Supporting Information

Unravelling Amino Acid–Graphene Interactions: Insights from Polarizable Force Field Simulations

*Sahil Soni, Ripan Halder, Mayank Luniwal, Sairam S. Mallajosyula**

Department of Chemistry, Indian Institute of Technology Gandhinagar, Gandhinagar, Gujarat, India – 382355

*msairam@iitgn.ac.in

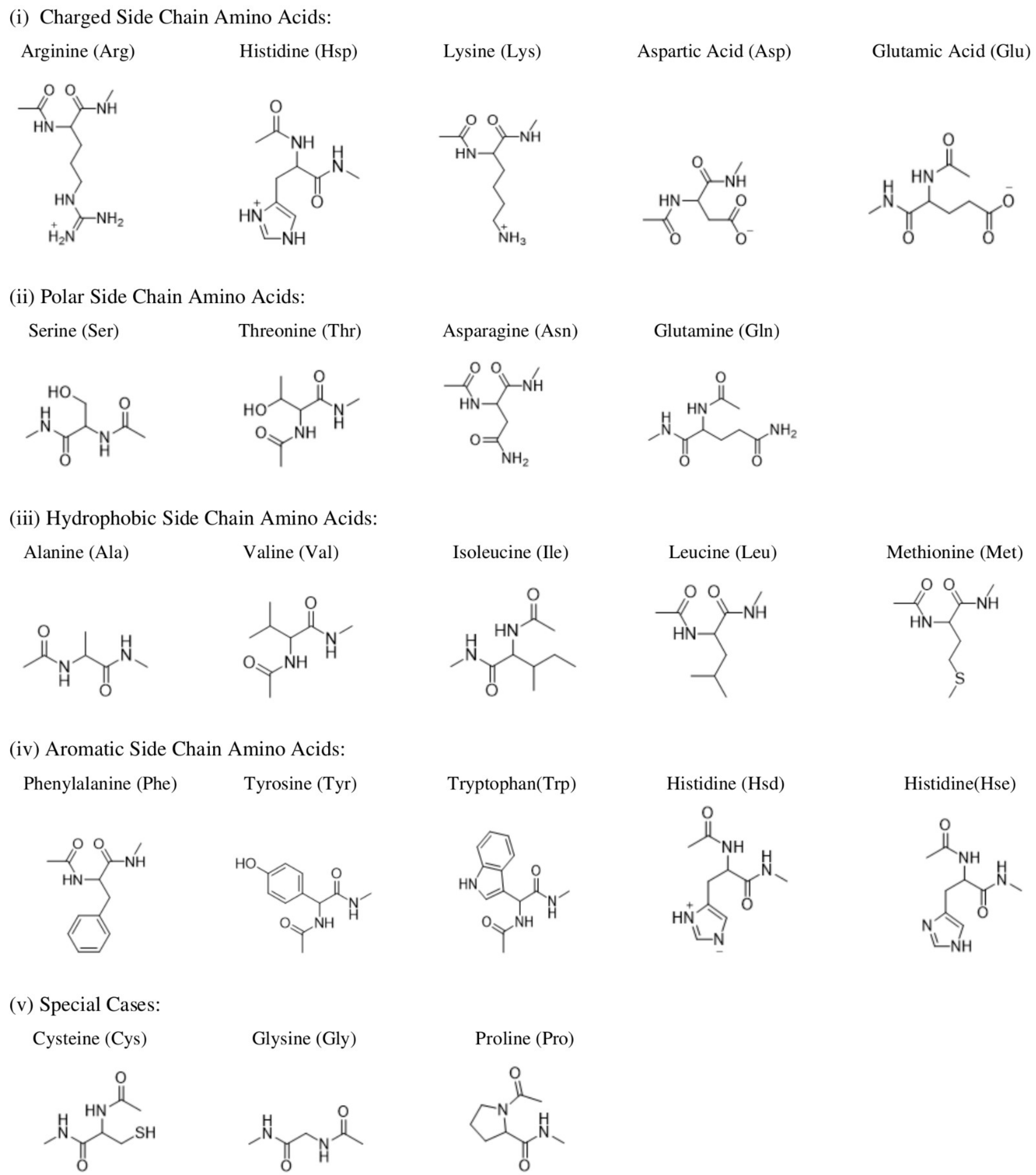


Figure S1: The chemical structures of all the amino acids considered in the study

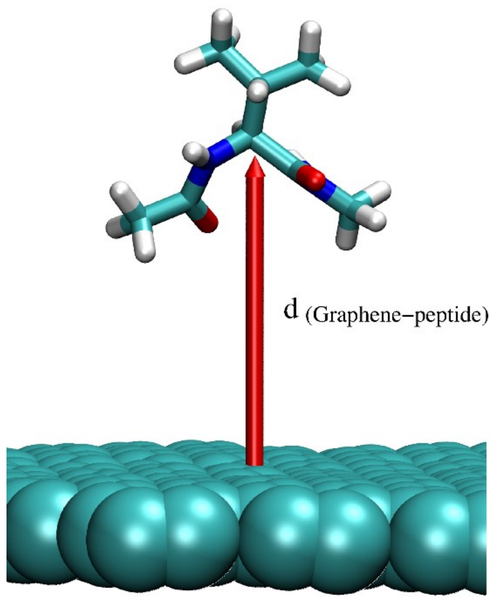


Figure S2: The z-axis projection between the center-of-mass of the peptide (valine) and center of mass of the top-most Graphene Sheet.

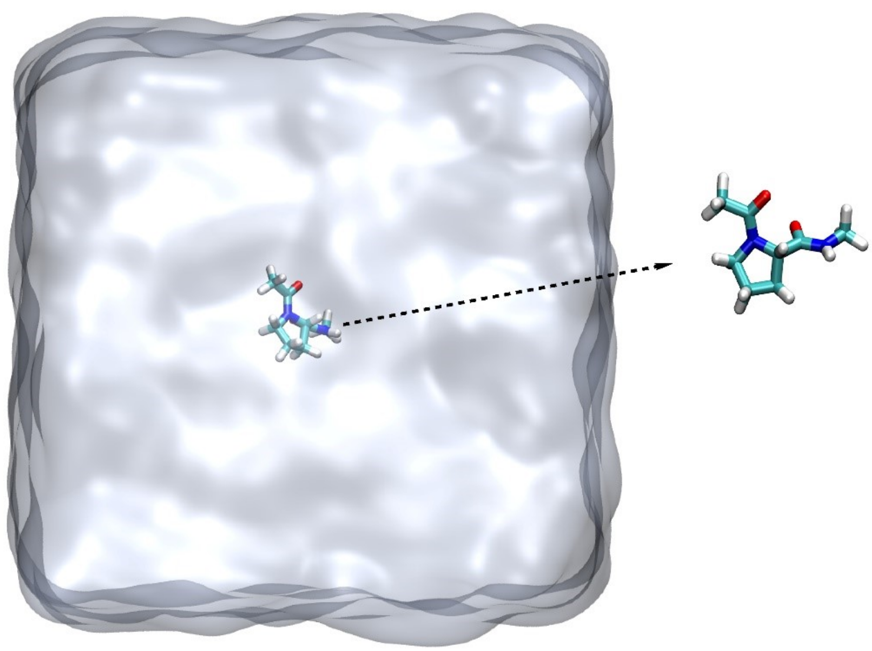
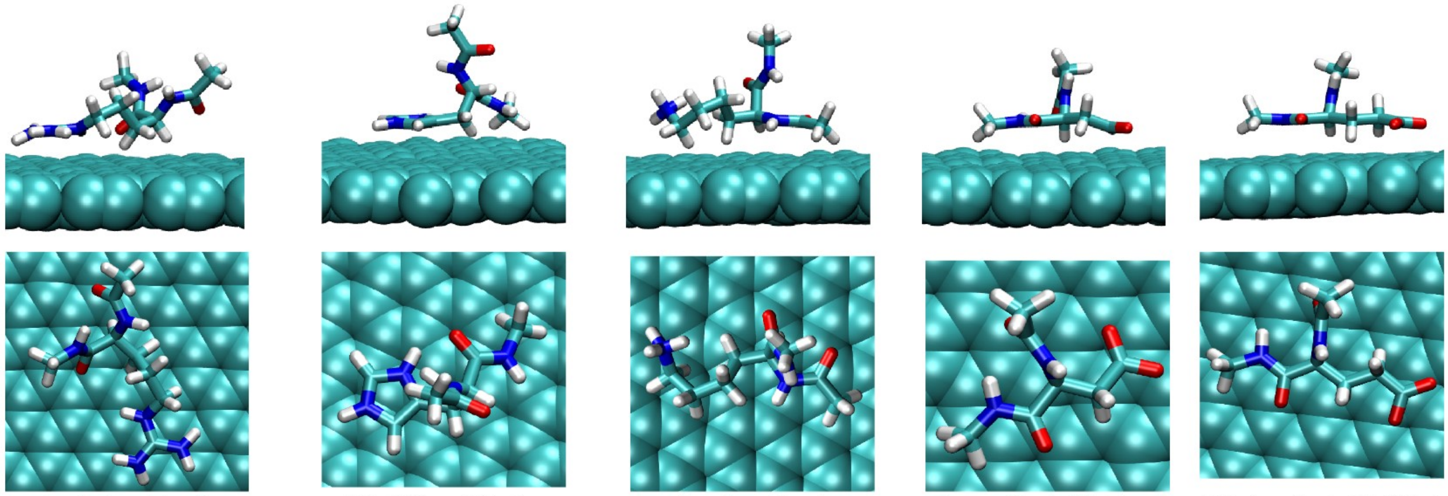


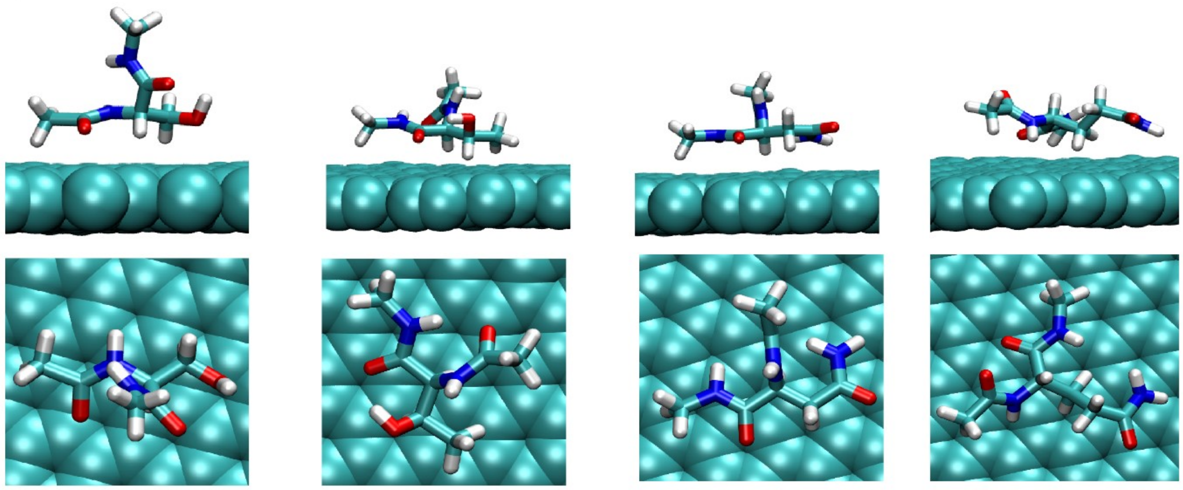
Figure S3: A representative image of the free-standing peptide (Proline) using Licorice representation in a TIP3P water box.

(i) Charged Side Chain Amino Acids:



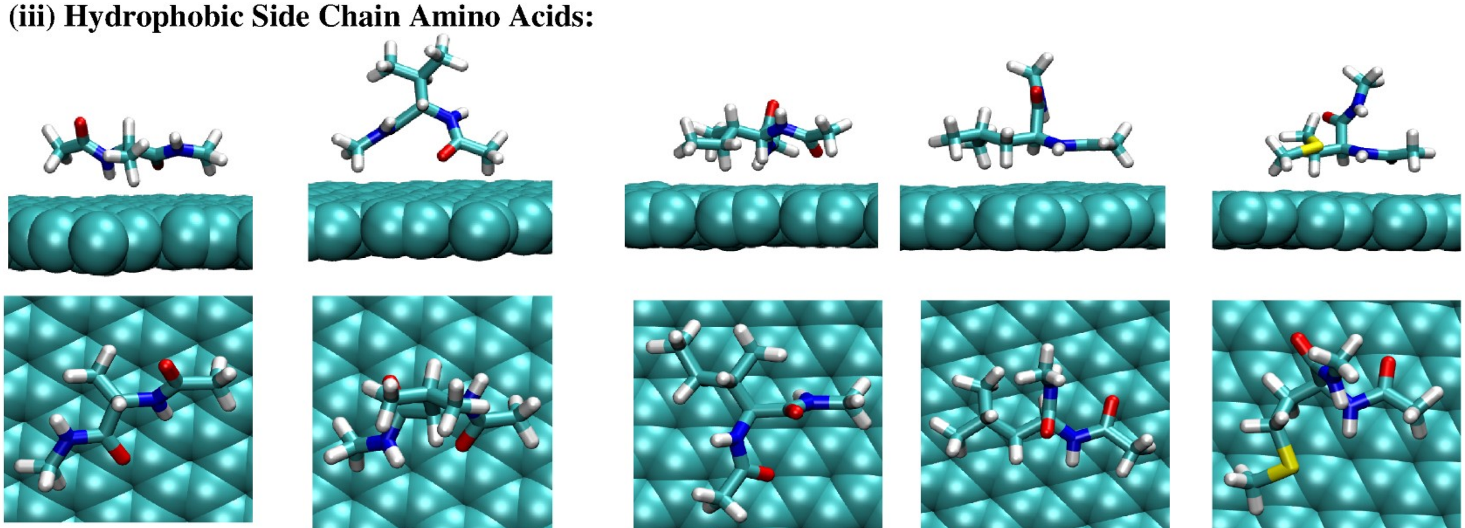
Arginine (Arg) Histidine (Hsp) Lysine (Lys) Aspartic Acid (Asp) Glutamic Acid (Glu)

(ii) Polar Side Chain Amino Acids:



Serine (Ser) Threonine (Thr) Asparagine (Asn) Glutamine (Gln)

(iii) Hydrophobic Side Chain Amino Acids:



Serine (Ser) Valine (Val) Isoleucine (Ile) Leucine (Leu) Methionine (Met)

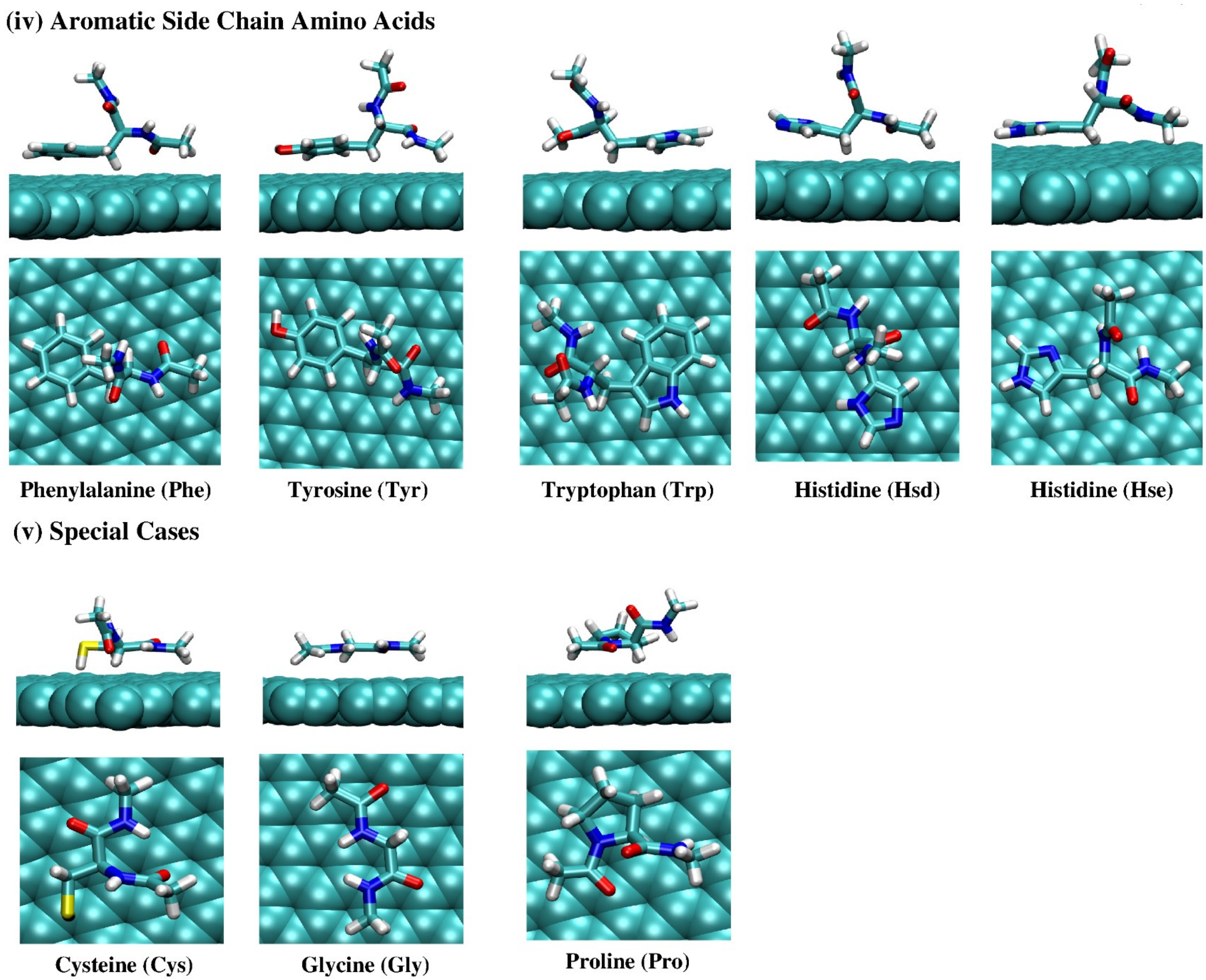


Figure S4: Representative structures showing the top and side views of dipeptides interacting with the graphene surface, corresponding to the minima in the PMF profiles from the polarizable simulations.

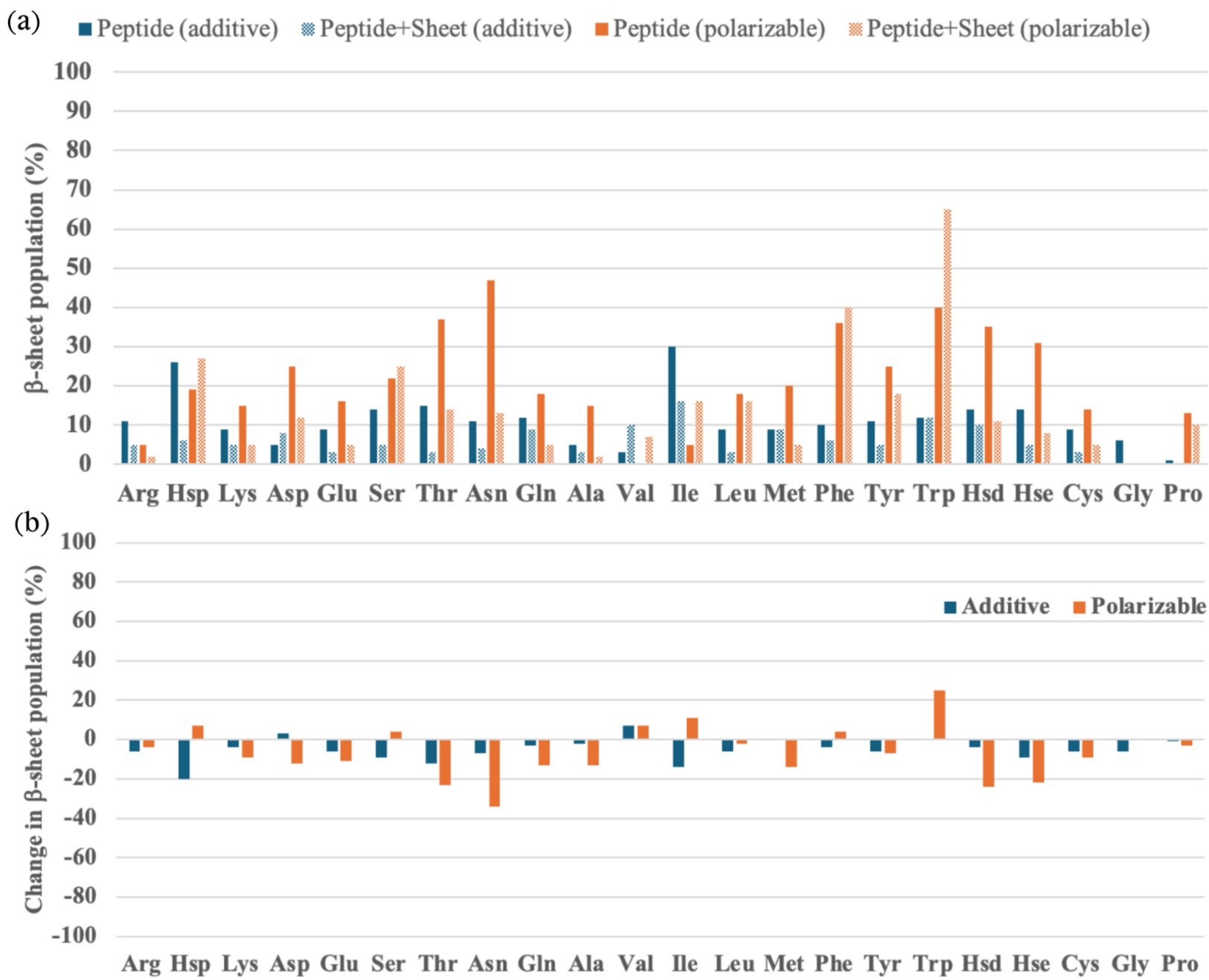


Figure S5: (a) Percentage population corresponding to the β-sheet ($-150° < \varphi < -90°$ and $80° < \psi < 160°$) region in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations. Percentage populations are evaluated for both the free peptide as well as the peptide adsorbed on graphene surface. (b) Change in the β-sheet populations upon adsorption of the peptide onto the graphene surface, calculated as the difference between the β-sheet populations observed in the peptide-graphene system and the free peptide only system for both additive and polarizable simulations.

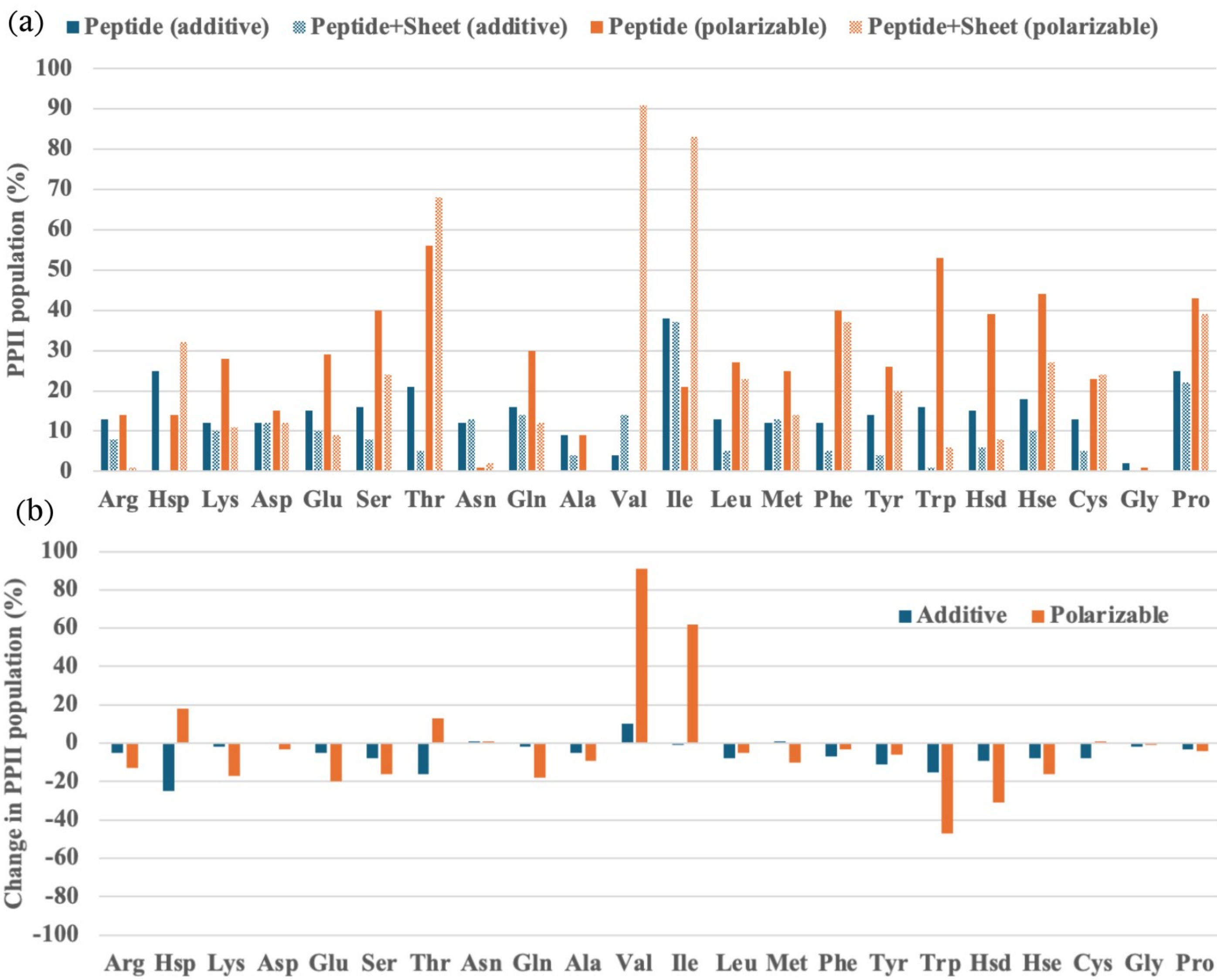


Figure S6: (a) Percentage population corresponding to the PPII ($-90° < \varphi < -25°$ and $80° < \psi < 160°$) region in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations. Percentage populations are evaluated for both the free peptide as well as the peptide adsorbed on graphene surface. (b) Change in the PPII populations upon adsorption of the peptide onto the graphene surface, calculated as the difference between the PPII populations observed in the peptide-graphene system and the free peptide only system for both additive and polarizable simulations.

Table S1: Minimum free energy of the di-peptides relative to the minimum free energy of the Gly di-peptide obtained from polarizable and additive simulations. The relative free energies using other force fields previously reported in literature are also presented for comparison.[1–3]

Di-peptide	Polarizable CHARMM/ SWM4	Additive CHARMM36m/ TIP3P	CHARMM36/ mTIP3P[2]	Amberff99SB-ILDN/ TIP3P [2]	OPLS-AA/ mTIP3P[2]	Amber03w/ TIP4P-2005[2]	GROMOS 54A8/ SPC[3]	GRAPPA/ CHARMM22*/ mTIP3P[1]
Arg	-12.6±5.7	-3.5±1.5	-3.24	-4.23	-2.69	-2.65	-2.51	-1.07
Glu	-10.4±4.8	2.3±0.6	0.65	1.59	1.54	2.31	-2.20	1.84
Asp	-10.3±4.0	2.7±0.7	1.22	1.69	1.96	2.71	-1.89	2.46
Trp	-2.5±0.5	-3.4±1.3	-5.24	-4.34	-4.34	-5.24	-4.35	-0.64
Tyr	-1.8±0.6	-2.2±0.7	-3.87	-4.06	-2.54	-2.18	-4.66	-0.50
His	-0.0±6.1	0.5±0.1	-0.94	-0.90	-0.29	-1.30	-2.44	1.27
Lys	0.00±1.5	1.6±0.3	-0.56	0.36	0.24	0.58	-0.81	2.82
Gly	0.00±0.0	0.0±0.0	0.00	0.00	0.00	0.00	0.00	0.00
Phe	0.1±0.2	-0.8±0.2	-3.24	-1.66	-0.89	-2.06	-2.48	0.91
Leu	0.3±0.8	1.4±0.3	-0.58	1.15	1.21	0.81	-1.74	2.75
Met	0.4±0.8	0.4±0.1	-1.76	-0.02	0.06	-0.94	-2.72	0.53
Ile	0.5±1.2	2.3±0.7	-0.20	1.35	1.97	0.72	-1.51	3.80
Cys	0.7±0.7	1.2±0.1	-0.64	1.15	1.06	1.65	-1.27	1.89
Gln	0.8±0.6	1.6±0.2	-0.64	0.00	0.00	0.15	-2.01	-0.74
Ala	0.8±0.5	2.3±0.4	0.27	1.37	1.33	2.29	-0.38	1.99
Asn	0.9±0.4	1.1±0.1	-0.94	0.80	0.78	0.62	-1.41	0.82
Thr	1.0±1.2	1.6±0.4	-0.40	1.97	1.87	2.11	-1.19	1.96
Pro	1.2±0.6	0.8±0.3	-0.89	0.80	0.58	1.82	0.48	2.75
Val	1.3±1.4	2.3±0.7	0.37	1.52	2.33	0.81	-1.10	2.65
Ser	1.5±0.9	2.1±0.4	-0.08	1.06	1.07	1.71	-0.77	1.29

Table S2: Percentage population corresponding to the α_R-helix ($-150° < \varphi < -25°$ and $-150° < \psi < 0°$) region in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations.

	Peptide (additive)	**Peptide+Sheet (additive)**	**Peptide (polarizable)**	**Peptide+Sheet (polarizable)**
Arg	51±8	45±57	62±26	32±40
Hsp	14±8	10±14	29±15	7±2
Lys	59±12	65±15	33±26	8±0
Asp	56±0	51±24	42±2	0±0
Glu	61±7	73±4	55±2	8±7
Ser	47±9	47±24	28±6	11±7
Thr	48±8	87±12	0±0	8±11
Asn	62±4	75±5	13±18	5±2
Gln	40±2	54±6	41±15	42±5
Ala	60±0	53±19	14±18	0±0
Val	82±11	63±28	100±0	0±0
Ile	17±19	34±18	63±20	0±0
Leu	60±9	78±3	36±25	0±0
Met	58±12	54±22	34±8	44±10
Phe	65±0	84±6	14±6	7±9
Tyr	61±16	87±1	30±7	34±2
Trp	64±3	68±1	0±0	3±4
Hsd	48±0	32±38	6±7	35±24
Hse	42±2	70±8	14±14	27±37
Cys	66±3	78±4	32±14	16±12
Gly	7±0	1±0	25±4	7±1
Pro	11±0	60±5	14±3	12±1

Table S3: Percentage population corresponding to the β-sheet ($-150° < \varphi < -90°$ and $80° < \psi < 160°$) region in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations.

	Peptide (additive)	Peptide+Sheet (additive)	Peptide (polarizable)	Peptide+Sheet (polarizable)
Arg	11±1	5±6	5±6	2±1
Hsp	26±1	6±2	19±1	27±2
Lys	9±3	5±3	15±8	5±4
Asp	5±1	8±5	25±4	12±6
Glu	9±2	3±0	16±0	5±1
Ser	14±6	5±1	22±2	25±1
Thr	15±3	3±3	37±1	14±6
Asn	11±1	4±1	47±6	13±10
Gln	12±3	9±2	18±2	5±2
Ala	5±0	3±0	15±3	2±0
Val	3±3	10±8	0±0	7±2
Ile	30±7	16±7	5±3	16±4
Leu	9±2	3±1	18±4	16±10
Met	9±3	9±4	20±2	5±8
Phe	10±0	6±3	36±3	40±5
Tyr	11±2	5±1	25±4	18±2
Trp	12±3	12±1	40±1	65±0
Hsd	14±1	10±4	35±8	11±3
Hse	14±0	5±4	31±15	8±1
Cys	9±2	3±1	14±4	5±4
Gly	6±0	0±0	0±0	0±0
Pro	1±0	0±0	13±0	10±2

Table S4: Percentage population corresponding to the PPII ($-90° < \varphi < -25°$ and $80° < \psi < 160°$) region in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations.

	Peptide (additive)	Peptide+Sheet (additive)	Peptide (polarizable)	Peptide+Sheet (polarizable)
Arg	13±2	8±9	14±18	1±1
Hsp	25±2	0±0	14±4	32±6
Lys	12±2	10±5	28±13	11±6
Asp	12±3	12±3	15±4	12±2
Glu	15±4	10±2	29±1	9±2
Ser	16±3	8±5	40±2	24±8
Thr	21±4	5±4	56±2	68±7
Asn	12±4	13±1	1±2	2±1
Gln	16±2	14±0	30±2	12±14
Ala	9±1	4±1	9±4	0±0
Val	4±4	14±12	0±0	91±2
Ile	38±8	37±4	21±14	83±4
Leu	13±4	5±2	27±8	23±29
Met	12±2	13±7	25±9	14±20
Phe	12±0	5±1	40±1	37±14
Tyr	14±1	4±0	26±0	20±5
Trp	16±1	1±0	53±2	6±3
Hsd	15±1	6±7	39±8	8±2
Hse	18±0	10±4	44±6	27±6
Cys	13±2	5±1	23±9	24±17
Gly	2±0	0±0	1±0	0±0
Pro	25±2	22±1	43±2	39±2

Table S5: Percentage population corresponding to the random coil structures that fall outside the defined regions in the Ramachandran ϕ/ψ surfaces corresponding to each di-peptide system from both additive and polarizable simulations.

	Peptide (additive)	**Peptide+Sheet (additive)**	**Peptide (polarizable)**	**Peptide+Sheet (polarizable)**
Arg	24±5	42±42	19±3	65±38
Hsp	35±5	84±12	43±11	33±2
Lys	21±7	20±7	24±6	75±10
Asp	24±5	28±16	18±2	75±4
Glu	16±1	13±2	0±1	79±5
Ser	24±0	40±28	11±2	40±2
Thr	15±1	6±5	7±2	10±2
Asn	16±6	8±6	39±10	81±9
Gln	31±3	24±8	12±11	41±20
Ala	25±0	40±20	62±12	98±0
Val	11±4	13±8	0±0	2±0
Ile	15±4	13±15	11±2	1±0
Leu	18±3	13±0	19±14	61±39
Met	20±7	24±12	21±2	37±18
Phe	14±0	5±2	10±2	17±0
Tyr	13±13	5±1	19±2	28±6
Trp	3±0	20±0	7±1	25±2
Hsd	22±1	52±50	21±9	45±24
Hse	26±2	15±0	11±6	38±31
Cys	12±1	14±4	31±2	54±33
Gly	84±1	99±1	74±4	93±1
Pro	64±2	61±5	30±0	39±1

References:

1. Z. E. Hughes and T. R. Walsh, *J Mater Chem B*, 2015, **3**, 3211–3221.
2. S. Dasetty, J. K. Barrows and S. Sarupria, *Soft Matter*, 2019, **15**, 2359–2372.
3. M. Barria-Urenda, A. Ruiz-Fernandez, C. Gonzalez, C. Oostenbrink and J. A. Garate, *J Chem Inf Model*, 2023, **63**, 6642–6654.