILVER itself. Aside from a few outliers

343   (acetic acid and acetamide dimers), STERLING performs quite well and might be a

344   viable option for a recalculation of S66x8. BRONZEnew would be the next best solution,

345   but is computationally much less expensive: the extra cost compared to our published

346   S66x8 revision is essentially that of the CCSD(F12*)(T)/cc-pVDZ-F12 counterpoise

347   steps. Considering that this cuts the interquartile range of the errors approximately in

348   half, we believe that the fairly modest extra cost is well justified.

349
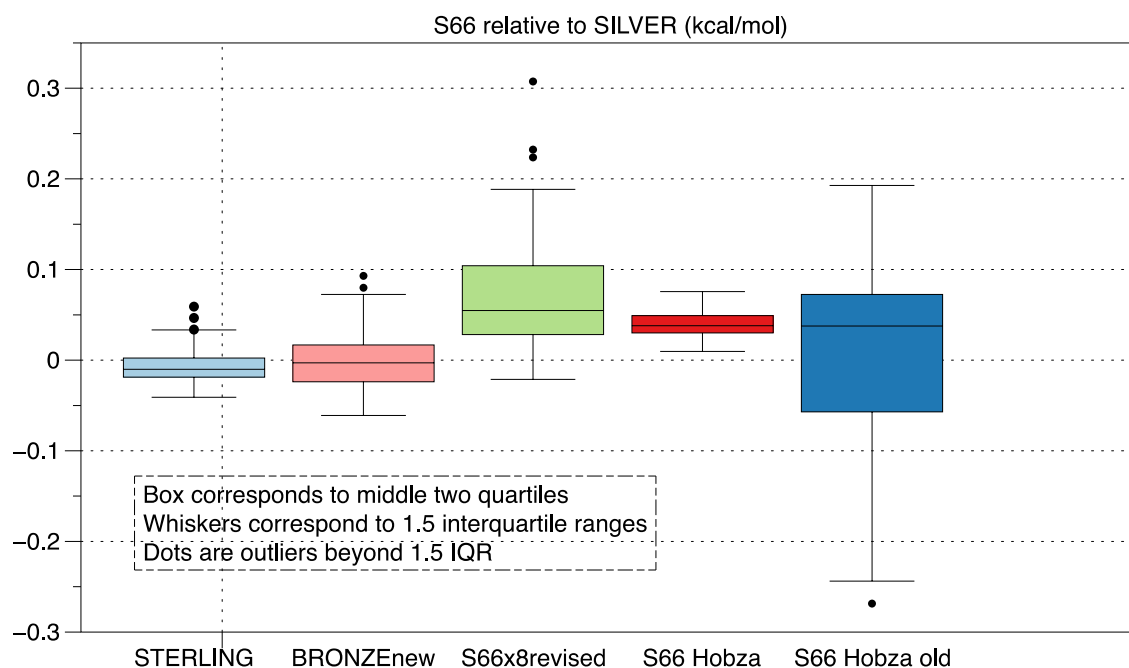
350 **Figure 1: box plot of errors in S66 association energies compared to SILVER**

351 **values (kcal/mol)**

352

353   Finally, the "old S66" level of theory, at which Hobza and coworkers calculated the

354   S66 set, clearly has an inadequate HLC (just CCSD(T)/AVDZ with full counterpoise), as

355   noted previously in Ref.[17]

356   CP-corrected [CCSD(T)-MP2]/AVDZ, as used in the S66x8 paper, clearly does benefit

357   from some error compensation between CCSD–MP2 and (T), as the RMSD relative to the

358   66-system silver standard is *substantially* smaller than the RMSDs on the two

359   constituent components.

360

361   <u>A preliminary update of S66x8</u>

362   It is computationally quite feasible to re-evaluate all of S66x8 at our new BRONZE

363   level. These data are presented in Table 7.

364   Differences with our previously published revision are small at equilibrium and

365   stretched distances (0.053 kcal/mol RMS), but more significant at compressed distances

366   (0.108 kcal/mol RMS). The largest differences are seen for dimers involving uracil. We

367   attempted aug-cc-pVDZ-F12 half-CP as well, but spot-checking against SILVER results

368   for a small subset of systems (20, 21, 24) suggests that any calculation in which (T) is

369   not evaluated with at least a haVTZ basis set needs to be considered with caution for the

370   compressed distances. Such a re-evaluation is presently in progress, but will take time

371   owing to its formidable computational cost for particularly the uracil dimers.

372

373   **Conclusions**

374   We have re-evaluated the S66 benchmark for noncovalent interactions at the highest

375   ab initio level that is currently feasible. Obtaining reliable MP2-F12 basis set limits does

376   not appear to represent a serious challenge: our aug-cc-pV{T,Q}Z-F12 extrapolated

377 values are probably as reliable as can be achieved, and are only a minor factor in the

378 cost of the overall benchmark calculations.

379   We can define three tiers of accuracy for the CCSD(T)-MP2 "high-level correction"

380 HLC:

381   • "GOLD" combining [CCSD(F12*)–MP2-F12]/cc-pVQZ-F12 half-CP with

382 (T)/haV{T,Q}Z half-CP

383   • "SILVER" combining [CCSD(F12*)–MP2-F12]/aug-cc-pVTZ-F12 half-CP with

384 (T)/haV{D,T}Z half-CP

385   •"BRONZE", i.e., half-counterpoise CCSD(F12*)(Tc$_{sc}$)/cc-pVDZ-F12

386   In addition, we can identify a reduced-cost variant of SILVER, which we will call

387   • "STERLING" combining [CCSD(F12*)–MP2-F12]/cc-pVTZ-F12 half-CP with

388 (T)/sano-PV{D,T}Z+ raw

389   SILVER is available for the entire set: for a subset of 18 systems where GOLD was

390 feasible, SILVER deviates from it by less than 0.01 kcal/mol RMS.

391   STERLING sacrifices about 0.02 kcal/mol RMS in accuracy, but cuts overall

392 computation time in half thanks to the smaller 'semi-augmented' basis sets used for the

393 (T).

394   BRONZE deviates by just over 0.03 kcal/mol RMS from SILVER, but at drastically

395 reduced cost (over an order of magnitude) and is a viable option for larger systems and

396 more extensive benchmarks.

397   The revised S66 benchmark of the Hobza group stands up well under scrutiny: the

398 fairly inexpensive CCSD(T)/AVDZ HLCs used in their S66x8 study are inadequate, but

399 still do benefit from error compensation. The revised S66x8 values from our group

400 could still have been improved further by adding half-counterpoise corrections to the

401 HLC. We have presented such values in the present work; however, we recommend that

402　they be treated with caution, particularly at compressed distances. A more thorough re-

403　evaluation is in progress.

404

416

417　**Conflict of interest statement**

418　The authors declare no conflict of interest.

419

420　**Supporting information**

421　Excel spreadsheet containing calculated total energies and interaction energies for the

422　S66 dataset at the levels of theory considered.

423

424

425

426

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Table 1: RMSD (kcal/mol) for the MP2-F12 limits of the S66 set

	relative to cc-pV{Q,5}Z-F12 half-CP			relative to aV{T,Q}Z-F12 half-CP		
	Raw	CP	Half	Raw	CP	Half
cc-pVDZ-F12	0.083	0.148	0.042	0.085	0.145	0.040
cc-pVTZ-F12	0.066	0.052	0.014	0.068	0.050	0.015
cc-pVQZ-F12	0.029	0.014	0.009	0.032	0.011	0.011
cc-pV5Z-F12	0.007	0.006	0.002			
cc-pV{T,Q}Z-F12	0.023	0.005	0.012	0.025	0.006	0.015
cc-pV{Q,5}Z-F12	0.003	0.003	REF			
aVDZ-F12	0.088	0.092	0.030	0.091	0.090	0.031
aVTZ-F12	0.038	0.019	0.011	0.040	0.017	0.014
aVQZ-F12	0.008	0.007	0.003	0.011	0.005	0.004
aV{D,T}Z-F12	0.040	0.009	0.024	0.043	0.011	0.027
aV{T,Q}Z-F12	0.007	0.003	0.004	0.004	0.004	REF
MP2/CBS[a]		0.019			0.017	

[a]MP2 basis set limit used by the Hobza and coworkers for S66 dataset

Table 2: RMS Deviations (kcal/mol) for the CCSD–MP2 components from the basis set

limit values of S66 interaction energies as calculated with various basis sets

	relative to GOLD[a] reference (for 18 systems)			relative to SILVER[b] reference (for complete S66 set)		
	Raw	CP	Half	Raw	CP	Half
CCSD-F12b–MP2-F12						
cc-pVDZ-F12	0.043	0.063	0.052	0.042	0.051	0.044
cc-pVTZ-F12	0.015	0.017	0.015	0.019	0.017	0.017
cc-pVQZ-F12	0.005	0.006	0.004			
CCSD-(F12*)–MP2-F12						
cc-pVDZ-F12	0.014	0.021	0.015	0.015	0.020	0.014
cc-pVTZ-F12	0.010	0.007	0.006	0.011	0.007	0.007
cc-pVQZ-F12	0.004	0.004	REF			
aVDZ-F12	0.016	0.015	0.006	0.029	0.020	0.009
aVTZ-F12	0.010	0.005	0.007	0.006	0.006	REF
CCSD–MP2						
haVDZ	0.074	0.098	0.080	0.093	0.183	0.133
haVTZ	0.018	0.063	0.036	0.020	0.088	0.044
haV{D,T}Z	0.018	0.066	0.039	0.031	0.060	0.025
haVQZ	0.014	0.053	0.022			
sano-pVDZ+	0.138	0.145	0.137	0.210	0.267	0.237
sano-pVTZ+	0.085	0.067	0.055	0.071	0.113	0.074
sano-pVQZ+	0.048	0.057	0.022			
AVDZ[c]		0.096			0.179	

3

4 [a] GOLD: CCSD(F12*)–MP2-F12/cc-pVQZ-F12 half-CP (for subset of 18 out of 66
5   systems)
6 [b] SILVER: CCSD(F12*)–MP2-F12/aVTZ-F12 half-CP (for complete S66 set)
7 [c]Level of theory used by the Hobza and coworkers in original S66 dataset

8   **Table 3:** RMS Deviations (kcal/mol) for the (T) term of conventional CCSD(T)

9   calculated for S66 interaction energies with various basis sets.

	For 18 sub-systems			For complete S66 set		
	Raw	CP	Half	Raw	CP	Half
haV{T,Q}Z	0.002	0.002	REF[a]			
haV{D,T}Z	0.007	0.011	0.008	0.007	0.007	REF[b]
haVQZ	0.005	0.019	0.012			
haVTZ	0.011	0.047	0.028	0.022	0.052	0.026
haVDZ	0.035	0.137	0.081	0.086	0.172	0.089
sano-pV{T,Q}Z+	0.010	0.007	0.007			
sano-pV{D,T}Z+	0.022	0.041	0.027	0.026	0.057	0.039
sano-pVQZ+	0.020	0.043	0.030			
sano-pVTZ+	0.047	0.095	0.069	0.073	0.132	0.102
sano-pVDZ+	0.128	0.226	0.176	0.199	0.312	0.254
AVDZ[c]		0.115			0.134	

10
11   [a] GOLD: [CCSD(T)−CCSD]/haV{T,Q}Z half-CP (for subset of 18 out of 66 systems)
12   [b] SILVER: [CCSD(T)−CCSD]/haV{D,T}Z half-CP reference (for complete S66 set)
13   [c]Level of theory used by the Hobza and coworkers in original S66 dataset

Table 4: RMS Deviations (kcal/mol) for the (T) term of explicitly correlated CCSD(T)-F12x calculated for S66 interaction energies with various basis sets.

	Raw (T*)	Raw (T)	Raw ($T_{b_{sc}}$)	Raw (T^*_{sc})	Raw (Ts)	CP (T*)	CP (T)	CP ($T_{b_{sc}}$)	CP (T^*_{sc})	CP (Ts)	Half (T*)	Half (T)	Half ($T_{b_{sc}}$)	Half (T^*_{sc})	Half (Ts)
relative to GOLD[a] reference (for 18 sub-systems)															
F12b/cc-pVQZ-F12	0.022	0.006	0.020	0.025	0.016	0.010	0.019	0.003	0.003	0.007	0.015	0.008	0.009	0.013	0.005
F12b/cc-pVTZ-F12	0.042	0.012	0.037	0.045	0.030	0.017	0.046	0.015	0.007	0.021	0.027	0.024	0.012	0.020	0.006
F12b/cc-pVDZ-F12	0.066	0.046	0.045	0.061	0.033	0.044	0.132	0.067	0.053	0.077	0.038	0.088	0.018	0.013	0.027
(F12*)/cc-pVDZ-F12	0.057	0.055	0.039	0.050	0.025	0.051	0.141	0.074	0.063	0.086	0.036	0.097	0.024	0.015	0.037
(F12*)/aVDZ-F12	0.055	0.043	0.045	0.058	0.032	0.035	0.117	0.048	0.037	0.060	0.036	0.079	0.013	0.017	0.020
relative to SILVER[b] (for complete S66 set)															
F12b/cc-pVTZ-F12	0.062	0.018	0.066	0.079	0.057	0.019	0.054	0.010	0.012	0.015	0.039	0.023	0.032	0.044	0.023
F12b/cc-pVDZ-F12	0.085	0.044	0.096	0.122	0.080	0.048	0.167	0.064	0.044	0.076	0.041	0.103	0.029	0.047	0.022
(F12*)/cc-pVDZ-F12	0.069	0.058	0.084	0.103	0.063	0.061	0.181	0.074	0.058	0.092	0.036	0.118	0.023	0.032	0.026
(F12*)/aVDZ-F12	0.080	0.032	0.121	0.142	0.102	0.035	0.140	0.036	0.028	0.049	0.045	0.081	0.055	0.072	0.040

[a]GOLD: [CCSD(T)–CCSD]/haV{T,Q}Z half-CP (for subset of 18 out of 66 systems)
[b]SILVER: [CCSD(T)–CCSD]/haV{D,T}Z half-CP reference (for complete S66 set)

Table 5: RMS Deviations (kcal/mol) for the high level corrections (HLC = [CCSD(T)-F12x – MP2-F12]/cc-pVnZ-F12)]) components of the S66 interaction energies.

	Raw HLC (T*)	Raw HLC (T)	Raw HLC (T(b/c)$_{sc}$)	Raw HLC (T*$_{sc}$)	Raw HLC (Ts)	CP HLC (T*)	CP HLC (T)	CP HLC (T(b/c)$_{sc}$)	CP HLC (T*$_{sc}$)	CP HLC (Ts)	Half HLC (T*)	Half HLC (T)	Half HLC (T(b/c)$_{sc}$)	Half HLC (T*$_{sc}$)	Half HLC (Ts)
relative to GOLD[a] reference (for 18 sub-systems)															
F12b/cc-pVQZ-F12	0.019	0.003	0.018	0.023	0.013	0.014	0.014	0.005	0.009	0.004	0.016	0.007	0.011	0.015	0.007
F12b/cc-pVTZ-F12	0.039	0.009	0.035	0.043	0.028	0.020	0.055	0.026	0.021	0.032	0.023	0.029	0.012	0.018	0.012
F12b/cc-pVDZ-F12	0.039	0.082	0.024	0.031	0.027	0.089	0.184	0.122	0.110	0.133	0.048	0.132	0.063	0.051	0.075
(F12*)/cc-pVDZ-F12	0.057	0.058	0.043	0.053	0.032	0.061	0.153	0.087	0.077	0.100	0.036	0.103	0.034	0.026	0.046
(F12*)/aVDZ-F12	0.067	0.031	0.060	0.073	0.047	0.042	0.130	0.062	0.052	0.074	0.036	0.079	0.016	0.020	0.023
relative to SILVER[b] (for complete S66 set)															
F12b/cc-pVTZ-F12	0.068	0.025	0.075	0.088	0.066	0.021	0.057	0.022	0.024	0.026	0.041	0.024	0.039	0.051	0.032
F12b/cc-pVDZ-F12	0.058	0.072	0.078	0.102	0.065	0.074	0.196	0.103	0.087	0.115	0.035	0.132	0.050	0.053	0.055
(F12*)/cc-pVDZ-F12	0.073	0.054	0.092	0.112	0.072	0.069	0.190	0.087	0.071	0.103	0.034	0.119	0.032	0.039	0.035
(F12*)/aVDZ-F12	0.105	0.035	0.149	0.170	0.130	0.044	0.158	0.053	0.041	0.067	0.048	0.078	0.061	0.078	0.047

[a]GOLD: half-counterpoise corrected [CCSD(F12*) –MP2-F12]/cc-pVQZ-F12 combined with half-counterpoise corrected [CCSD(T)–CCSD]/haV{T,Q}Z
[b]SILVER: half-counterpoise corrected [CCSD(F12*)–MP2-F12]/aVTZ-F12 combined with half-counterpoise corrected [CCSD(T)–CCSD]/haV{D,T}Z

Table 6: Systems in the S66 dataset and final recommended dissociation energies (kcal/mol) obtained in the present work.

Systems	GOLD[a]	SILVER[b]	Systems	GOLD[a]	SILVER[b]
01 Water ... Water	4.979	4.982	34 Pentane ... Pentane		3.741
02 Water ... MeOH	5.666	5.666	35 Neopentane ... Pentane		2.582
03 Water ... MeNH$_2$	6.985	6.986	36 Neopentane ... Neopentane		1.745
04 Water ... Peptide		8.183	37 Cyclopentane ... Neopentane		2.376
05 MeOH ... MeOH	5.824	5.822	38 Cyclopentane ... Cyclopentane		2.967
06 MeOH ... MeNH$_2$	7.625	7.617	39 Benzene ... Cyclopentane		3.488
07 MeOH ... Peptide		8.307	40 Benzene ... Neopentane		2.824
08 MeOH ... Water	5.065	5.064	41 Uracil ... Pentane		4.761
09 MeNH$_2$ ... MeOH	3.088	3.087	42 Uracil ... Cyclopentane		4.052
10 MeNH$_2$ ... MeNH$_2$	4.189	4.184	43 Uracil ... Neopentane		3.652
11 MeNH$_2$ ... Peptide		5.436	44 Ethene ... Pentane		1.973
12 MeNH$_2$ ... Water	7.354	7.349	45 Ethyne ... Pentane		1.696
13 Peptide ... MeOH		6.251	46 Peptide ... Pentane		4.215
14 Peptide ... MeNH$_2$		7.516	47 Benzene ... Benzene (TS)		2.801
15 Peptide ... Peptide		8.689	48 Pyridine ... Pyridine (TS)		3.472
16 Peptide ... Water		5.180	49 Benzene ... Pyridine (TS)		3.260
17 Uracil ... Uracil (BP)		17.407	50 Benzene ... Ethyne (CH-π)	2.839	2.828
18 Water ... Pyridine		6.927	51 Ethyne ... Ethyne (TS)	1.526	1.519
19 MeOH ... Pyridine	7.464	7.467	52 Benzene ... AcOH (OH-π)		4.691
20 AcOH ... AcOH	19.364	19.361	53 Benzene ... AcNH$_2$ (NH-π)		4.376
21 AcNH$_2$ ... AcNH$_2$	16.468	16.474	54 Benzene ... Water (OH-π)		3.267
22 AcOH ... Uracil		19.736	55 Benzene ... MeOH (OH-π)		4.139
23 AcNH$_2$ ... Uracil		19.420	56 Benzene ... MeNH$_2$ (NH-π)		3.174
24 Benzene ... Benzene (π-π)		2.685	57 Benzene ... Peptide (NH-π)		5.222
25 Pyridine ... Pyridine (π-π)		3.751	58 Pyridine ... Pyridine (CH-N)		4.189
26 Uracil ... Uracil (π-π)		9.672	59 Ethyne ... Water (CH-O)	2.912	2.905
27 Benzene ... Pyridine (π-π)		3.300	60 Ethyne ... AcOH (OH-π)	4.925	4.917
28 Benzene ... Uracil (π-π)		5.517	61 Pentane ... AcOH		2.876
29 Pyridine ... Uracil (π-π)		6.629	62 Pentane ... AcNH$_2$		3.491
30 Benzene ... Ethene	1.348	1.358	63 Benzene ... AcOH		3.709
31 Uracil ... Ethene		3.291	64 Peptide ... Ethene		2.967
32 Uracil ... Ethyne		3.651	65 Pyridine ... Ethyne		4.064
33 Pyridine ... Ethene	1.790	1.779	66 MeNH$_2$ ... Pyridine		3.930

[a]GOLD: MP2-F12/aV{T,Q}Z-F12 half-CP + [CCSD(F12*) −MP2-F12]/cc-pVQZ-F12 half-CP + [CCSD(T)−CCSD]/haV{T,Q}Z half-CP

[b]SILVER: MP2-F12/aV{T,Q}Z-F12 half-CP + [CCSD(F12*)−MP2-F12]/aVTZ-F12 half-CP + [CCSD(T)−CCSD]/haV{D,T}Z half-CP

Table 7: Preliminary re-evaluation of the S66x8 dataset at our new BRONZE level (kcal/mol)

	$0.9r_e$	$0.95r_e$	$1.0r_e$	$1.05r_e$	$1.1r_e$	$1.25r_e$	$1.5r_e$	$2.0r_e$
01 Water ... Water	4.610	4.912	4.915	4.739	4.462	3.460	2.108	0.871
02 Water ... MeOH	5.232	5.578	5.589	5.396	5.086	3.947	2.385	0.952
03 Water ... MeNH$_2$	6.530	6.897	6.894	6.660	6.291	4.916	2.973	1.140
04 Water ... Peptide	7.666	8.076	8.089	7.851	7.465	5.991	3.828	1.437
05 MeOH ... MeOH	5.328	5.727	5.773	5.599	5.299	4.147	2.526	1.010
06 MeOH ... MeNH$_2$	7.006	7.497	7.558	7.346	6.971	5.497	3.342	1.273
07 MeOH ... Peptide	7.689	8.186	8.255	8.051	7.680	6.190	3.649	1.099
08 MeOH ... Water	4.629	4.985	5.023	4.867	4.601	3.595	2.201	0.908
09 MeNH$_2$ ... MeOH	2.813	3.037	3.029	2.889	2.680	1.970	1.097	0.394
10 MeNH$_2$ ... MeNH$_2$	3.671	4.068	4.127	3.985	3.730	2.777	1.302	0.388
11 MeNH$_2$ ... Peptide	4.922	5.334	5.387	5.221	4.926	3.204	1.402	0.457
12 MeNH$_2$ ... Water	6.777	7.224	7.259	7.036	6.659	5.217	3.149	1.195
13 Peptide ... MeOH	5.725	6.149	6.213	6.053	5.762	4.615	2.952	1.308
14 Peptide ... MeNH$_2$	6.860	7.379	7.478	7.310	6.978	5.611	3.552	1.492
15 Peptide ... Peptide	8.085	8.590	8.673	8.485	8.131	6.677	4.426	1.782
16 Peptide ... Water	4.740	5.097	5.146	5.006	4.758	3.805	2.458	1.136
17 Uracil ... Uracil (BP)	16.042	17.190	17.432	17.078	16.352	13.263	8.410	3.357
18 Water ... Pyridine	6.453	6.853	6.872	6.653	6.294	4.939	3.013	1.189
19 MeOH ... Pyridine	6.855	7.366	7.451	7.263	6.911	5.490	3.385	1.336
20 AcOH ... AcOH	17.793	19.070	19.328	18.923	18.106	14.657	9.246	3.595
21 AcNH$_2$ ... AcNH$_2$	15.185	16.242	16.441	16.085	15.386	12.485	8.022	3.009
22 AcOH ... Uracil	18.241	19.470	19.732	19.358	18.581	15.243	9.907	4.161
23 AcNH$_2$ ... Uracil	18.011	19.157	19.419	19.094	18.391	15.309	10.276	4.672
24 Benzene ... Benzene (π-π)	-0.030	1.905	2.634	2.739	2.546	1.543	0.499	0.067
25 Pyridine ... Pyridine (π-π)	1.063	2.997	3.716	3.788	3.543	2.360	0.974	0.241
26 Uracil ... Uracil (π-π)	7.693	9.396	9.765	9.406	8.688	6.110	3.138	1.013
27 Benzene ... Pyridine (π-π)	0.463	2.523	3.265	3.338	3.096	1.976	0.735	0.151
28 Benzene ... Uracil (π-π)	3.278	5.041	5.588	5.475	5.034	3.296	1.380	0.260
29 Pyridine ... Uracil (π-π)	3.460	5.990	6.698	6.513	5.936	3.876	1.796	0.543
30 Benzene ... Ethene	0.048	0.977	1.310	1.333	1.210	0.678	0.176	-0.008
31 Uracil ... Ethene	2.424	3.130	3.300	3.181	2.921	1.981	0.937	0.257
32 Uracil ... Ethyne	2.628	3.442	3.649	3.528	3.247	2.213	1.045	0.275
33 Pyridine ... Ethene	0.699	1.487	1.764	1.762	1.621	1.013	0.367	0.047
34 Pentane ... Pentane	2.789	3.569	3.734	3.581	3.278	2.223	1.050	0.273
35 Neopentane ... Pentane	1.817	2.466	2.590	2.467	2.240	1.491	0.699	0.187
36 Neopentane ... Neopentane	1.428	1.713	1.753	1.667	1.524	1.042	0.504	0.136
37 Cyclopentane ... Neopentane	1.574	2.225	2.384	2.306	2.122	1.458	0.705	0.191
38 Cyclopentane ... Cyclopentane	2.199	2.811	2.971	2.839	2.578	1.705	0.791	0.207
39 Benzene ... Cyclopentane	2.013	3.135	3.496	3.420	3.135	2.062	0.903	0.194

40 Benzene ... Neopentane	1.753	2.597	2.839	2.767	2.544	1.703	0.773	0.191
41 Uracil ... Pentane	3.732	4.624	4.792	4.569	4.064	2.451	0.986	0.220
42 Uracil ... Cyclopentane	2.963	3.910	4.094	3.895	3.526	2.298	1.026	0.253
43 Uracil ... Neopentane	2.807	3.560	3.678	3.478	3.142	2.055	0.932	0.235
44 Ethene ... Pentane	1.589	1.918	1.948	1.830	1.648	1.078	0.490	0.121
45 Ethyne ... Pentane	0.997	1.526	1.669	1.616	1.473	0.958	0.418	0.097
46 Peptide ... Pentane	3.673	4.144	4.195	4.009	3.700	2.615	1.190	0.290
47 Benzene ... Benzene (TS)	1.549	2.513	2.823	2.790	2.590	1.772	0.839	0.230
48 Pyridine ... Pyridine (TS)	2.444	3.248	3.492	3.426	3.202	2.294	1.188	0.378
49 Benzene ... Pyridine (TS)	1.992	2.975	3.280	3.229	3.004	2.103	1.060	0.339
50 Benzene ... Ethyne (CH-π)	1.784	2.585	2.822	2.764	2.563	1.785	0.895	0.274
51 Ethyne ... Ethyne (TS)	1.183	1.449	1.506	1.449	1.335	0.930	0.462	0.135
52 Benzene ... AcOH (OH-π)	3.895	4.523	4.661	4.519	4.228	3.121	1.705	0.558
53 Benzene ... AcNH$_2$ (NH-π)	3.763	4.247	4.346	4.216	3.961	2.974	1.651	0.486
54 Benzene ... Water (OH-π)	2.710	3.139	3.212	3.089	2.869	2.090	1.153	0.417
55 Benzene ... MeOH (OH-π)	3.316	3.941	4.106	4.005	3.760	2.786	1.529	0.521
56 Benzene ... MeNH$_2$ (NH-π)	2.376	2.983	3.153	3.062	2.823	1.939	0.941	0.264
57 Benzene ... Peptide (NH-π)	3.620	4.866	5.220	5.105	4.759	3.419	1.818	0.626
58 Pyridine ... Pyridine (CH-N)	2.890	3.887	4.194	3.921	3.474	2.199	1.025	0.281
59 Ethyne ... Water (CH-O)	2.573	2.844	2.883	2.788	2.618	1.994	1.177	0.460
60 Ethyne ... AcOH (OH-π)	4.295	4.788	4.863	4.692	4.385	3.248	1.769	0.557
61 Pentane ... AcOH	2.642	2.852	2.839	2.697	2.488	1.775	0.784	0.171
62 Pentane ... AcNH$_2$	3.079	3.442	3.458	3.283	3.013	2.102	1.041	0.276
63 Benzene ... AcOH	2.574	3.483	3.715	3.591	3.296	2.226	1.024	0.265
64 Peptide ... Ethene	2.528	2.893	2.945	2.820	2.605	1.846	0.878	0.191
65 Pyridine ... Ethyne	3.647	4.002	4.065	3.948	3.727	2.870	1.684	0.623
66 MeNH$_2$ ... Pyridine	3.357	3.803	3.907	3.803	3.582	2.697	1.502	0.497