SUPPLEMENTARY INFORMATION

DEPENDENCE OF BINDING FREE ENERGIES BETWEEN RNA NUCLEOBASES AND PROTEIN SIDE CHAINS ON LOCAL DIELECTRIC PROPERTIES

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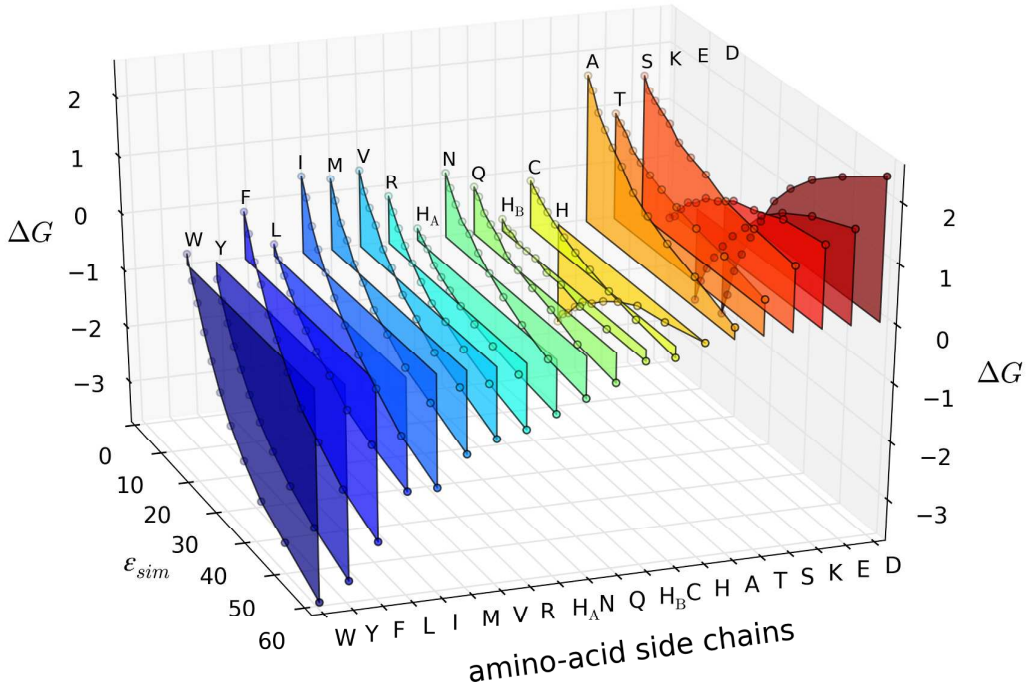

Figure S1. Absolute binding free energies of amino-acid side chains and CYT, as a function of the dielectric constant of the environment. Please, see Figure 5 in the main manuscript for a more detailed description.

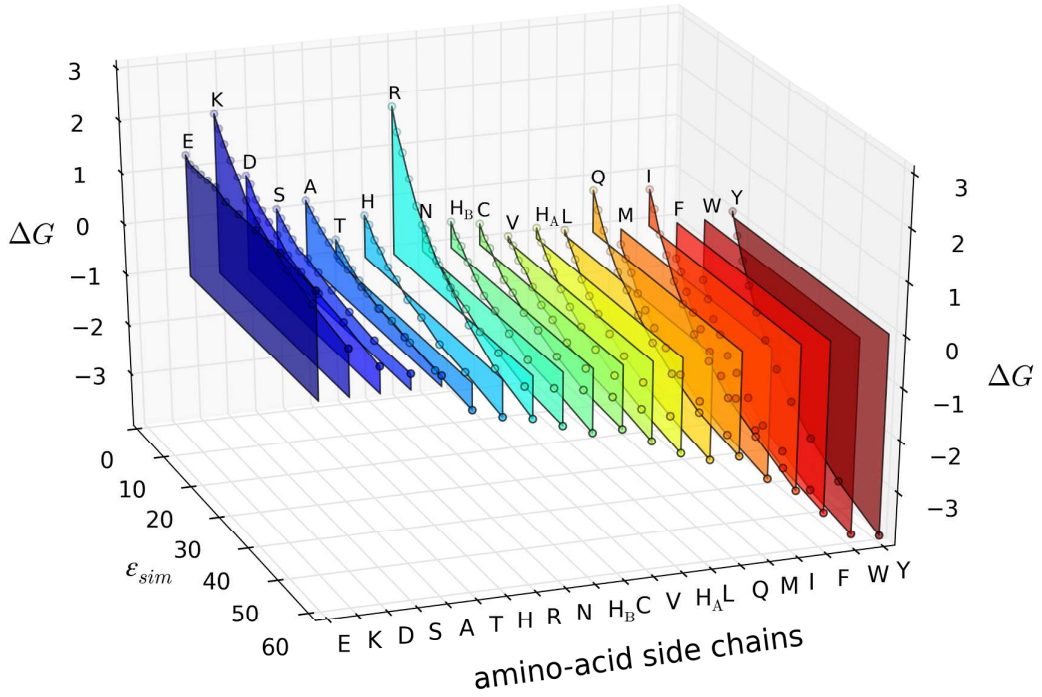

Figure S2. Absolute binding free energies of amino-acid side chains and ADE, as a function of the dielectric constant of the environment. Please, see Figure 5 in the main manuscript for a more detailed description.

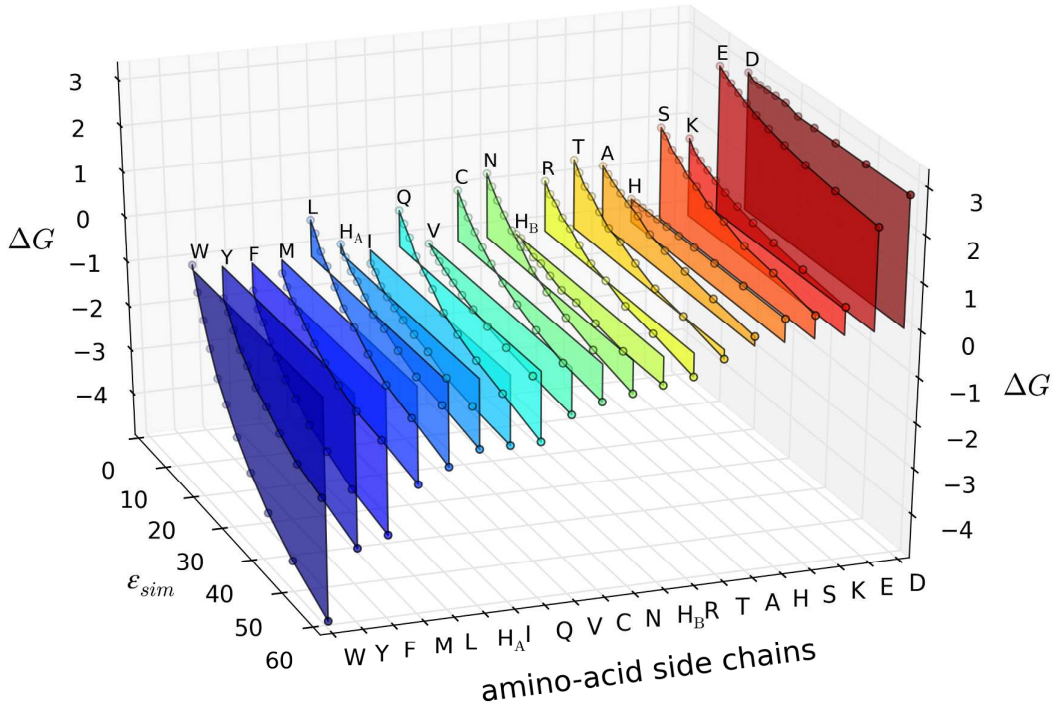

Figure S3. Absolute binding free energies of amino acid-side chains and URA, as a function of the dielectric constant of the environment. Please, see Figure 5 in the main manuscript for a more detailed description.

X_{met}	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0
ε_{sim}	61.0	49.9	42.1	36.5	32.2	28.8	26.1	23.8	21.8	20.1	18.6
ε_{exp}	77.6	71.1	65.2	59.8	54.8	50.2	46.1	42.2	38.7	35.5	32.5

Table S1. Simulated dielectric permittivity (ε_{sim}) and the experimental dielectric permittivity (ε_{exp}) as a function of the corresponding values of mole fraction of methanol (X_{met}).

GUA-Asp											
X_{met}	**0.0**	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1.0**
mindist (nm)	nb	nb	0.51	0.54	0.52	0.52	0.52	0.52	0.53	0.53	0.54
N1_H1 OD1	nb	nb	43.8 (6.4)	44.3 (3.7)	48.3 (3.4)	46.5 (3.6)	48.8 (4.8)	50.5 (4.3)	50.0 (2.2)	48.4 (4.4)	47.5 (1.1)
N1_H1 OD2	nb	nb	48.2 (6.2)	41.2 (5.2)	48.0 (1.3)	51.6 (1.8)	50.3 (1.9)	50.6 (3.2)	49.1 (3.3)	47.5 (3.1)	47.2 (1.5)
N2_H21 OD1	nb	nb	28.8 (5.5)	29.2 (3.4)	31.9 (2.4)	38.8 (0.5)	38.1 (2.0)	38.2 (3.4)	38.8 (3.5)	39.2 (4.0)	42.5 (2.2)
N2_H21 OD2	nb	nb	24.8 (6.8)	32.8 (4.1)	32.6 (3.8)	32.7 (4.2)	35.8 (3.1)	38.1 (4.5)	40.4 (3.0)	41.0 (4.0)	43.3 (0.7)
N2_H22 OD1	nb	nb	1.2 (0.6)	1.5 (0.6)	1.4 (0.2)	1.3 (1.5)	1.9 (1.8)	0.4 (0.3)	0.2 (0.3)	1.2 (1.0)	0.0 (0.1)
N2_H22 OD2	nb	nb	1.0 (0.5)	1.7 (0.4)	1.5 (1.8)	0.4 (0.4)	0.6 (0.3)	0.9 (0.9)	0.2 (0.3)	0.3 (0.3)	0.1 (0.1)
CYT-Asp											
X_{met}	**0.0**	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1.0**
mindist (nm)	nb	nb	nb	nb	nb	nb	nb	0.51	nb	0.51	0.51
N4_H41 OD1	nb	nb	nb	nb	nb	nb	nb	40.4 (4.2)	nb	43.1 (3.2)	45.5 (1.2)
N4_H41 OD2	nb	nb	nb	nb	nb	nb	nb	38.6 (2.3)	nb	41.8 (2.6)	45.0 (2.8)
N4_H42 OD1	nb	nb	nb	nb	nb	nb	nb	2.8 (1.5)	nb	1.0 (0.7)	1.2 (1.5)
N4_H42 OD2	nb	nb	nb	nb	nb	nb	nb	1.9 (0.9)	nb	0.6 (0.5)	1.1 (0.3)

Table S2. Analysis of H-bonding occupancies with Asp for all conformers in the neighborhood of a distance at which a given PMF attains its lowest value (mindist) for all systems with a negative ΔG for binding ("nb" refers to non-binders with $\Delta G \geq 0$ for which structural analysis was not performed). Please, see Methods section for detailed definitions. URA-Asp and ADE-Asp systems are not included as they do not exhibit negative ΔGs for binding at any values of X_{met}. All trajectories were divided into 4 equally sized parts and the reported values, given here in %, refer to the average occupancies and the standard deviations (in parentheses) over the 4 parts.

X_{met}	ADE		CYT		GUA		URA	
	mindist (nm)	% stacked	mindist (nm)	% stacked	mindist (nm)	% stacked	mindist (nm)	% stacked
0.0	0.54	17.9 (1.9)	0.40	94.2 (0.5)	0.40	98.5 (0.2)	0.39	97.7 (0.3)
0.1	0.54	15.8 (2.4)	0.39	94.6 (0.4)	0.40	98.4 (0.3)	0.36	99.7 (0.1)
0.2	0.57	9.3 (0.6)	0.39	93.0 (0.6)	0.50	29.0 (1.2)	0.40	96.1 (0.5)
0.3	0.57	8.3 (0.5)	0.46	41.7 (1.8)	0.51	27.8 (5.5)	0.39	96.3 (0.3)
0.4	0.58	7.2 (1.2)	0.47	37.9 (2.2)	0.57	11.1 (0.5)	0.39	96.3 (0.4)
0.5	0.58	9.0 (0.6)	0.50	18.8 (1.8)	0.57	9.9 (1.3)	0.40	95.8 (0.4)
0.6	0.61	5.4 (0.5)	0.50	17.7 (1.7)	0.54	13.8 (0.8)	0.39	96.4 (0.4)
0.7	0.61	5.1 (0.6)	0.50	19.0 (1.0)	0.57	9.1 (2.1)	0.40	nb
0.8	0.58	7.3 (0.3)	0.50	17.8 (1.8)	0.64	4.2 (0.7)	0.40	nb
0.9	0.61	5.5 (1.1)	0.50	nb	0.57	8.8 (2.0)	0.40	nb
1.0	0.61	4.8 (0.7)	0.50	nb	0.64	4.1 (1.1)	0.40	nb

Table S3. Analysis of stacking occupancies with Trp for all conformers in the neighborhood of a distance at which a given PMF attains its lowest value (mindist) for all systems with a negative ΔG for binding ("nb" refers to non-binders with $\Delta G \geq 0$ for which structural analysis was not performed). Please, see Methods section for further details. All trajectories were divided into 4 equally sized parts and the reported values, given here in %, refer to the average occupancies and the standard deviations (in parentheses) over the 4 parts.