Supporting Information

Enthalpic and Entropic Contributions to Hydrophobicity

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Further decomposition of calculated thermodynamic properties

As outlined in the methodology section total solvation free energies, enthalpies, and entropies, these thermodynamic values are further decomposed. According to Eq. (3), the total enthalpy ΔH_{Solv} can be split into the enthalpic interactions between the solute and the water ΔH_{SW} and an enthalpy term describing the distortion of the water-water interactions ΔH_{WW}. The total entropy ΔS_{Solv} is split into an orientational ΔS_{orient} and a translational term ΔS_{trans} (compare Eq. (4)). The origin of these terms is explained in the methods section of the main text.

Table S1: Decomposition of the thermodynamic properties for the TIP3P water model.

Amino Acid	ΔH_{SW}	ΔH_{WW}	ΔH_{Solv}	$-T\Delta S_{orient}$	$-T\Delta S_{trans}$	$-T\Delta S_{Solv}$	ΔG_{Solv}
ALA	-43.2±1.8	20.6±1.0	-22.5±0.8	9.5±0.0	5.3±0.1	14.8±0.1	-7.7±0.7
ARG(+)	-121.9±4.2	57.2±2.1	-64.7±2.1	14.7±0.3	9.3±0.2	24.1±0.5	-40.7±1.6
ASN	-63.5±7.0	29.7±3.0	-33.8±4.0	12.2±0.6	6.9±0.3	19.1±0.9	-14.7±3.2
ASP(-)	-141.8±0.7	61.2±0.4	-80.5±0.3	18.2±0.1	8.2±0.1	26.4±0.0	-54.2±0.3
CYS	-46.8±3.5	22.9±1.5	-23.9±2.0	9.6±0.2	5.7±0.2	15.3±0.4	-8.5±1.7
GLN	-68.1±2.5	32.3±1.4	-35.8±1.1	13.2±0.2	7.4±0.2	20.6±0.4	-15.2±0.7
GLU(-)	-137.6±3.4	59.3±1.5	-78.3±1.9	19.0±0.0	8.7±0.2	27.7±0.2	-50.6±1.7
GLY	-42.9±1.1	20.5±0.7	-22.4±0.4	8.9±0.0	5.2±0.0	14.0±0.1	-8.4±0.4
HIS	-67.6±1.2	31.6±0.3	-36.0±1.0	13.5±0.2	7.6±0.0	21.1±0.2	-14.9±0.8
HIS(+)	-108.5±3.9	50.9±2.3	-57.7±1.6	13.2±0.3	8.3±0.1	21.5±0.3	-36.2±1.3
ILE	-49.7±0.5	24.2±0.2	-25.4±0.5	11.3±0.0	6.8±0.1	18.1±0.1	-7.3±0.6
LEU	-49.0±1.2	24.1±0.5	-24.9±0.7	11.2±0.2	6.6±0.1	17.8±0.3	-7.1±0.5
LYS(+)	-126.6±4.5	60.5±2.0	-66.1±2.5	14.3±0.3	8.5±0.5	22.8±0.7	-43.4±1.9
MET	-54.1±0.6	26.5±0.5	-27.6±0.6	11.4±0.1	6.7±0.0	18.1±0.1	-9.5±0.5
PHE	-57.9±0.2	28.8±0.3	-29.1±0.1	12.6±0.0	7.3±0.1	19.9±0.2	-9.2±0.1
PRO	-43.6±1.6	20.7±0.8	-22.9±0.8	10.2±0.1	5.8±0.0	16.0±0.2	-6.9±0.6
SER	-52.5±2.2	24.5±1.0	-28.0±1.2	9.8±0.1	5.8±0.0	15.6±0.1	-12.4±1.1
THR	-51.7±2.0	24.6±1.0	-27.1±1.1	10.6±0.2	6.2±0.2	16.7±0.4	-10.3±0.9
TRP	-65.5±1.0	31.7±0.6	-33.8±0.5	14.1±0.1	8.3±0.1	22.3±0.2	-11.5±0.4
TYR	-63.1±3.6	30.7±1.5	-32.4±2.1	12.5±0.2	7.7±0.1	20.2±0.3	-12.2±1.9
VAL	-47.5±1.4	23.0±0.6	-24.5±0.8	10.8±0.1	6.4±0.2	17.2±0.3	-7.3±0.5

Table S2: Decomposition of the thermodynamic properties for the TIP4P water model.

Amino Acid	ΔH_{SW}	ΔH_{WW}	ΔH_{Solv}	$-T\Delta S_{orient}$	$-T\Delta S_{trans}$	$-T\Delta S_{Solv}$	ΔG_{Solv}
ALA	-46.5±1.1	24.4±0.6	-22.0±0.5	10.3±0.1	5.5±0.1	15.8±0.2	-6.3±0.4
ARG(+)	-127.8±1.6	65.0±1.1	-62.8±0.5	15.5±0.1	9.0±0.2	24.5±0.3	-38.3±0.4
ASN	-68.3±5.6	34.8±2.5	-33.5±3.1	13.4±0.5	7.0±0.2	20.4±0.7	-13.1±2.5
ASP(-)	-145.8±6.9	63.1±2.8	-82.8±4.2	20.5±0.1	8.7±0.1	29.2±0.1	-53.5±4.1
CYS	-49.4±2.1	27.1±1.1	-22.3±1.0	10.4±0.2	5.9±0.1	16.3±0.3	-6.0±0.8
GLN	-70.7±2.0	36.0±1.1	-34.7±0.8	14.2±0.1	7.5±0.0	21.7±0.1	-12.9±0.8
GLU(-)	-151.1±2.7	65.2±1.5	-85.9±1.3	21.5±0.2	9.2±0.1	30.6±0.1	-55.2±1.1
GLY	-46.3±0.3	24.7±0.1	-21.6±0.2	9.7±0.0	5.1±0.0	14.8±0.1	-6.8±0.2
HIS	-71.6±2.2	37.1±1.2	-34.5±1.2	14.6±0.3	7.6±0.2	22.2±0.4	-12.3±0.8
HIS(+)	-114.7±1.2	58.6±0.5	-56.0±0.7	14.3±0.2	8.2±0.0	22.5±0.2	-33.5±0.7
ILE	-53.1±0.8	27.6±0.6	-25.4±0.2	12.5±0.0	7.2±0.2	19.7±0.1	-5.7±0.2
LEU	-53.4±0.8	28.5±0.9	-24.9±0.1	12.4±0.1	7.0±0.1	19.4±0.2	-5.5±0.1
LYS(+)	-129.3±1.6	66.3±1.0	-63.0±0.9	15.1±0.2	8.4±0.1	23.5±0.2	-39.5±0.7
MET	-55.7±2.3	30.1±0.7	-25.7±1.7	12.3±0.2	7.1±0.2	19.5±0.3	-6.2±1.4
PHE	-55.8±3.8	30.6±1.7	-25.2±2.2	13.4±0.2	7.6±0.2	20.9±0.4	-4.3±1.8
PRO	-46.5±1.0	24.9±0.4	-21.6±0.7	10.9±0.1	5.8±0.1	16.8±0.2	-4.8±0.5
SER	-58.4±5.2	29.1±2.9	-29.3±2.7	10.8±0.5	5.8±0.3	16.7±0.8	-12.7±2.0
THR	-55.7±0.9	28.6±0.8	-27.1±0.2	11.5±0.1	6.5±0.1	18.0±0.2	-9.1±0.2
TRP	-70.1±0.6	37.8±0.3	-32.3±0.4	15.4±0.1	8.5±0.1	23.9±0.2	-8.4±0.3
TYR	-67.5±1.1	36.3±0.7	-31.3±0.8	13.8±0.3	8.0±0.3	21.9±0.6	-9.4±0.3
VAL	-51.2±0.4	27.0±0.3	-24.2±0.1	11.8±0.1	6.6±0.0	18.4±0.1	-5.8±0.1

Table S3: Decomposition of the thermodynamic properties for the TIP5P water model.

Amino Acid	ΔH_{SW}	ΔH_{WW}	ΔH_{Solv}	$-T\Delta S_{orient}$	$-T\Delta S_{trans}$	$-T\Delta S_{Solv}$	ΔG_{Solv}
ALA	-41.0±0.9	19.7±0.2	-21.3±0.7	9.8±0.1	6.0±0.1	15.8±0.2	-5.5±0.5
ARG(+)	-129.1±2.4	57.0±0.6	-72.1±1.9	18.1±0.4	11.3±0.2	29.4±0.6	-42.8±1.5
ASN	-67.2±1.2	30.0±0.4	-37.1±0.9	14.2±0.2	8.5±0.1	22.6±0.3	-14.5±1.0
ASP(-)	-123.0±4.9	55.9±2.2	-67.0±2.8	16.7±0.1	8.6±0.1	25.3±0.1	-41.7±2.7
CYS	-47.5±3.6	23.3±1.7	-24.2±1.9	9.9±0.1	6.2±0.1	16.1±0.1	-8.1±1.8
GLN	-66.3±1.0	30.3±0.5	-35.9±0.5	14.6±0.1	8.6±0.1	23.2±0.2	-12.7±0.6
GLU(-)	-126.3±2.4	57.7±0.9	-68.6±1.6	17.8±0.0	8.7±0.1	26.5±0.1	-42.1±1.6
GLY	-40.3±0.7	19.9±0.7	-20.5±0.0	8.9±0.1	5.7±0.0	14.6±0.1	-5.9±0.0
HIS	-61.3±2.9	29.0±0.8	-32.3±2.1	14.0±0.5	8.3±0.3	22.4±0.8	-9.9±1.3
HIS(+)	-112.6±5.4	52.4±2.6	-60.2±2.8	15.1±0.5	9.2±0.2	24.3±0.5	-35.9±2.3
ILE	-46.6±1.6	22.3±1.1	-24.4±0.5	12.1±0.2	7.6±0.3	19.7±0.4	-4.7±0.4
LEU	-45.5±0.8	22.6±0.9	-22.9±0.3	11.5±0.1	7.2±0.1	18.7±0.2	-4.2±0.1
LYS(+)	-127.2±0.9	58.3±0.5	-69.0±0.6	16.2±0.1	9.4±0.2	25.6±0.4	-43.3±0.3
MET	-47.9±1.1	24.0±0.5	-23.9±0.7	11.7±0.2	7.2±0.1	18.9±0.2	-5.0±0.6
PHE	-52.7±0.6	26.1±0.4	-26.6±0.7	12.9±0.3	8.1±0.1	21.0±0.5	-5.6±0.2
PRO	-39.2±0.4	19.6±0.2	-19.6±0.3	9.9±0.0	6.2±0.1	16.1±0.1	-3.5±0.3
SER	-55.1±4.2	25.0±2.1	-30.0±2.8	10.8±0.9	6.3±0.3	17.1±1.2	-12.9±1.5
THR	-50.7±0.2	23.1±0.2	-27.6±0.4	11.4±0.0	6.9±0.0	18.3±0.0	-9.4±0.4
TRP	-58.4±4.0	29.3±1.8	-29.1±2.5	14.3±0.4	8.8±0.2	23.0±0.5	-6.0±2.0
TYR	-61.5±3.2	28.8±1.6	-32.7±1.7	13.7±0.4	8.3±0.2	22.0±0.5	-10.7±1.1
VAL	-44.0±0.6	14.4±10.2	-22.4±0.3	10.9±0.2	4.6±3.3	17.9±0.3	-3.0±2.2