

Volume 73 (2017)

**Supporting information for article:**

**Interplay of point multipole moments and charge penetration for intermolecular electrostatic interaction energies from the University at Buffalo pseudoatom databank model of electron density**

**Sławomir A. Bojarowski, Prashant Kumar and Paulina M. Dominiak**

Table S1: List of dimers in the S66 dataset indicating dominant components (electrostatic or dispersion) to total interaction energy (Hobza et. al., J. Chem. Theory Comput., 2011, 7 (8), pp 2427-2438). The third column shows subgroups found in this publication.

| Dimer               | Dominant component | Type of interaction (subgroup) |
|---------------------|--------------------|--------------------------------|
| 01_ Water-Water     | Electrostatic      | single-H-bonded (SHB)          |
| 02_ Water-MeOH      | Electrostatic      | single-H-bonded (SHB)          |
| 03_ Water-MeNH2     | Electrostatic      | single-H-bonded (SHB)          |
| 04_ Water-Peptide   | Electrostatic      | single-H-bonded (SHB)          |
| 05_ MeOH-MeOH       | Electrostatic      | single-H-bonded (SHB)          |
| 06_ MeOH-MeNH2      | Electrostatic      | single-H-bonded (SHB)          |
| 07_ MeOH-Peptide    | Electrostatic      | single-H-bonded (SHB)          |
| 08_ MeOH-Water      | Electrostatic      | single-H-bonded (SHB)          |
| 09_ MeNH2-MeOH      | Mixed              | single-H-bonded (SHB)          |
| 12_ MeNH2-Water     | Electrostatic      | single-H-bonded (SHB)          |
| 13_ Peptide-MeOH    | Electrostatic      | single-H-bonded (SHB)          |
| 14_ Peptide-MeNH2   | Electrostatic      | single-H-bonded (SHB)          |
| 15_ Peptide-Peptide | Electrostatic      | single-H-bonded (SHB)          |

|                              |               |   |
|------------------------------|---------------|---|
| 16_Peptide-Water             | Electrostatic | single-H-bonded (SHB)                         |
| 18_Water-Pyridine            | Electrostatic | single-H-bonded (SHB)                         |
| 19_MeOH-Pyridine             | Electrostatic | single-H-bonded (SHB)                         |
| 59_Ethyne-Water_CH-O         | Electrostatic | single-H-bonded (SHB)                         |
| 17_Uracil-Uracil_BP          | Electrostatic | double-H-bonded (DHB)                         |
| 20_AcOH-AcOH                 | Electrostatic | double-H-bonded (DHB)                         |
| 21_AcNH2-AcNH2               | Electrostatic | double-H-bonded (DHB)                         |
| 22_AcOH-Uracil               | Electrostatic | double-H-bonded (DHB)                         |
| 23_AcNH2-Uracil              | Electrostatic | double-H-bonded (DHB)                         |
| 10_MeNH2-MeNH2               | Mixed         | weak-H-bonded (WHB)                           |
| 11_MeNH2-Peptide             | Mixed         | weak-H-bonded (WHB)                           |
| 58_Pyridine-Pyridine_CH-N    | Mixed         | weak-H-bonded (WHB)                           |
| 65_Pyridine-Ethyne           | Electrostatic | weak-H-bonded (WHB)                           |
| 24_Benzene-Benzene_pi-pi     | Dispersion    | $\pi-\pi$ without uracil (PP)                 |
| 25_Pyridine-Pyridine_pi-pi   | Dispersion    | $\pi-\pi$ without uracil (PP)                 |
| 27_Benzene-Pyridine_pi-pi    | Dispersion    | $\pi-\pi$ without uracil (PP)                 |
| 30_Benzene-Ethene            | Dispersion    | $\pi-\pi$ without uracil (PP)                 |
| 33_Pyridine-Ethene           | Dispersion    | $\pi-\pi$ without uracil (PP)                 |
| 26_Uracil-Uracil_pi-pi       | Mixed         | $\pi-\pi$ with uracil (PPU)                   |
| 28_Benzene-Uracil_pi-pi      | Dispersion    | $\pi-\pi$ with uracil (PPU)                   |
| 29_Pyridine-Uracil_pi-pi     | Mixed         | $\pi-\pi$ with uracil (PPU)                   |
| 31_Uracil-Ethene             | Dispersion    | $\pi-\pi$ with uracil (PPU)                   |
| 32_Uracil-Ethyne             | Mixed         | $\pi-\pi$ with uracil (PPU)                   |
| 34_Pentane-Pentane           | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 35_Neopentane-Pentane        | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 36_Neopentane-Neopentane     | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 37_Cyclopentane-Neopentane   | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 38_Cyclopentane-Cyclopentane | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 39_Benzene-Cyclopentane      | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 40_Benzene-Neopentane        | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 41_Uracil-Pentane            | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 42_Uracil-Cyclopentane       | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 43_Uracil-Neopentane         | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 44_Ethene-Pentane            | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 45_Ethyne-Pentane            | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 46_Peptide-Pentane           | Dispersion    | $\pi$ -aliphatic or aliphatic-aliphatic (PAA) |
| 47_Benzene-Benzene_TS        | Dispersion    | T-shaped (TS)                                 |
| 48_Pyridine-Pyridine_TS      | Dispersion    | T-shaped (TS)                                 |
| 49_Benzene-Pyridine_TS       | Dispersion    | T-shaped (TS)                                 |
| 50_Benzene-Ethyne_CH-pi      | Mixed         | T-shaped (TS)                                 |
| 51_Ethyne-Ethyne_TS          | Mixed         | T-shaped (TS)                                 |
| 56_Benzene-MeNH2_NH-pi       | Dispersion    | T-shaped (TS)                                 |
| 52_Benzene-AcOH_OH-pi        | Mixed         | H- $\pi$ (HP)                                 |
| 53_Benzene-AcNH2_NH-pi       | Mixed         | H- $\pi$ (HP)                                 |
| 54_Benzene-Water_OH-pi       | Mixed         | H- $\pi$ (HP)                                 |
| 55_Benzene-MeOH_OH-pi        | Mixed         | H- $\pi$ (HP)                                 |

|                           |               |                      |
|---------------------------|---------------|----------------------|
| 57_ Benzene-Peptide_NH-pi | Mixed         | H- $\pi$ (HP)        |
| 60_ Ethyne-AcOH_OH-pi     | Electrostatic | H- $\pi$ (HP)        |
| 61_ Pentane-AcOH          | Dispersion    | polar-nonpolar (PNP) |
| 62_ Pentane-AcNH2         | Dispersion    | polar-nonpolar (PNP) |
| 63_ Benzene-AcOH          | Dispersion    | polar-nonpolar (PNP) |
| 64_ Peptide-Ethene        | Mixed         | polar-nonpolar (PNP) |
| 66_ MeNH2-Pyridine        | Mixed         | polar-nonpolar (PNP) |

Table S2. The electrostatic interaction energies ( $\text{kJ mol}^{-1}$ ) computed with the EP, EPMM ( $r_{\text{Crit1}} = 5.0 \text{ \AA}$ ) and MM methods for interactions between H(1) and N(1) pseudoatoms from the first molecule of uracil with all other pseudoatoms from the second molecule of uracil in Uracil-Uracil\_BP dimer at 1.00 fraction of equilibrium distance. The interatomic distances are given in  $\text{\AA}$ . The H(1) and N(1) pseudoatoms from the first molecule are engaged in H-bond. The single horizontal lines mark the interatomic distances higher than  $r_{\text{Crit1}}$ .

| Molecule 1 | Molecule 2 | Distance | EP     | EPMM   | MM     | EPMM-MM |
|------------|------------|----------|--------|--------|--------|---------|
| H(1)       | O(4)       | 7.67     | -44.67 | -44.67 | -28.76 | -15.91  |
| H(1)       | H(8)       | 10.74    | 15.40  | 15.40  | 15.46  | -0.06   |
| H(1)       | C(8)       | 11.43    | -28.25 | -28.25 | -26.23 | -2.02   |
| H(1)       | N(4)       | 12.80    | 6.39   | 6.39   | 6.55   | -0.16   |
| H(1)       | N(3)       | 16.85    | 4.67   | 4.67   | 4.68   | -0.01   |
| H(1)       | H(5)       | 18.03    | 8.11   | 8.11   | 8.11   | 0.00    |
| H(1)       | C(7)       | 18.49    | 5.54   | 5.54   | 5.55   | 0.00    |
| H(1)       | H(7)       | 20.55    | -2.95  | -2.95  | -2.95  | 0.00    |
| <hr/>      |            |          |        |        |        |         |
| H(1)       | C(5)       | 21.89    | -6.05  | -6.05  | -6.05  | 0.00    |
| H(1)       | C(6)       | 22.33    | 3.63   | 3.64   | 3.64   | 0.00    |
| H(1)       | O(3)       | 26.31    | -4.52  | -4.52  | -4.52  | 0.00    |
| H(1)       | H(6)       | 26.67    | -2.64  | -2.64  | -2.64  | 0.00    |
| <hr/>      |            |          |        |        |        |         |
| N(1)       | O(4)       | 11.96    | -8.06  | -8.06  | -5.62  | -2.44   |
| N(1)       | H(8)       | 12.70    | 6.49   | 6.49   | 6.65   | -0.16   |
| N(1)       | C(8)       | 15.38    | -5.64  | -5.64  | -5.10  | -0.53   |
| N(1)       | N(4)       | 15.71    | 2.02   | 2.02   | 2.13   | -0.11   |
| <hr/>      |            |          |        |        |        |         |
| N(1)       | N(3)       | 20.95    | 1.53   | 1.53   | 1.53   | 0.00    |
| N(1)       | C(7)       | 21.20    | 2.20   | 2.21   | 2.21   | 0.00    |
| N(1)       | H(5)       | 22.32    | 2.73   | 2.73   | 2.73   | 0.00    |
| N(1)       | H(7)       | 22.52    | -0.89  | -0.89  | -0.89  | 0.00    |
| N(1)       | C(6)       | 25.59    | 1.42   | 1.42   | 1.42   | 0.00    |
| N(1)       | C(5)       | 25.75    | -2.23  | -2.23  | -2.23  | 0.00    |
| N(1)       | H(6)       | 29.77    | -0.92  | -0.92  | -0.92  | 0.00    |
| N(1)       | O(3)       | 30.33    | -1.73  | -1.73  | -1.73  | 0.00    |

Table S3. Errors ( $\text{kJ mol}^{-1}$ ) of  $E_{es}^4(\text{UBDB})$  for particular subgroups in S66a8 dataset. The errors were quantified by computing RMS difference of  $E_{es}^4(\text{UBDB})$  with  $E_{es}(\text{REF})$  at the B3LYP/aug-cc-pVTZ level of theory.

| <b>S66a8</b> |  | Rotation angles around the equilibrium geometry |       |       |       |       |       |       |       |
|--------------|--|---|-------|-------|-------|-------|-------|-------|-------|
| Subgroups    |  | 1y-30   | 1y+30 | 1z-30 | 1z+30 | 2y-30 | 2y+30 | 2z-30 | 2z+30 |
| SHB          |  | 6.32  | 5.65  | 5.73  | 6.19  | 4.69  | 4.77  | 3.10  | 4.69  |
| DHB          |  | 8.03  | 8.12  | 2.47  | 6.99  | 8.12  | 7.95  | 5.69  | 10.04 |
| WHB          |  | 5.23  | 7.78  | 5.44  | 4.02  | 5.94  | 5.52  | 6.69  | 3.77  |
| PP           |  | 3.56  | 4.48  | 4.77  | 3.77  | 2.05  | 1.92  | 1.97  | 1.80  |
| PPU          |  | 3.68  | 2.26  | 3.97  | 2.59  | 1.59  | 1.84  | 2.38  | 3.18  |
| PAA          |  | 1.34  | 1.17  | 1.21  | 1.88  | 1.34  | 1.05  | 1.72  | 1.72  |
| TS           |  | 1.09  | 1.21  | 1.21  | 2.80  | 1.13  | 0.92  | 1.97  | 2.55  |
| HP           |  | 2.09  | 1.97  | 2.59  | 3.22  | 2.59  | 2.30  | 2.09  | 2.47  |
| PNP          |  | 1.92  | 0.92  | 2.26  | 3.18  | 3.97  | 1.76  | 2.13  | 2.38  |
| GLOBAL       |  | 4.48  | 4.44  | 3.89  | 4.39  | 3.97  | 3.77  | 3.18  | 4.18  |

Table S4. Errors ( $\text{kJ mol}^{-1}$ ) of  $E_{mtp}^4(\text{UBDB})$  for particular subgroups in the S66×8 dataset. The errors were quantified by computing RMS difference of  $E_{mtp}^4(\text{UBDB})$  with  $E_{es}(\text{REF})$  at the B3LYP/aug-cc-pVTZ level of theory.

| <b>S66×8</b> |  | Fractions of equilibrium distance |       |       |       |       |       |       |      |
|--------------|--|-----------------------------------|-------|-------|-------|-------|-------|-------|------|
| Subgroup     |  | 0.90                              | 0.95  | 1.00  | 1.05  | 1.10  | 1.25  | 1.50  | 2.00 |
| SHB          |  | 33.89                             | 26.40 | 20.71 | 16.36 | 13.01 | 6.90  | 2.85  | 0.79 |
| DHB          |  | 93.85                             | 75.35 | 60.84 | 49.33 | 40.21 | 22.72 | 10.17 | 3.22 |
| WHB          |  | 31.30                             | 23.22 | 16.90 | 12.76 | 9.92  | 4.73  | 1.80  | 0.54 |
| PPS          |  | 36.19                             | 21.80 | 13.22 | 8.08  | 4.98  | 1.26  | 0.17  | 0.04 |
| PPU          |  | 37.45                             | 24.06 | 13.72 | 8.41  | 5.23  | 1.63  | 0.71  | 0.25 |
| PAA          |  | 19.04                             | 12.09 | 7.66  | 4.90  | 3.10  | 0.84  | 0.17  | 0.04 |
| TSH          |  | 13.51                             | 8.37  | 5.19  | 3.22  | 1.97  | 0.54  | 0.21  | 0.08 |
| HPI          |  | 14.64                             | 9.67  | 6.44  | 4.35  | 3.01  | 1.26  | 0.59  | 0.21 |
| PNP          |  | 18.45                             | 12.64 | 8.79  | 6.23  | 4.48  | 1.92  | 0.67  | 0.21 |
| GLOBAL       |  | 36.90                             | 27.82 | 21.34 | 16.82 | 13.43 | 7.32  | 3.18  | 0.96 |

Table S5. Errors ( $\text{kJ mol}^{-1}$ ) of  $E_{es}^4$  from UBDB and  $E_{es}^4$  from tailored pseudoatoms for equilibrium geometries in the S66 dataset. The errors were quantified by computing RMS difference of  $E_{es}^4$  (UBDB) with  $E_{es}$  (REF). The transferability error was quantified by computing RMS difference ( $\text{kJ mol}^{-1}$ ) of  $E_{es}^4$  (UBDB) with  $E_{es}^4$  from tailored pseudoatoms.

| Subgroup | $E_{es}^4$ (UBDB) | $E_{es}^4$ (tailored) | Transferability Error |
|----------|-------------------|-----------------------|-----------------------|
| SHB      | 7.03              | 5.02                  | 2.89                  |
| DHB      | 4.98              | 12.34                 | 7.91                  |
| WHB      | 8.54              | 5.82                  | 3.01                  |
| PP       | 3.14              | 2.93                  | 0.50                  |
| PPU      | 6.82              | 3.14                  | 4.81                  |
| PAA      | 1.80              | 1.72                  | 0.96                  |
| TS       | 2.13              | 2.51                  | 0.75                  |
| HP       | 4.31              | 4.27                  | 1.30                  |
| PNP      | 3.05              | 2.51                  | 1.38                  |
| GLOBAL   | 5.19              | 4.98                  | 3.14                  |

Table S6: Mean  $E_{es}^{l_{max}}$  (kJ mol<sup>-1</sup>) at different  $l_{max}$  in sub-groups of the S66×8 dataset.

| Nr | Name          | 0.90    | 0.95    | 1.00    | 1.05    | 1.10   | 1.25   | 1.50   | 2.00   | Subgroup |
|----|---------------|---------|---------|---------|---------|--------|--------|--------|--------|----------|
| 1  | $E_{es}^0$    | -33.93  | -24.48  | -17.70  | -12.80  | -9.37  | -3.89  | -1.21  | -0.38  | SHB      |
| 2  | $E_{es}^1$    | -37.45  | -31.59  | -26.86  | -23.10  | -20.08 | -13.81 | -8.28  | -3.68  | SHB      |
| 3  | $E_{es}^2$    | -52.34  | -41.80  | -33.76  | -27.53  | -22.80 | -14.02 | -7.66  | -3.35  | SHB      |
| 4  | $E_{es}^3$    | -52.97  | -42.13  | -33.85  | -27.49  | -22.68 | -13.77 | -7.49  | -3.31  | SHB      |
| 5  | $E_{es}^4$    | -52.84  | -42.05  | -33.81  | -27.49  | -22.68 | -13.77 | -7.49  | -3.26  | SHB      |
| 6  | $E_{es}(REF)$ | -56.27  | -46.15  | -38.24  | -31.97  | -26.99 | -17.20 | -9.41  | -3.85  | SHB      |
| 7  | $E_{es}^0$    | -125.81 | -96.11  | -73.35  | -56.32  | -43.68 | -21.55 | -8.66  | -3.05  | DHB      |
| 8  | $E_{es}^1$    | -106.40 | -90.83  | -77.66  | -66.90  | -58.03 | -39.33 | -22.93 | -9.83  | DHB      |
| 9  | $E_{es}^2$    | -164.89 | -134.89 | -110.62 | -91.38  | -76.23 | -46.61 | -24.56 | -10.17 | DHB      |
| 10 | $E_{es}^3$    | -164.81 | -134.47 | -110.04 | -90.71  | -75.52 | -46.07 | -24.35 | -10.17 | DHB      |
| 11 | $E_{es}^4$    | -170.87 | -139.79 | -114.64 | -94.73  | -79.04 | -48.24 | -25.40 | -10.50 | DHB      |
| 12 | $E_{es}(REF)$ | -168.91 | -142.17 | -120.46 | -102.72 | -88.24 | -58.16 | -32.55 | -13.31 | DHB      |
| 13 | $E_{es}^0$    | -27.82  | -18.74  | -12.05  | -7.91   | -5.27  | -1.30  | -0.08  | 0.00   | WHB      |
| 14 | $E_{es}^1$    | -24.14  | -19.96  | -16.44  | -13.89  | -11.92 | -7.53  | -3.89  | -1.42  | WHB      |
| 15 | $E_{es}^2$    | -32.68  | -24.56  | -18.12  | -13.89  | -10.88 | -5.52  | -2.43  | -0.88  | WHB      |
| 16 | $E_{es}^3$    | -29.33  | -21.80  | -15.94  | -12.13  | -9.46  | -4.73  | -2.09  | -0.79  | WHB      |
| 17 | $E_{es}^4$    | -29.08  | -21.46  | -15.69  | -11.88  | -9.25  | -4.60  | -2.05  | -0.75  | WHB      |
| 18 | $E_{es}(REF)$ | -39.87  | -30.92  | -23.72  | -18.70  | -15.10 | -8.16  | -3.68  | -1.30  | WHB      |
| 19 | $E_{es}^0$    | -32.47  | -18.79  | -10.71  | -5.98   | -3.14  | -0.17  | 0.29   | 0.08   | PPS      |
| 20 | $E_{es}^1$    | -21.80  | -9.08   | -2.09   | 1.55    | 3.43   | 4.10   | 2.34   | 0.59   | PPS      |
| 21 | $E_{es}^2$    | -21.25  | -11.76  | -6.28   | -3.14   | -1.30  | 0.33   | 0.33   | 0.00   | PPS      |
| 22 | $E_{es}^3$    | -21.17  | -11.63  | -6.15   | -3.01   | -1.17  | 0.42   | 0.33   | 0.00   | PPS      |
| 23 | $E_{es}^4$    | -22.93  | -12.76  | -6.82   | -3.39   | -1.42  | 0.38   | 0.38   | 0.00   | PPS      |
| 24 | $E_{es}(REF)$ | -31.46  | -18.12  | -10.25  | -5.65   | -2.97  | -0.13  | 0.25   | 0.04   | PPS      |
| 25 | $E_{es}^0$    | -51.09  | -35.52  | -20.04  | -12.80  | -8.41  | -2.68  | -0.75  | -0.29  | PPU      |
| 26 | $E_{es}^1$    | -55.02  | -37.91  | -22.84  | -15.19  | -10.42 | -3.89  | -1.26  | -0.38  | PPU      |
| 27 | $E_{es}^2$    | -41.55  | -31.09  | -19.62  | -14.18  | -10.67 | -5.44  | -2.59  | -1.00  | PPU      |
| 28 | $E_{es}^3$    | -43.18  | -32.59  | -20.59  | -14.94  | -11.30 | -5.77  | -2.72  | -1.05  | PPU      |
| 29 | $E_{es}^4$    | -49.83  | -37.32  | -23.43  | -16.82  | -12.51 | -6.07  | -2.76  | -1.05  | PPU      |
| 30 | $E_{es}(REF)$ | -47.78  | -34.31  | -22.26  | -15.90  | -11.80 | -5.94  | -2.89  | -1.09  | PPU      |
| 31 | $E_{es}^0$    | -34.23  | -21.59  | -13.56  | -8.49   | -5.27  | -1.26  | -0.04  | 0.00   | PAA      |
| 32 | $E_{es}^1$    | -16.48  | -10.59  | -6.95   | -4.73   | -3.31  | -1.38  | -0.50  | -0.17  | PAA      |
| 33 | $E_{es}^2$    | -16.95  | -11.00  | -7.15   | -4.73   | -3.14  | -1.00  | -0.21  | -0.04  | PAA      |
| 34 | $E_{es}^3$    | -15.19  | -9.83   | -6.44   | -4.23   | -2.76  | -0.84  | -0.13  | 0.00   | PAA      |
| 35 | $E_{es}^4$    | -15.23  | -9.92   | -6.49   | -4.27   | -2.80  | -0.84  | -0.13  | 0.00   | PAA      |
| 36 | $E_{es}(REF)$ | -18.37  | -11.72  | -7.49   | -4.81   | -3.10  | -0.88  | -0.17  | 0.00   | PAA      |
| 37 | $E_{es}^0$    | -27.41  | -17.45  | -11.09  | -6.86   | -4.31  | -1.09  | -0.13  | 0.00   | TSH      |
| 38 | $E_{es}^1$    | -22.68  | -18.03  | -14.94  | -12.59  | -10.84 | -7.45  | -4.35  | -1.72  | TSH      |
| 39 | $E_{es}^2$    | -23.05  | -16.48  | -12.01  | -8.74   | -6.61  | -3.31  | -1.51  | -0.54  | TSH      |
| 40 | $E_{es}^3$    | -22.22  | -16.07  | -11.84  | -8.70   | -6.61  | -3.35  | -1.51  | -0.54  | TSH      |
| 41 | $E_{es}^4$    | -21.46  | -15.61  | -11.55  | -8.49   | -6.49  | -3.31  | -1.51  | -0.54  | TSH      |
| 42 | $E_{es}(REF)$ | -18.74  | -13.14  | -9.50   | -7.03   | -5.40  | -2.89  | -1.46  | -0.59  | TSH      |

|    |               |        |        |        |        |        |        |       |       |     |
|----|---------------|--------|--------|--------|--------|--------|--------|-------|-------|-----|
| 43 | $E_{es}^0$    | -24.06 | -14.85 | -8.95  | -5.15  | -2.76  | 0.21   | 0.84  | 0.38  | HPI |
| 44 | $E_{es}^1$    | -40.50 | -32.17 | -26.23 | -21.76 | -18.41 | -12.01 | -6.86 | -2.72 | HPI |
| 45 | $E_{es}^2$    | -34.31 | -25.77 | -19.83 | -15.61 | -12.55 | -7.28  | -3.77 | -1.42 | HPI |
| 46 | $E_{es}^3$    | -34.02 | -25.98 | -20.25 | -16.15 | -13.14 | -7.78  | -4.06 | -1.51 | HPI |
| 47 | $E_{es}^4$    | -33.35 | -25.61 | -20.08 | -16.07 | -13.14 | -7.87  | -4.14 | -1.55 | HPI |
| 48 | $E_{es}(REF)$ | -28.91 | -22.34 | -17.66 | -14.23 | -11.67 | -7.07  | -3.77 | -1.42 | HPI |
| 49 | $E_{es}^0$    | -27.41 | -18.28 | -12.22 | -8.16  | -5.44  | -1.63  | -0.17 | 0.00  | PNP |
| 50 | $E_{es}^1$    | -19.41 | -13.89 | -10.21 | -7.70  | -5.98  | -3.26  | -1.59 | -0.59 | PNP |
| 51 | $E_{es}^2$    | -19.20 | -13.64 | -9.83  | -7.20  | -5.36  | -2.51  | -0.96 | -0.33 | PNP |
| 52 | $E_{es}^3$    | -17.57 | -12.47 | -8.95  | -6.53  | -4.85  | -2.30  | -0.92 | -0.29 | PNP |
| 53 | $E_{es}^4$    | -17.70 | -12.51 | -8.95  | -6.49  | -4.81  | -2.22  | -0.88 | -0.29 | PNP |
| 54 | $E_{es}(REF)$ | -21.34 | -15.23 | -11.05 | -8.20  | -6.19  | -3.05  | -1.30 | -0.42 | PNP |

Table S7: Mean  $E_{es}^{l_{max}}$  (kJ mol<sup>-1</sup>) at different  $l_{max}$  in subgroups of S66a8 dataset.

| No | Name          | 1y-30  | 1y+30  | 1z-30  | 1z+30  | 2y-30  | 2y+30  | 2z-30  | 2z-30  | Subgroup |
|----|---------------|--------|--------|--------|--------|--------|--------|--------|--------|----------|
| 1  | $E_{es}^0$    | -11.92 | -11.76 | -12.30 | -12.26 | -15.56 | -15.56 | -14.52 | -15.77 | SHB      |
| 2  | $E_{es}^1$    | -21.97 | -21.80 | -21.21 | -22.01 | -23.22 | -24.14 | -23.35 | -22.93 | SHB      |
| 3  | $E_{es}^2$    | -24.14 | -24.52 | -23.10 | -24.94 | -27.15 | -28.66 | -27.99 | -26.90 | SHB      |
| 4  | $E_{es}^3$    | -24.06 | -24.31 | -22.64 | -24.89 | -26.11 | -28.37 | -27.99 | -25.94 | SHB      |
| 5  | $E_{es}^4$    | -24.06 | -24.31 | -22.68 | -24.89 | -26.15 | -28.24 | -27.87 | -25.98 | SHB      |
| 6  | $E_{es}(REF)$ | -28.62 | -28.41 | -26.44 | -29.54 | -28.07 | -29.50 | -29.75 | -27.41 | SHB      |
| 7  | $E_{es}^0$    | -54.56 | -54.39 | -36.48 | -31.09 | -56.99 | -57.11 | -35.94 | -29.46 | DHB      |
| 8  | $E_{es}^1$    | -65.19 | -65.14 | -44.35 | -39.04 | -67.36 | -67.40 | -43.72 | -36.48 | DHB      |
| 9  | $E_{es}^2$    | -84.68 | -84.47 | -58.07 | -50.79 | -86.99 | -87.15 | -56.53 | -46.36 | DHB      |
| 10 | $E_{es}^3$    | -84.10 | -83.76 | -60.04 | -49.29 | -86.44 | -86.69 | -59.33 | -43.05 | DHB      |
| 11 | $E_{es}^4$    | -87.61 | -87.28 | -61.71 | -51.34 | -89.75 | -89.96 | -60.29 | -44.85 | DHB      |
| 12 | $E_{es}(REF)$ | -94.93 | -94.77 | -62.38 | -56.32 | -97.49 | -97.49 | -58.32 | -51.92 | DHB      |
| 13 | $E_{es}^0$    | -10.00 | -9.37  | -9.92  | -8.83  | -10.13 | -8.54  | -6.53  | -7.78  | WHB      |
| 14 | $E_{es}^1$    | -12.89 | -14.06 | -12.38 | -12.93 | -12.64 | -11.76 | -10.00 | -10.13 | WHB      |
| 15 | $E_{es}^2$    | -12.97 | -15.52 | -12.80 | -15.40 | -13.39 | -12.34 | -11.42 | -10.29 | WHB      |
| 16 | $E_{es}^3$    | -11.59 | -13.51 | -11.05 | -13.47 | -11.84 | -10.71 | -11.25 | -9.25  | WHB      |
| 17 | $E_{es}^4$    | -11.55 | -13.31 | -11.00 | -13.26 | -11.67 | -10.46 | -11.05 | -9.08  | WHB      |
| 18 | $E_{es}(REF)$ | -16.69 | -20.63 | -16.15 | -17.03 | -17.57 | -15.27 | -17.70 | -12.09 | WHB      |
| 19 | $E_{es}^0$    | -5.52  | -5.65  | -4.77  | -5.36  | -6.86  | -7.07  | -6.28  | -6.82  | PPS      |
| 20 | $E_{es}^1$    | 3.14   | 2.59   | 4.23   | 2.34   | -1.09  | -1.46  | 0.13   | -1.84  | PPS      |
| 21 | $E_{es}^2$    | 0.21   | -0.13  | 0.96   | -0.46  | -3.35  | -3.60  | -2.80  | -3.47  | PPS      |
| 22 | $E_{es}^3$    | -0.92  | -0.96  | 0.25   | -1.30  | -3.14  | -3.64  | -2.80  | -3.47  | PPS      |
| 23 | $E_{es}^4$    | -1.00  | -1.00  | 0.25   | -1.26  | -3.43  | -3.89  | -3.05  | -3.72  | PPS      |
| 24 | $E_{es}(REF)$ | -4.02  | -4.73  | -3.51  | -4.27  | -5.48  | -5.82  | -4.94  | -5.40  | PPS      |
| 25 | $E_{es}^0$    | -12.76 | -14.31 | -10.63 | -11.55 | -10.67 | -11.38 | -12.09 | -14.90 | PPU      |
| 26 | $E_{es}^1$    | -15.77 | -18.62 | -14.60 | -12.51 | -10.96 | -9.46  | -13.14 | -19.83 | PPU      |
| 27 | $E_{es}^2$    | -11.92 | -14.02 | -11.00 | -11.25 | -10.79 | -10.88 | -12.30 | -15.40 | PPU      |
| 28 | $E_{es}^3$    | -12.89 | -14.73 | -12.47 | -11.67 | -11.51 | -11.13 | -12.26 | -15.86 | PPU      |
| 29 | $E_{es}^4$    | -13.72 | -15.73 | -12.38 | -12.34 | -12.30 | -11.97 | -13.35 | -17.41 | PPU      |

|    |               |        |        |        |        |        |        |        |        |     |
|----|---------------|--------|--------|--------|--------|--------|--------|--------|--------|-----|
| 30 | $E_{es}(REF)$ | -15.44 | -16.02 | -15.36 | -13.68 | -13.05 | -12.64 | -14.35 | -15.90 | PPU |
| 31 | $E_{es}^0$    | -6.53  | -7.15  | -7.15  | -7.95  | -6.02  | -6.36  | -6.69  | -7.78  | PAA |
| 32 | $E_{es}^1$    | -2.93  | -3.51  | -3.31  | -3.68  | -1.42  | -1.63  | -3.26  | -1.09  | PAA |
| 33 | $E_{es}^2$    | -3.89  | -4.27  | -4.02  | -4.52  | -3.31  | -3.93  | -4.60  | -4.44  | PAA |
| 34 | $E_{es}^3$    | -3.47  | -3.81  | -3.77  | -4.02  | -3.51  | -3.93  | -4.31  | -4.52  | PAA |
| 35 | $E_{es}^4$    | -3.51  | -3.85  | -3.89  | -3.97  | -3.64  | -4.06  | -4.48  | -4.73  | PAA |
| 36 | $E_{es}(REF)$ | -4.06  | -4.06  | -3.93  | -4.77  | -3.05  | -3.43  | -3.81  | -3.81  | PAA |
| 37 | $E_{es}^0$    | -6.23  | -6.07  | -5.61  | -5.82  | -9.62  | -9.75  | -8.16  | -8.49  | TSH |
| 38 | $E_{es}^1$    | -9.08  | -9.16  | -6.95  | -8.12  | -13.10 | -13.56 | -11.76 | -11.80 | TSH |
| 39 | $E_{es}^2$    | -5.77  | -5.69  | -4.69  | -5.40  | -9.46  | -9.71  | -9.58  | -9.04  | TSH |
| 40 | $E_{es}^3$    | -6.65  | -6.57  | -5.61  | -6.23  | -9.29  | -9.58  | -9.58  | -9.08  | TSH |
| 41 | $E_{es}^4$    | -6.86  | -6.74  | -5.73  | -6.36  | -9.08  | -9.41  | -9.33  | -8.91  | TSH |
| 42 | $E_{es}(REF)$ | -7.41  | -7.32  | -5.82  | -7.28  | -8.54  | -9.12  | -7.91  | -7.41  | TSH |
| 43 | $E_{es}^0$    | -7.03  | -6.82  | -6.19  | -6.53  | -7.95  | -7.87  | -3.97  | -6.02  | HPI |
| 44 | $E_{es}^1$    | -21.80 | -22.09 | -19.37 | -18.95 | -22.13 | -21.46 | -12.38 | -18.49 | HPI |
| 45 | $E_{es}^2$    | -15.06 | -14.90 | -14.27 | -12.51 | -16.02 | -15.40 | -8.24  | -13.85 | HPI |
| 46 | $E_{es}^3$    | -16.07 | -15.86 | -14.94 | -12.34 | -16.61 | -16.02 | -9.00  | -14.06 | HPI |
| 47 | $E_{es}^4$    | -16.57 | -16.36 | -15.02 | -12.64 | -16.78 | -16.23 | -8.87  | -14.23 | HPI |
| 48 | $E_{es}(REF)$ | -16.28 | -16.36 | -12.72 | -14.35 | -15.73 | -15.73 | -9.29  | -12.22 | HPI |
| 49 | $E_{es}^0$    | -5.48  | -6.32  | -7.36  | -6.15  | -7.20  | -9.20  | -7.87  | -8.20  | PNP |
| 50 | $E_{es}^1$    | -5.90  | -4.39  | -3.89  | -5.61  | -6.11  | -8.03  | -8.45  | -5.40  | PNP |
| 51 | $E_{es}^2$    | -5.69  | -5.36  | -5.52  | -6.02  | -6.23  | -7.45  | -6.69  | -5.27  | PNP |
| 52 | $E_{es}^3$    | -5.61  | -5.23  | -5.90  | -5.61  | -5.77  | -6.99  | -6.11  | -4.98  | PNP |
| 53 | $E_{es}^4$    | -5.48  | -5.19  | -6.23  | -5.65  | -5.61  | -6.99  | -6.02  | -5.15  | PNP |
| 54 | $E_{es}(REF)$ | -7.24  | -5.19  | -5.90  | -6.74  | -8.12  | -7.07  | -7.74  | -6.28  | PNP |

Table S8: Mean  $E_{mtp}^{l_{max}}$  (kJ mol<sup>-1</sup>) at different  $l_{max}$  in sub-groups of the S66×8 dataset.

| Nr | Name                   | 0.90   | 0.95   | 1.00   | 1.05   | 1.10   | 1.25   | 1.50   | 2.00   | Subgroup |
|----|------------------------|--------|--------|--------|--------|--------|--------|--------|--------|----------|
| 1  | $E_{mtp}^0$            | -2.22  | -1.97  | -1.76  | -1.59  | -1.46  | -1.13  | -0.75  | -0.38  | SHB      |
| 2  | $E_{mtp}^1$            | -26.86 | -23.85 | -21.30 | -19.08 | -17.15 | -12.72 | -8.12  | -3.68  | SHB      |
| 3  | $E_{mtp}^2$            | -23.97 | -21.34 | -19.04 | -17.03 | -15.31 | -11.34 | -7.24  | -3.35  | SHB      |
| 4  | $E_{mtp}^3$            | -24.48 | -21.59 | -19.12 | -17.03 | -15.23 | -11.13 | -7.03  | -3.26  | SHB      |
| 5  | $E_{mtp}^4$            | -24.35 | -21.46 | -19.04 | -16.99 | -15.19 | -11.13 | -7.03  | -3.26  | SHB      |
| 6  | $E_{mtp}(\text{RESP})$ | -33.05 | -29.16 | -25.90 | -23.10 | -20.67 | -15.19 | -9.67  | -4.52  | SHB      |
| 7  | $E_{mtp}^0$            | -18.66 | -16.86 | -15.27 | -13.85 | -12.59 | -9.54  | -6.28  | -2.97  | DHB      |
| 8  | $E_{mtp}^1$            | -71.13 | -63.55 | -56.99 | -51.21 | -46.19 | -34.31 | -21.80 | -9.79  | DHB      |
| 9  | $E_{mtp}^2$            | -70.33 | -63.05 | -56.65 | -51.00 | -46.07 | -34.39 | -22.01 | -10.08 | DHB      |
| 10 | $E_{mtp}^3$            | -71.09 | -63.51 | -56.90 | -51.13 | -46.07 | -34.27 | -21.92 | -10.08 | DHB      |
| 11 | $E_{mtp}^4$            | -76.07 | -67.78 | -60.58 | -54.31 | -48.87 | -36.11 | -22.89 | -10.38 | DHB      |
| 12 | $E_{mtp}(\text{RESP})$ | -94.93 | -84.56 | -75.56 | -67.78 | -61.00 | -45.19 | -28.74 | -13.10 | DHB      |
| 13 | $E_{mtp}^0$            | 0.00   | 0.00   | 0.00   | 0.00   | 0.00   | 0.00   | 0.00   | 0.00   | WHD      |
| 14 | $E_{mtp}^1$            | -19.75 | -17.28 | -14.90 | -12.97 | -11.34 | -7.53  | -3.89  | -1.42  | WHD      |
| 15 | $E_{mtp}^2$            | -12.68 | -10.96 | -9.29  | -7.99  | -6.90  | -4.44  | -2.30  | -0.88  | WHD      |

|    |                  |        |        |        |        |        |        |       |       |     |
|----|------------------|--------|--------|--------|--------|--------|--------|-------|-------|-----|
| 16 | $E_{mtp}^3$      | -9.33  | -8.20  | -7.20  | -6.32  | -5.56  | -3.68  | -1.97 | -0.79 | WHB |
| 17 | $E_{mtp}^4$      | -8.83  | -7.78  | -6.82  | -6.02  | -5.27  | -3.51  | -1.92 | -0.75 | WHB |
| 18 | $E_{mtp}$ (RESP) | -17.74 | -15.36 | -13.22 | -11.51 | -10.04 | -6.57  | -3.47 | -1.34 | WHB |
| 19 | $E_{mtp}^0$      | 1.92   | 1.63   | 1.38   | 1.21   | 1.00   | 0.63   | 0.29  | 0.08  | PP  |
| 20 | $E_{mtp}^1$      | 14.52  | 12.38  | 10.59  | 9.08   | 7.82   | 4.98   | 2.34  | 0.59  | PP  |
| 21 | $E_{mtp}^2$      | 3.60   | 2.97   | 2.47   | 2.05   | 1.67   | 0.92   | 0.33  | 0.00  | PP  |
| 22 | $E_{mtp}^3$      | 3.97   | 3.31   | 2.72   | 2.26   | 1.84   | 1.00   | 0.33  | 0.00  | PP  |
| 23 | $E_{mtp}^4$      | 3.77   | 3.18   | 2.68   | 2.22   | 1.84   | 1.05   | 0.38  | 0.00  | PP  |
| 24 | $E_{mtp}$ (RESP) | 5.10   | 4.18   | 3.47   | 2.85   | 2.34   | -6.57  | 0.50  | 0.04  | PP  |
| 25 | $E_{mtp}^0$      | -2.38  | -2.85  | -1.84  | -1.63  | -1.46  | -1.05  | -0.63 | -0.29 | PPU |
| 26 | $E_{mtp}^1$      | -6.69  | -5.40  | -4.81  | -4.10  | -3.51  | -2.26  | -1.13 | -0.38 | PPU |
| 27 | $E_{mtp}^2$      | -10.21 | -9.54  | -7.91  | -6.95  | -6.15  | -4.31  | -2.51 | -1.00 | PPU |
| 28 | $E_{mtp}^3$      | -12.05 | -11.13 | -8.95  | -7.78  | -6.78  | -4.69  | -2.68 | -1.05 | PPU |
| 29 | $E_{mtp}^4$      | -11.76 | -10.79 | -8.83  | -7.70  | -6.74  | -4.64  | -2.68 | -1.05 | PPU |
| 30 | $E_{mtp}$ (RESP) | -13.01 | -11.92 | -9.92  | -8.70  | -7.70  | -5.36  | -3.10 | -1.21 | PPU |
| 31 | $E_{mtp}^0$      | 0.08   | 0.08   | 0.08   | 0.08   | 0.08   | 0.04   | 0.00  | 0.00  | PAA |
| 32 | $E_{mtp}^1$      | -5.73  | -4.35  | -3.35  | -2.59  | -2.05  | -1.13  | -0.50 | -0.17 | PAA |
| 33 | $E_{mtp}^2$      | -0.88  | -0.71  | -0.63  | -0.54  | -0.46  | -0.29  | -0.13 | -0.04 | PAA |
| 34 | $E_{mtp}^3$      | -0.25  | -0.25  | -0.25  | -0.21  | -0.21  | -0.13  | -0.08 | 0.00  | PAA |
| 35 | $E_{mtp}^4$      | -0.17  | -0.17  | -0.17  | -0.17  | -0.17  | -0.13  | -0.04 | 0.00  | PAA |
| 36 | $E_{mtp}$ (RESP) | -0.33  | -0.29  | -0.25  | -0.21  | -0.17  | -0.13  | -0.04 | 0.00  | PAA |
| 37 | $E_{mtp}^0$      | -0.38  | -0.29  | -0.25  | -0.21  | -0.17  | -0.08  | -0.04 | 0.00  | TS  |
| 38 | $E_{mtp}^1$      | -17.15 | -15.10 | -13.35 | -11.80 | -10.50 | -7.45  | -4.35 | -1.72 | TS  |
| 39 | $E_{mtp}^2$      | -6.53  | -5.56  | -4.81  | -4.18  | -3.64  | -2.51  | -1.42 | -0.54 | TS  |
| 40 | $E_{mtp}^3$      | -6.28  | -5.44  | -4.77  | -4.18  | -3.68  | -2.55  | -1.46 | -0.54 | TS  |
| 41 | $E_{mtp}^4$      | -5.90  | -5.19  | -4.56  | -4.02  | -3.56  | -2.47  | -1.46 | -0.54 | TS  |
| 42 | $E_{mtp}$ (RESP) | -8.33  | -8.33  | -6.28  | -5.48  | -4.81  | -3.26  | -1.84 | -0.71 | TS  |
| 43 | $E_{mtp}^0$      | 3.81   | 3.35   | 2.97   | 2.64   | 2.34   | 1.67   | 0.96  | 0.38  | HP  |
| 44 | $E_{mtp}^1$      | -24.27 | -21.59 | -19.25 | -17.20 | -15.36 | -11.13 | -6.74 | -2.72 | HP  |
| 45 | $E_{mtp}^2$      | -15.23 | -13.22 | -11.55 | -10.13 | -8.95  | -6.28  | -3.64 | -1.42 | HP  |
| 46 | $E_{mtp}^3$      | -15.69 | -13.85 | -12.26 | -10.84 | -9.62  | -6.78  | -3.97 | -1.51 | HP  |
| 47 | $E_{mtp}^4$      | -15.31 | -13.60 | -12.13 | -10.79 | -9.58  | -6.82  | -4.02 | -1.55 | HP  |
| 48 | $E_{mtp}$ (RESP) | -18.66 | -16.40 | -14.43 | -12.72 | -11.17 | -7.91  | -4.60 | -1.76 | HP  |
| 49 | $E_{mtp}^0$      | 0.08   | 0.04   | 0.00   | 0.00   | 0.00   | 0.00   | 0.00  | 0.00  | PNP |
| 50 | $E_{mtp}^1$      | -5.44  | -4.90  | -4.39  | -3.97  | -3.56  | -2.59  | -1.55 | -0.59 | PNP |
| 51 | $E_{mtp}^2$      | -4.73  | -3.97  | -3.39  | -2.89  | -2.51  | -1.67  | -0.88 | -0.33 | PNP |
| 52 | $E_{mtp}^3$      | -3.72  | -3.22  | -2.80  | -2.43  | -2.13  | -1.46  | -0.84 | -0.29 | PNP |
| 53 | $E_{mtp}^4$      | -3.31  | -2.89  | -2.51  | -2.22  | -1.97  | -1.34  | -0.79 | -0.29 | PNP |
| 54 | $E_{mtp}$ (RESP) | -5.69  | -4.85  | -4.18  | -3.64  | -3.14  | -2.13  | -1.17 | -0.42 | PNP |

Table S9: Mean  $E_{mtp}^{l_{max}}$  (kJ mol<sup>-1</sup>) at different  $l_{max}$  in subgroups of S66a8 dataset.

| Nr | Name        | 1y-30 | 1y+30 | 1z-30 | 1z+30 | 2y-30 | 2y+30 | 2z-30 | 2z-30 | Subgroup |
|----|-------------|-------|-------|-------|-------|-------|-------|-------|-------|----------|
| 1  | $E_{mtp}^0$ | -1.51 | -1.46 | -1.30 | -1.63 | -1.38 | -1.59 | -1.38 | -1.55 | SHB      |

|    |                  |        |        |        |        |        |        |        |        |     |
|----|------------------|--------|--------|--------|--------|--------|--------|--------|--------|-----|
| 2  | $E_{mtp}^1$      | -17.11 | -17.45 | -16.53 | -16.99 | -18.16 | -19.04 | -18.70 | -17.49 | SHB |
| 3  | $E_{mtp}^2$      | -15.86 | -15.94 | -15.06 | -15.90 | -15.27 | -16.23 | -15.69 | -15.23 | SHB |
| 4  | $E_{mtp}^3$      | -15.98 | -15.90 | -14.94 | -15.94 | -14.64 | -16.15 | -15.73 | -14.77 | SHB |
| 5  | $E_{mtp}^4$      | -15.94 | -15.86 | -14.85 | -15.90 | -14.60 | -15.98 | -15.61 | -14.69 | SHB |
| 6  | $E_{mtp}$ (RESP) | -20.79 | -20.88 | -19.71 | -20.59 | -20.50 | -22.34 | -21.84 | -20.38 | SHB |
| 7  | $E_{mtp}^0$      | -13.51 | -13.47 | -9.54  | -8.66  | -13.68 | -13.68 | -9.12  | -7.82  | DHB |
| 8  | $E_{mtp}^1$      | -47.45 | -47.28 | -34.85 | -29.25 | -47.66 | -47.66 | -32.97 | -26.69 | DHB |
| 9  | $E_{mtp}^2$      | -48.53 | -48.45 | -33.76 | -31.13 | -49.12 | -49.08 | -31.97 | -28.79 | DHB |
| 10 | $E_{mtp}^3$      | -48.83 | -48.66 | -35.73 | -29.87 | -49.45 | -49.50 | -34.81 | -26.53 | DHB |
| 11 | $E_{mtp}^4$      | -51.71 | -51.55 | -37.11 | -31.42 | -52.30 | -52.30 | -35.73 | -27.95 | DHB |
| 12 | $E_{mtp}$ (RESP) | -63.35 | -63.14 | -46.19 | -39.16 | -64.56 | -64.60 | -46.94 | -34.69 | DHB |
| 13 | $E_{mtp}^0$      | -0.04  | 0.00   | 0.00   | 0.08   | 0.00   | 0.04   | 0.00   | 0.00   | WHB |
| 14 | $E_{mtp}^1$      | -11.00 | -13.05 | -11.21 | -13.64 | -10.50 | -11.13 | -9.54  | -10.00 | WHB |
| 15 | $E_{mtp}^2$      | -6.82  | -8.58  | -6.40  | -7.32  | -7.28  | -6.69  | -6.11  | -5.48  | WHB |
| 16 | $E_{mtp}^3$      | -5.73  | -6.49  | -4.69  | -5.82  | -5.86  | -5.10  | -5.82  | -4.64  | WHB |
| 17 | $E_{mtp}^4$      | -5.40  | -6.23  | -4.48  | -5.56  | -5.61  | -4.90  | -5.56  | -4.44  | WHB |
| 18 | $E_{mtp}$ (RESP) | -10.33 | -11.55 | -8.12  | -11.84 | -10.71 | -9.12  | -9.41  | -7.91  | WHB |
| 19 | $E_{mtp}^0$      | 0.88   | 0.79   | 0.79   | 0.84   | 0.84   | 0.75   | 0.67   | 0.84   | PP  |
| 20 | $E_{mtp}^1$      | 9.71   | 9.04   | 9.79   | 8.12   | 6.23   | 5.69   | 6.44   | 5.10   | PP  |
| 21 | $E_{mtp}^2$      | 4.94   | 4.35   | 5.06   | 3.72   | 1.21   | 0.75   | 1.21   | 0.96   | PP  |
| 22 | $E_{mtp}^3$      | 2.68   | 2.34   | 3.47   | 1.88   | 1.38   | 0.67   | 1.17   | 0.96   | PP  |
| 23 | $E_{mtp}^4$      | 2.80   | 2.47   | 3.72   | 2.05   | 1.34   | 0.63   | 1.17   | 0.96   | PP  |
| 24 | $E_{mtp}$ (RESP) | 2.13   | 1.30   | 2.09   | 1.46   | 1.72   | -9.12  | 1.80   | 1.59   | PP  |
| 25 | $E_{mtp}^0$      | -1.55  | -1.72  | -1.05  | -1.38  | -1.30  | -1.55  | -1.46  | -0.63  | PPU |
| 26 | $E_{mtp}^1$      | -6.07  | -7.28  | -6.07  | -2.85  | -2.01  | -0.08  | -2.72  | -9.46  | PPU |
| 27 | $E_{mtp}^2$      | -4.10  | -5.40  | -4.48  | -3.31  | -4.60  | -4.48  | -5.65  | -6.57  | PPU |
| 28 | $E_{mtp}^3$      | -6.74  | -8.20  | -7.15  | -5.94  | -5.31  | -4.73  | -5.77  | -7.36  | PPU |
| 29 | $E_{mtp}^4$      | -7.32  | -8.41  | -6.99  | -6.36  | -5.44  | -4.81  | -5.69  | -8.16  | PPU |
| 30 | $E_{mtp}$ (RESP) | -8.20  | -8.16  | -9.00  | -6.61  | -6.32  | -5.73  | -6.53  | -8.37  | PPU |
| 31 | $E_{mtp}^0$      | 0.17   | 0.00   | 0.00   | 0.08   | -0.04  | -0.04  | 0.17   | -0.04  | PAA |
| 32 | $E_{mtp}^1$      | -1.38  | -2.22  | -2.30  | -1.97  | -0.33  | -0.71  | -2.55  | 0.21   | PAA |
| 33 | $E_{mtp}^2$      | -0.38  | -0.46  | -0.25  | -0.59  | -0.08  | -0.25  | -0.42  | -0.17  | PAA |
| 34 | $E_{mtp}^3$      | 0.00   | -0.08  | 0.00   | -0.21  | -0.13  | -0.21  | -0.17  | -0.13  | PAA |
| 35 | $E_{mtp}^4$      | -0.04  | -0.08  | 0.00   | -0.13  | -0.13  | -0.17  | -0.21  | -0.13  | PAA |
| 36 | $E_{mtp}$ (RESP) | -0.25  | -0.25  | -0.13  | -0.25  | 0.00   | -0.08  | -0.21  | -0.04  | PAA |
| 37 | $E_{mtp}^0$      | -0.21  | -0.21  | -0.13  | -0.17  | -0.17  | -0.17  | -0.21  | -0.25  | TS  |
| 38 | $E_{mtp}^1$      | -8.24  | -8.28  | -6.23  | -7.36  | -10.33 | -10.29 | -11.17 | -10.92 | TS  |
| 39 | $E_{mtp}^2$      | -2.01  | -2.09  | -1.34  | -1.80  | -4.06  | -4.31  | -4.10  | -3.77  | TS  |
| 40 | $E_{mtp}^3$      | -3.01  | -3.10  | -2.43  | -2.85  | -3.97  | -4.18  | -3.97  | -3.81  | TS  |
| 41 | $E_{mtp}^4$      | -3.01  | -3.10  | -2.38  | -2.80  | -3.81  | -4.06  | -3.85  | -3.72  | TS  |
| 42 | $E_{mtp}$ (RESP) | -4.64  | -4.64  | -3.56  | -4.56  | -4.81  | -5.40  | -5.27  | -4.56  | TS  |
| 43 | $E_{mtp}^0$      | 2.26   | 2.30   | 2.30   | 1.92   | 2.38   | 2.38   | 1.51   | 1.97   | HP  |
| 44 | $E_{mtp}^1$      | -16.53 | -16.61 | -14.60 | -14.85 | -15.69 | -14.69 | -8.66  | -14.14 | HP  |
| 45 | $E_{mtp}^2$      | -9.00  | -9.12  | -8.20  | -7.61  | -9.16  | -8.83  | -5.36  | -7.99  | HP  |
| 46 | $E_{mtp}^3$      | -10.04 | -10.13 | -8.95  | -7.74  | -9.92  | -9.62  | -6.28  | -8.16  | HP  |

|    |                  |        |        |        |       |        |        |       |       |     |
|----|------------------|--------|--------|--------|-------|--------|--------|-------|-------|-----|
| 47 | $E_{mtp}^4$      | -10.42 | -10.46 | -8.95  | -7.87 | -10.04 | -9.79  | -6.15 | -8.20 | HP  |
| 48 | $E_{mtp}$ (RESP) | -11.59 | -11.72 | -10.38 | -9.58 | -11.42 | -11.05 | -7.07 | -9.46 | HP  |
| 49 | $E_{mtp}^0$      | 0.08   | -0.08  | -0.21  | 0.04  | 0.33   | -0.21  | 0.04  | -0.17 | PNP |
| 50 | $E_{mtp}^1$      | -3.51  | -2.89  | -1.21  | -3.51 | -2.80  | -5.15  | -5.36 | -1.92 | PNP |
| 51 | $E_{mtp}^2$      | -2.55  | -1.51  | -1.42  | -2.22 | -2.01  | -2.30  | -2.80 | -1.00 | PNP |
| 52 | $E_{mtp}^3$      | -2.55  | -1.26  | -1.97  | -1.88 | -1.80  | -1.92  | -2.26 | -0.92 | PNP |
| 53 | $E_{mtp}^4$      | -2.38  | -1.13  | -1.92  | -1.84 | -1.63  | -1.84  | -2.18 | -0.79 | PNP |
| 54 | $E_{mtp}$ (RESP) | -3.77  | -1.88  | -2.64  | -2.89 | -3.05  | -2.38  | -3.43 | -1.26 | PNP |

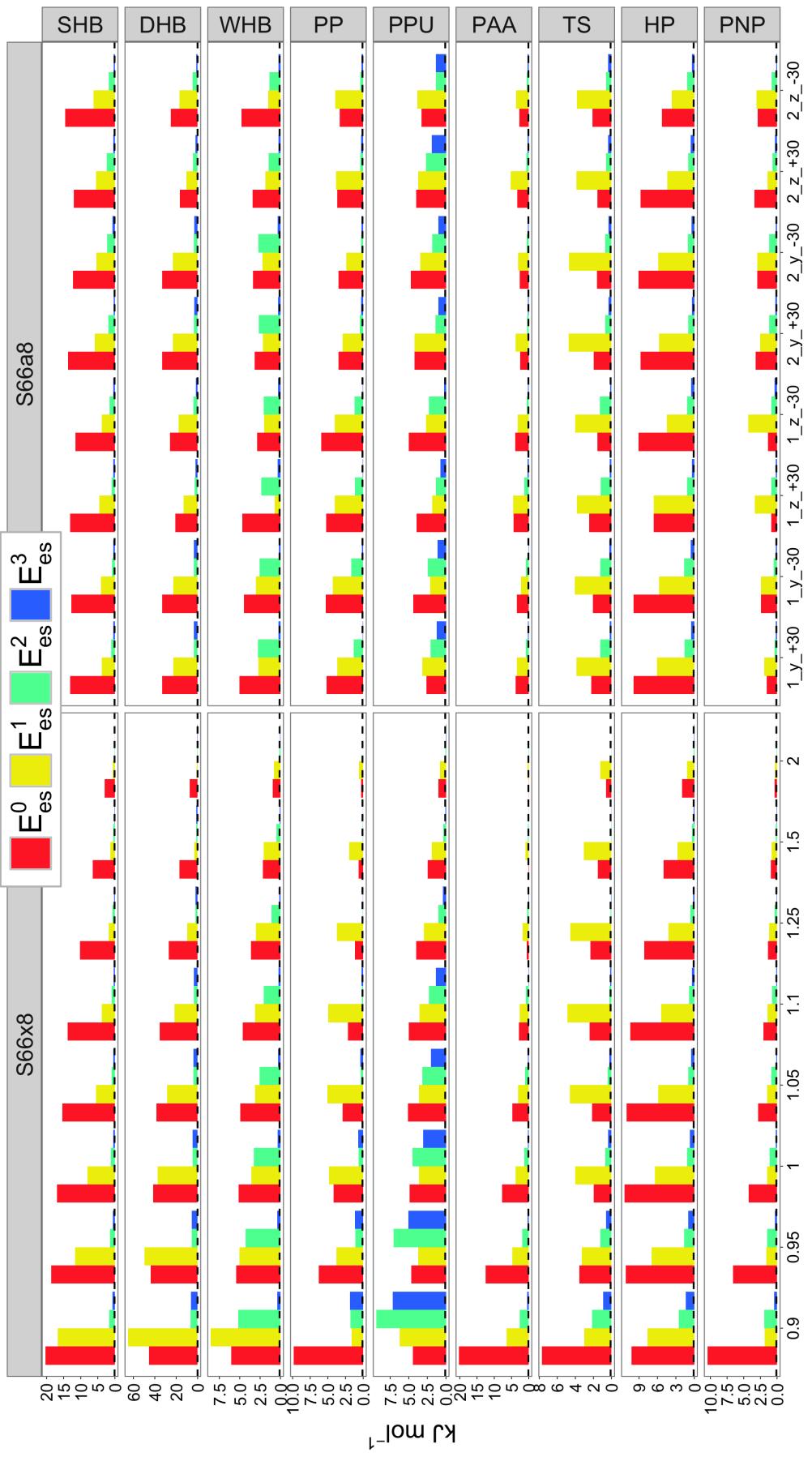


Fig. S1. Visualization of convergence of electrostatic interaction energies ( $E_{es}$ ) computed from UBDB (kJ mol<sup>-1</sup>) at different intermolecular distances (left) and angles (right) in nine subsets of the benchmark datasets. Only the differences of particular  $E_{es}^0, E_{es}^1, E_{es}^2, E_{es}^3$  from  $E_{es}^4$  are shown. The differences are quantified by RMS difference. The dashed horizontal lines along the x axis correspond to the value of 0.1 kJ mol<sup>-1</sup>. 13

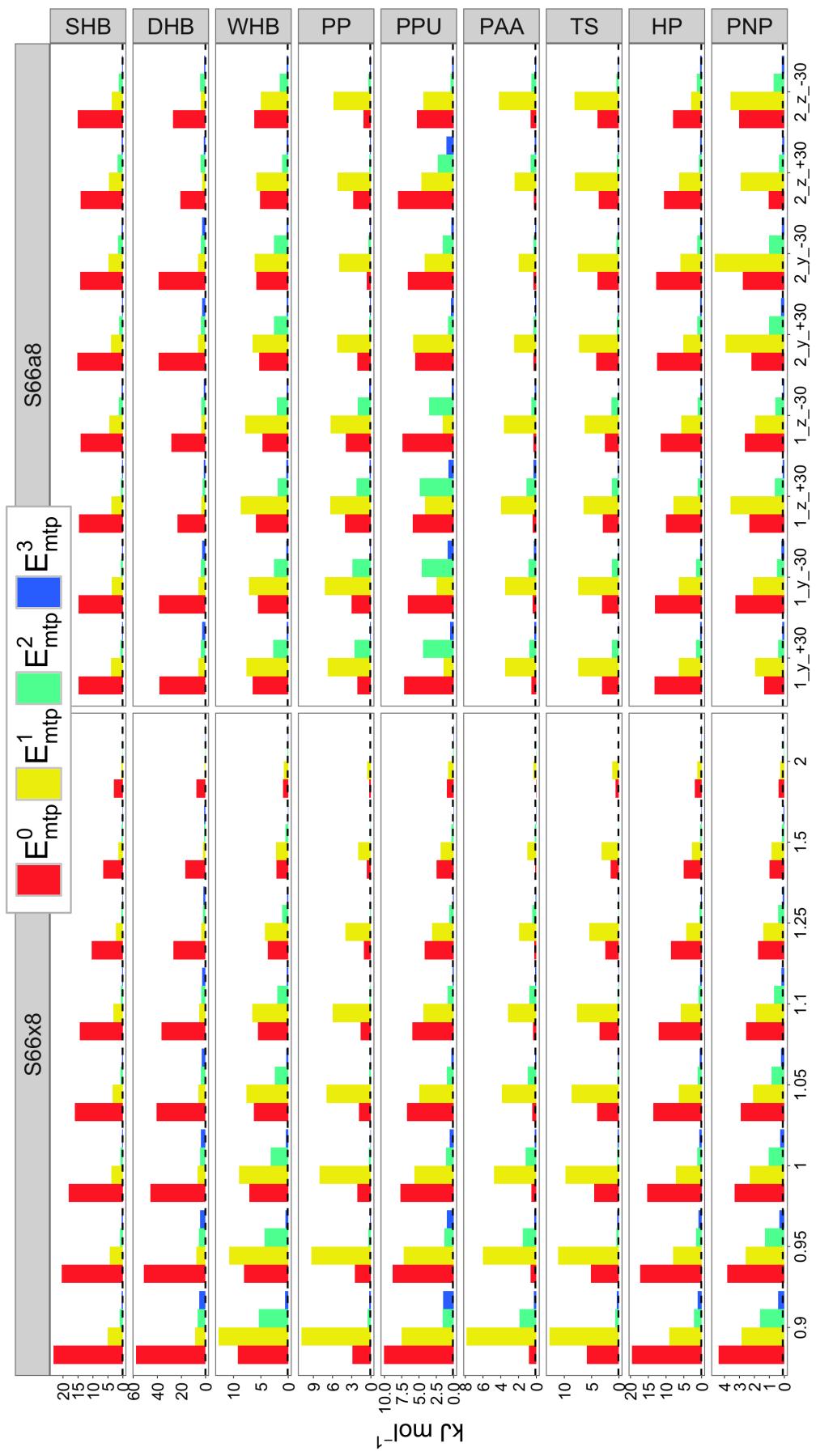


Fig. S2. Visualization of convergence of electrostatic interaction energies ( $E_{mtp}$ ) computed from UBDB ( $\text{kJ mol}^{-1}$ ) at different intermolecular distances (left) and angles (right) in nine subsets of the benchmark datasets. Only the differences of particular  $E_{mtp}^0, E_{mtp}^1, E_{mtp}^2, E_{mtp}^3$  from  $E_{mtp}^4$  are shown. The differences are quantified by RMS difference. The dashed horizontal lines along the x axis correspond to the value of  $0.1 \text{ kJ mol}^{-1}$ .