Interpretation of Interfacial Protein Spectra with Enhanced Molecular Simulation Ensembles

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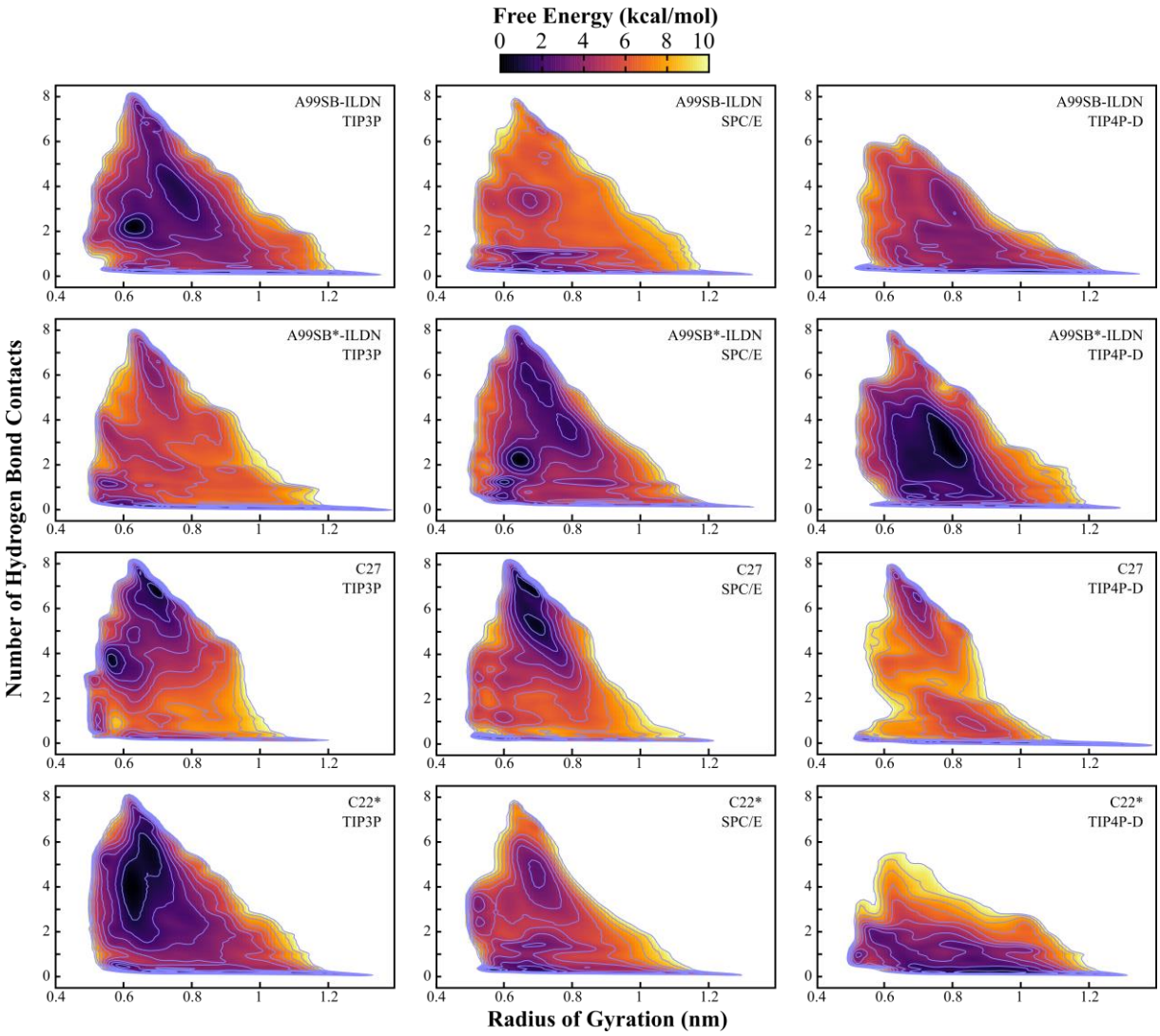

Figure S1. Free energy in CV space obtained from twelve 1 μs long WT-MetaD simulations of mastoparan X. The CVs are denoted on the x- and y-axis as Cα radius of gyration and number of α helix hydrogen bonds. The protein/water force field combination used in each simulation is indicated in the top right corner of the free energy surface.

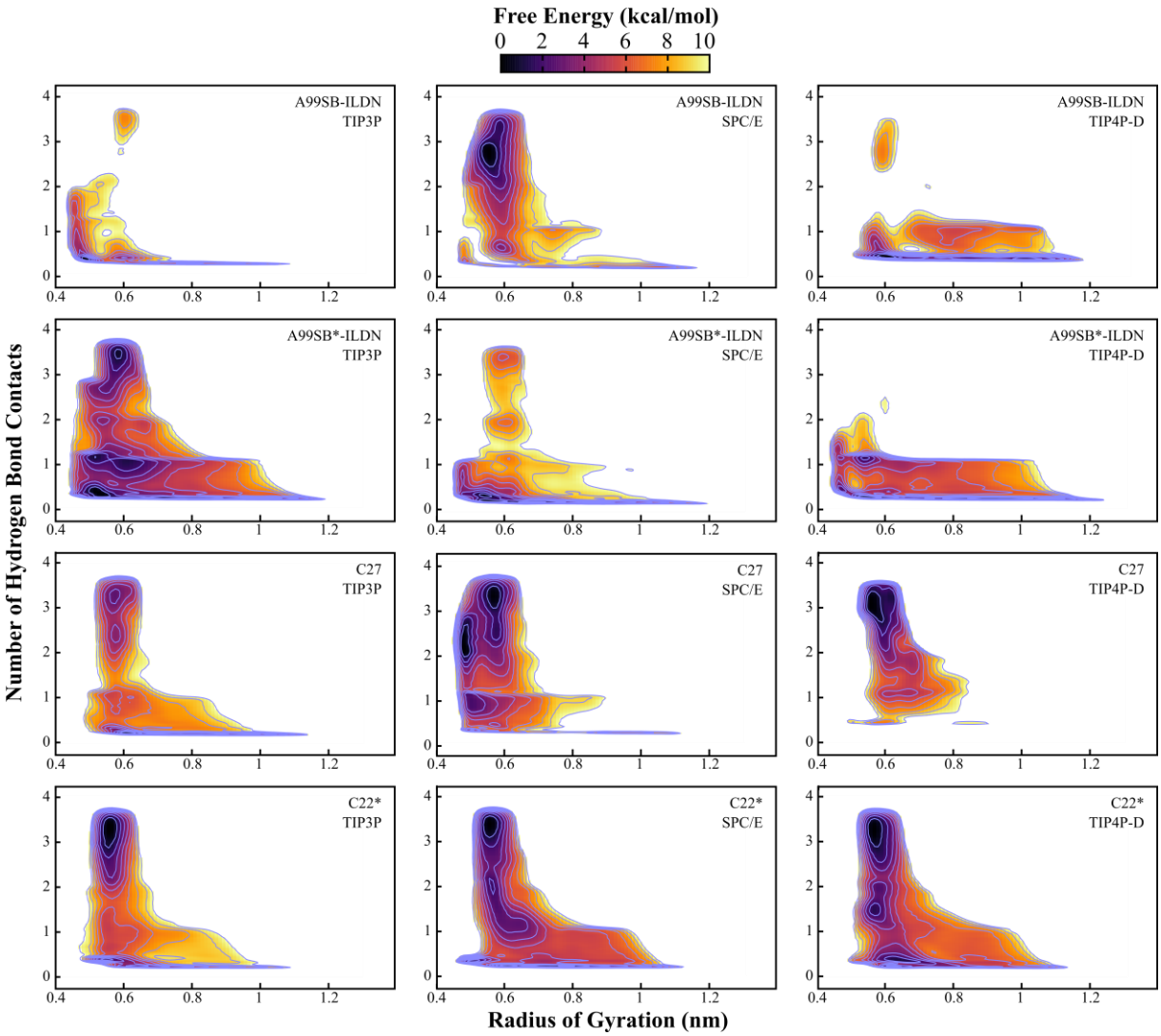

Figure S2. Free energy in CV space obtained from twelve 1 μs long WT-MetaD simulations of tryptophan zipper 2. The CVs are denoted on the x- and y-axis as Cα radius of gyration and number of β sheet hydrogen bonds. The protein/water force field combination used in each simulation is indicated in the top right corner of the free energy surface.

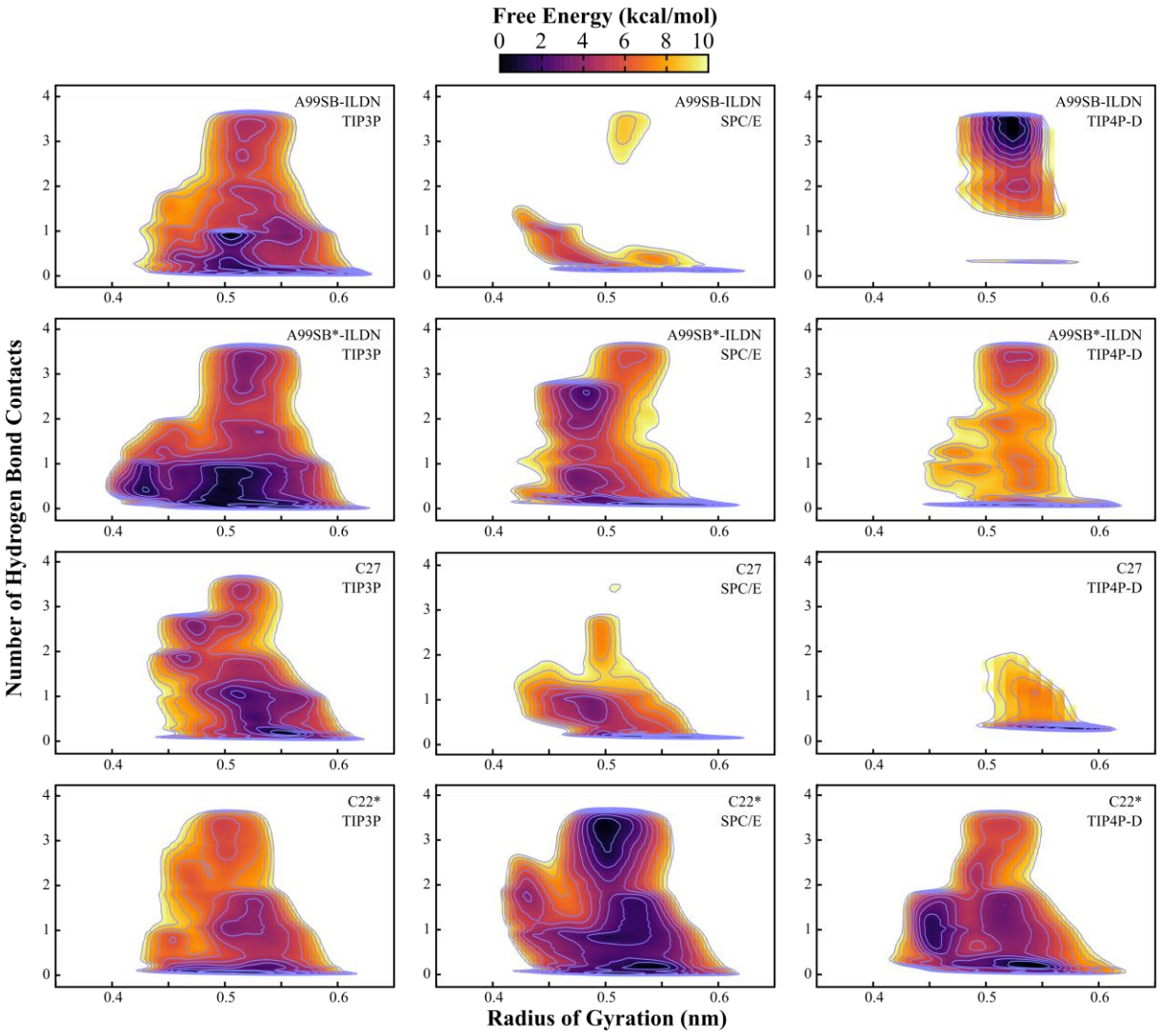

Figure S3. Free energy in CV space obtained from twelve 1 μs long WT-MetaD simulations of the minimal beta-hairpin peptide. The CVs are denoted on the x- and y-axis as Cα radius of gyration and number of β sheet hydrogen bonds. The protein/water force field combination used in each simulation is indicated in the top right corner of the free energy surface.

Table S1. (a) A1.2 fit parameters before setting the non-resonant amplitude and phase and the low frequency vibrational modes (w1 and w2) to zero. (b) Fit parameters used for the comparison to theoretical VSFG spectra.

	(a) SSP	**(b) SSP**	**(a) SPS**	**(b) SPS**
NR	0.3	0	0.1	0
phi	2.7	0	2.6	0
A1	-0.5	0	0.8	0
w1	1586.7	1586.7	1586.7	1586.7
G1	11.1	0	11.1	0
A2	0.6	0	-1.0	0
w2	1609.5	1609.5	1609.5	1609.5
G2	11.9	0	11.9	0
A3	2.7	2.7	0.8	0.8
w3	1627.4	1627.4	1627.4	1627.4
G3	18.1	18.1	18.1	18.1
A4	2.9	2.9	0.7	0.7
w4	1643.7	1643.8	1643.8	1643.8
G4	14.9	14.9	14.9	14.9
A5	0.9	0.9	0.4	0.4
w5	1656.4	1656.4	1656.4	1656.4
G5	15.3	15.3	15.3	15.3
A6	1.0	1.0	0.2	0.2
w6	1675.9	1675.9	1675.9	1675.9
G6	18.1	18.1	18.1	18.1

Table S2. MBH fit parameters. (a) Fit parameters before setting the non-resonant amplitude and phase and the low frequency vibrational modes (w1, w2, w3, and w7) to zero. (b) Fit parameters used for the comparison to theoretical VSFG spectra.

	(a) SSP	**(b) SSP**	**(a) SPS**	**(b) SPS**
NR	0.1	0	0.1	0
phi	1.3	0	1.0	0
A1	7.3	0	1.1	0
w1	1449.7	1449.7	1448.2	1448.2
G1	15.7	0	14.7	0
A2	0.4	0	1.0	0
w2	1546.0	1546.0	1561.8	1561.8
G2	11.9	0	12.0	0
A3	-4.7	0	-2.8	0
w3	1586.3	1586.3	1576.1	1576.1
G3	26.2	0	13.88	0
A4	-2.3	-2.3	-0.1	-0.1
w4	1610.5	1610.5	1613.2	1613.2
G4	14.5	14.5	6.1	6.1
A5	1.3	1.3	0	0
w5	1647.6	1647.6	1647.6	1647.6
G5	13.9	13.9	17.9	17.9
A6	-4.7	-4.7	-0.7	-0.7
w6	1683.0	1683.0	1678.4	1678.4
G6	20.8	20.8	31.4	31.4
A7	-13.8	0	-11.6	0
w7	1953.3	1953.3	1952.8	1952.8
G7	21.7	0	26.5	0

Table S3. MPX fit parameters. (a) Fit parameters before setting the non-resonant amplitude and phase to zero. (b) Fit parameters used for the comparison to theoretical VSFG spectra.

	(a) SSP	**(b) SSP**	**(a) SPS**	**(b) SPS**
NR	0.1	0	0.1	0
Phi	2.6	0	3.0	0
A1	2.6	2.6	0.6	0.6
w1	1655.0	1655.0	1644.0	1644.0
G1	15.7	15.7	17.2	17.2

Table S4. TZ2 fit parameters. (a) Fit parameters before setting the non-resonant amplitude and phase and the low frequency vibrational modes (w1, w2, and w5) to zero. (b) Fit parameters used for the comparison to theoretical VSFG spectra.

	(a) SSP	**(b) SSP**	**(a) SPS**	**(b) SPS**
NR	0.0	0	0.1	0
phi	0.0	0	3.1	0
A1	14.4	0	1.7	0
w1	1505.0	1505.0	1506.7	1506.7
G1	23.2	0	11.1	0
A2	8.3	0	3.5	0
w2	1576.7	1576.7	1565.5	1565.5
G2	37.5	0	28.2	0
A3	0	0	0.9	0.9
w3	0	0	1634.4	1634.4
G3	0	0	17.3	17.3
A4	1.4	1.4	3.4	3.4
w4	1652.9	1652.9	1674.3	1674.3
G4	16.7	16.7	31.2	31.2
A5	6.8	0	0.3	0
w5	1726.6	1726.6	1719.0	1719.0
G5	23.2	0	9.2	0

Convergence: To demonstrate a measure of convergence for the plots in Figure 3 in the main text, we plot the metadynamics hill height over the time of the simulation. While a low hill height does not prove the convergence of the metadynamics simulations, it does mean that for the last half of the simulations, no new regions of conformational space are being explored.

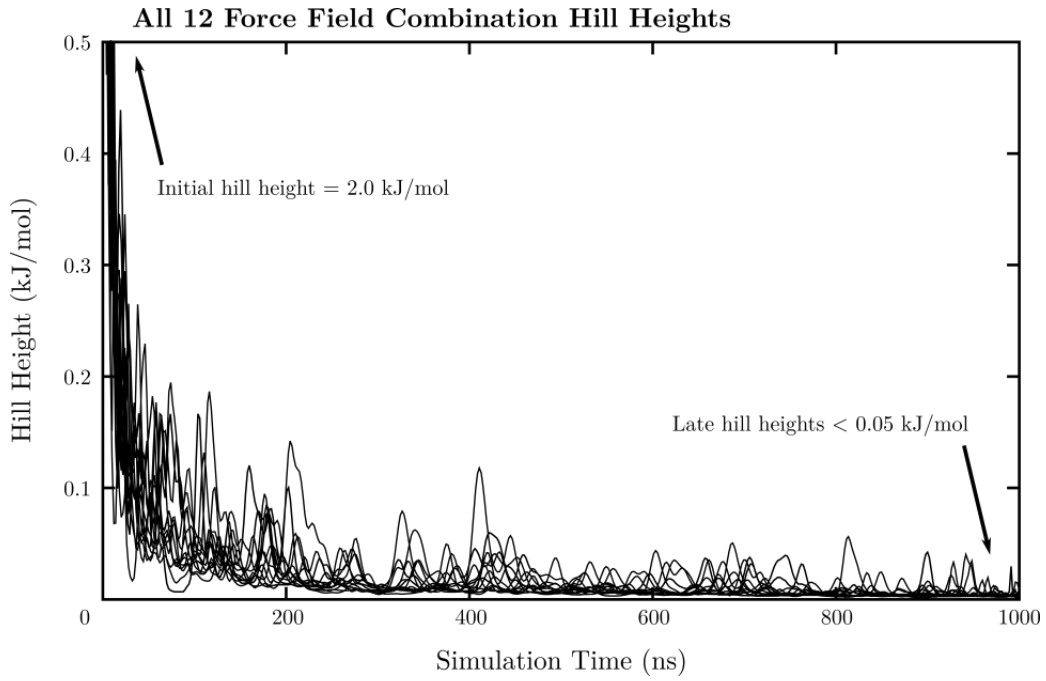

Figure S4. Metadynamics hill heights for all 12 aurein 1.2 simulations plotted over time. All hill height traces are uniformly plotted in black because the intention here is only to show that late hill heights are smaller than 0.05 kJ/mol. Lines are Bezier smoothed to make small peaks clearer. Hill height quickly decays from its initial height of 2.0 kJ/mol.

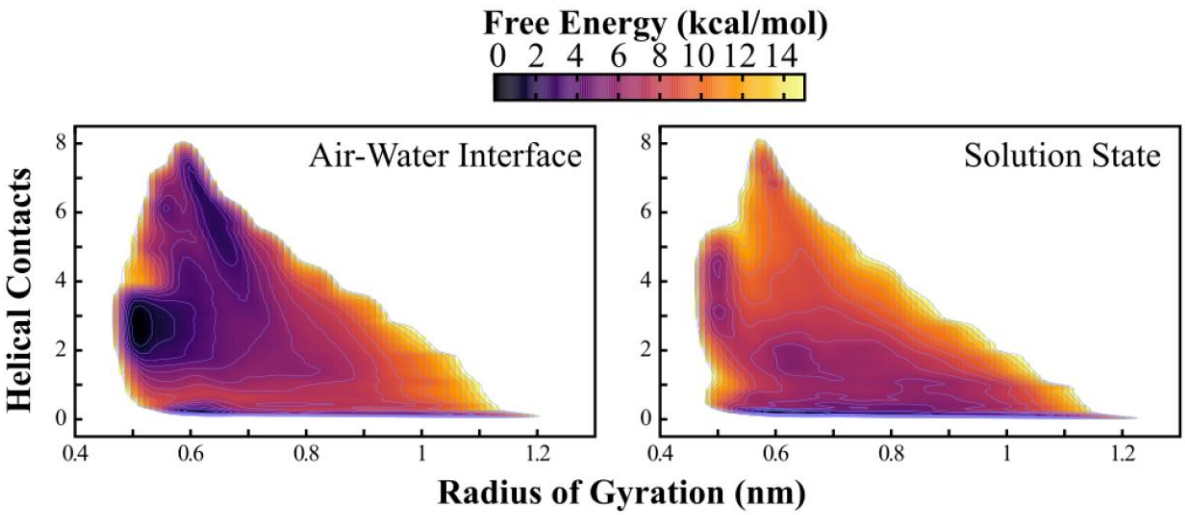

Figure S5. Free energy surfaces of A1.2 using AMBER99SB*-ILDN with SPC/E at the air water interface versus in solution. Certain highly probable structures observed at the air-water interface are no longer favored in the solution state.