SUPPLEMENTARY INFORMATION

Microtubule-Inspired Functionalization of Carbon Nanotubes: A Biomimetic Carrier Design

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Figure S1

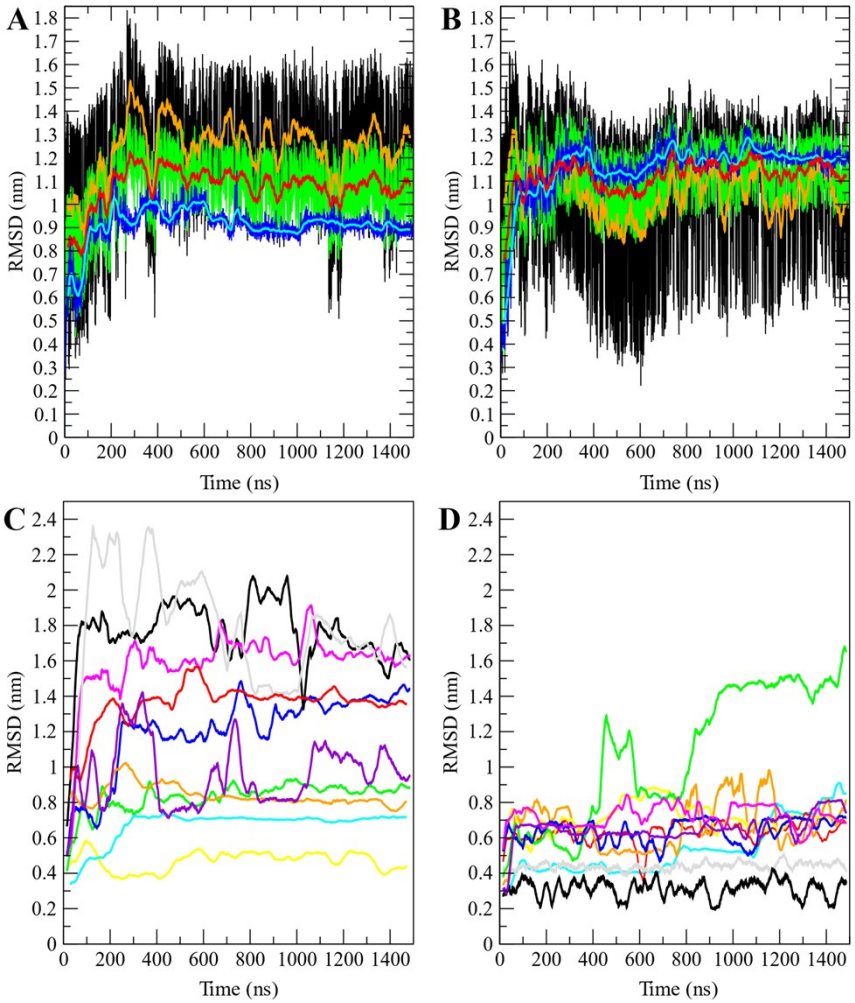

Figure S1: The root mean square deviation (RMSD) of the carbon nanotube (CNT) (black, orange average), peptides (blue, cyan average), and peptides–CNT complex (green, red average) of the (**A**) C1 system (the P1–P5), (**B**) C2 (the P6–P10) system, (**C**) each peptide on the CNT: P1 (cyan), P2 (red), P3 (gray), P4 (orange), P5 (yellow), P6

(green), P7 (blue), P8 (black), P9 (magenta), and P10 (violet); and (**D**) the CNT-free peptides (the P1'–P10') with exact coloring as in (C). Average lines were generated by averaging every 300 frames.

Figure S2

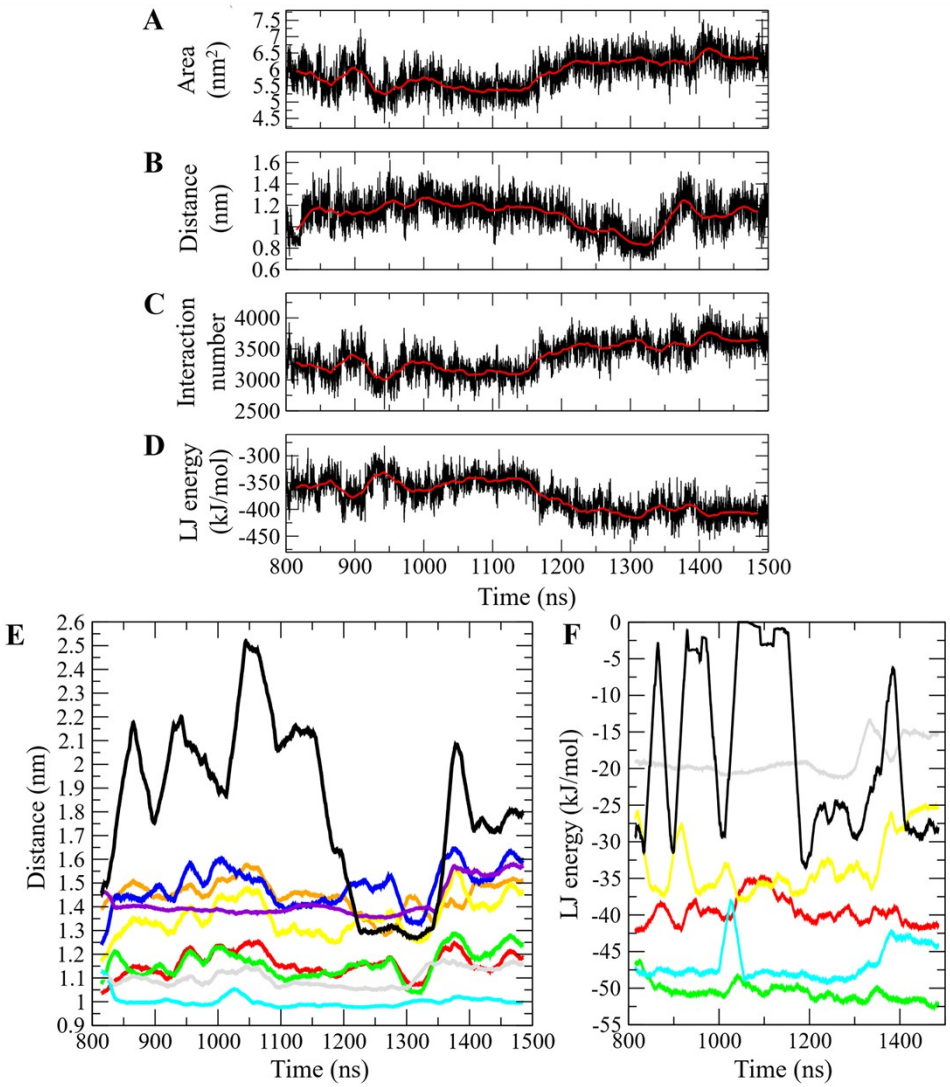

Figure S2: The time evolution of properties between the CNT and the P9 (β-M-loop): (**A**) solvent-accessible surface (SAS) area, (**B**) distance of center-of-mass (DCOM), (**C**) interaction frequency (< 6 Å), and (**D**) Lennard-Jones (LJ) energy. (**E**) The average DCOM between the CNT and the P9 residues: Tyr283 (red), Arg278 (green), Gly279(blue), Gln282(yellow), Arg284 (cyan), Ala285 (gray), Leu286 (violet), Thr287 (orange), and Glu290 (black). (**F**) The average LJ energy of the CNT with the P9 residues: Arg278 (green), Arg284 (cyan), Tyr283 (red), Ala285 (gray), Gln282 (yellow), and Glu290 (black). Graphs were generated with averaging every 300 frames of the 1.5 μs MD trajectory.

Figure S3

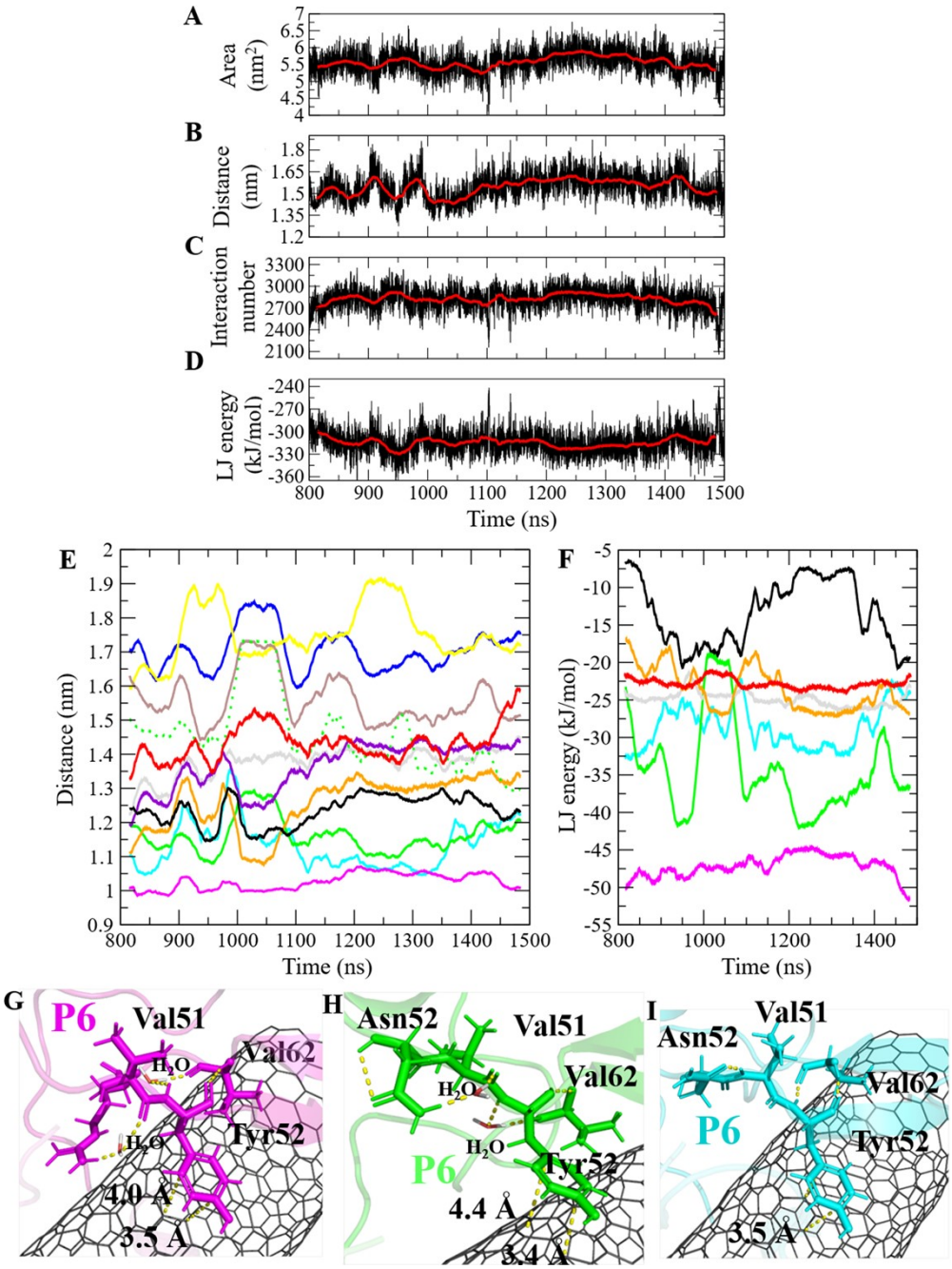

Figure S3: The time evolution of properties between the CNT and the P6: (**A**) SAS area, (**B**) DCOM, (**C**) interaction frequency (< 6 Å), and (**D**) LJ energy. (**E**) The average DCOM between the CNT and the P6 residues: Ile24 (cyan), Pro63 (violet), Arg64 (magenta), Tyr53 (blue), Asn54 (red), Tyr52 (green), Ser25 (black), Tyr61 (yellow), Val51 (brown), Val62 (gray), Ala65 (orange), and Asn50 (dotted green). (**F**) The average LJ energy of the CNT with the P6 residues: Arg64 (magenta), Tyr52 (green), Ile24 (cyan), Val62 (gray), Asn54 (red), and Ser25 (black). Graphs were generated with averaging

every 300 frames. Mediating-water molecules favored a tilt Tyr52 ring at (**G**) 3.5–4.4 Å and (**H**) 4.4 Å to the CNT. (**I**) Intramolecular H-bond network bringing a parallel Tyr52 ring at 3.5 Å to the CNT.

Figure S4

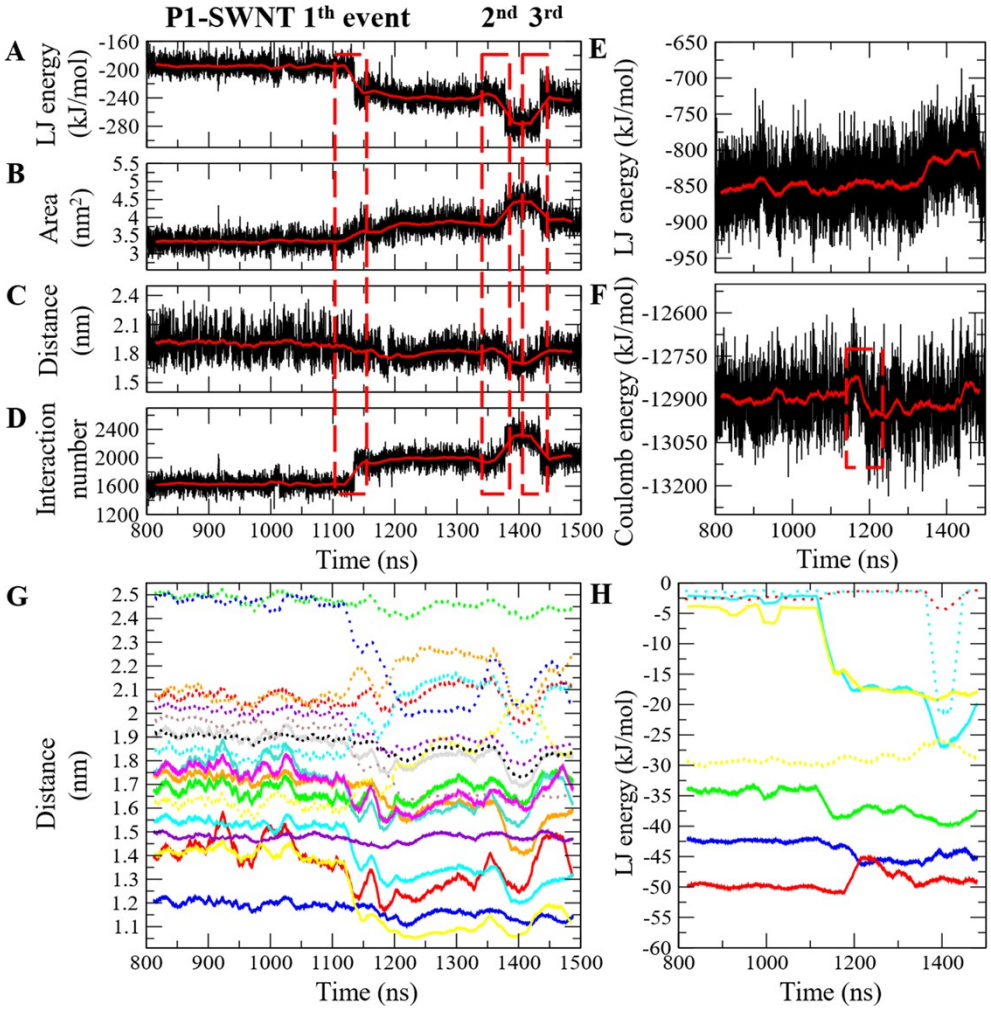

Figure S4: The properties between the CNT and the P1: (**A**) LJ energy, (**B**) SAS area, (**C**) DCOM, and (**D**) interaction number (<6 Å). The P1 intramolecular (**E**) LJ and (**F**) coulomb energy. (**G**) The average DCOM between the CNT and: the P1 (gray), Phe52 (green), Asp46 (turquoise), Asn50 (magenta), Cys25 (orange), Glu27 (violet), Phe49 (red), His28 (cyan), Tyr24 (blue), and Gly44 (yellow), Pro63 (dotted yellow), Leu26 (dotted black), Ile30 (dotted violet), Ile42 (dotted brown), Val62 (dotted cyan), Phe53 (dotted red), Pro32 (dotted green), Pro37 (dotted blue), and His61 (dotted orange). (**H**) The average LJ energy between the CNT and: Tyr24 (blue), Phe49 (red), His28 (cyan), Phe52 (green), Gly44 (yellow), Pro63 (dotted yellow), and Val62 (dotted cyan). Graphs were generated with averaging every 300 frames. (**K**) Tyr24 (P1) from parallel to (**L**) tilt at ~30° to the CNT length axis due to a water molecule bridging its hydroxyl to Glu28.

Figure S5

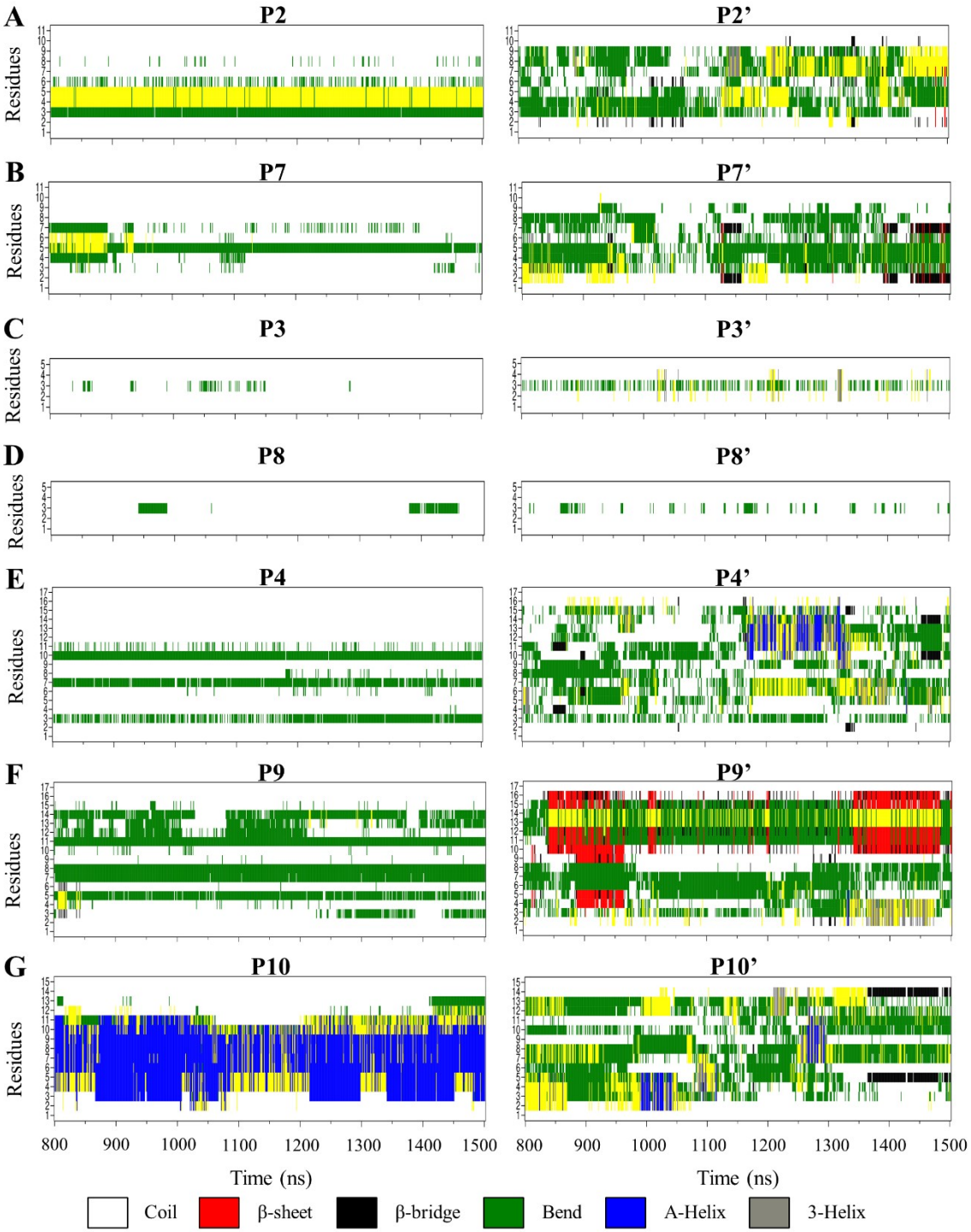

Figure S5: The secondary structure analysis based on the dictionary secondary structure of protein (DSSP) algorithm of (**A**) the P2 and P2' (residue numbering of 1–11 refers to Arg79–Pro89 in 1JFF.pdb [1]), (**B**) the P7 and P7' (1–11 refers to Gly81–Asn91 [1]), (**C**) the

P3 and P3' (1–5 refers to Leu157–Tyr161 [1]), (**D**) the P8 and P8' (1–5 refers to Glu159–Asp163 [1]), (**E**) the P4 and P4' (1–17 refers to Tyr272–Val288 [1]), (**F**) the P9 and P9' (1–17 refers to Pro274–Glu290 [1]), and (**G**) the P10 and P10' (1–15 refers to Asp329–Phe343 [1]).

Figure S6

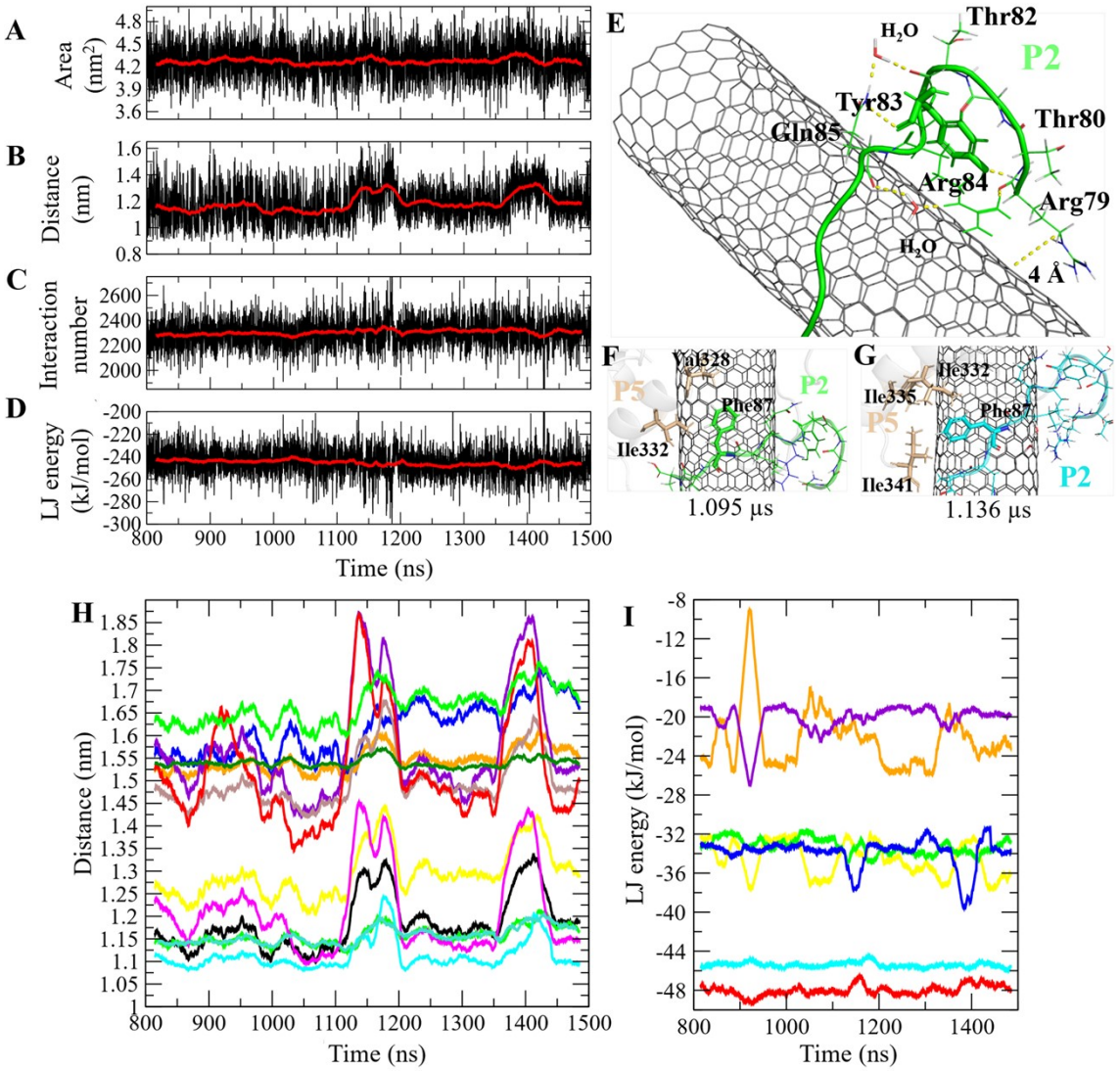

Figure S6: The time evolution of properties between the CNT and the P2 (α-H2-B3): (**A**) SAS area, (**B**) DCOM, (**C**) interaction frequency (< 6 Å), and (**D**) LJ energy. (**E**) Tyr83 (stick) of the P2 caused steric hindrance and induced bend conformation. (**F**–**G**) Phe57 non-parallel orientations on the CNT. (**H**) The average DCOM between the CNT and: the P2 (black), Arg79 (blue), Thr80 (green), Gly81 (orange), Thr82 (dark green), Tyr83 (turquoise), Arg84 (yellow), Gln85 (cyan), Leu86 (brown), Phe87 (magenta), His88 (violet), Pro89 (red). (**I**) The average LJ energy between the CNT and: Arg79 (red), Tyr83 (green), Arg84 (cyan), Gln85 (blue), and Phe87 (yellow), His88 (orange), and Pro89

(violet). Graphs were generated with averaging every 300 frames of the 1.5 μs MD trajectory.

Figure S7

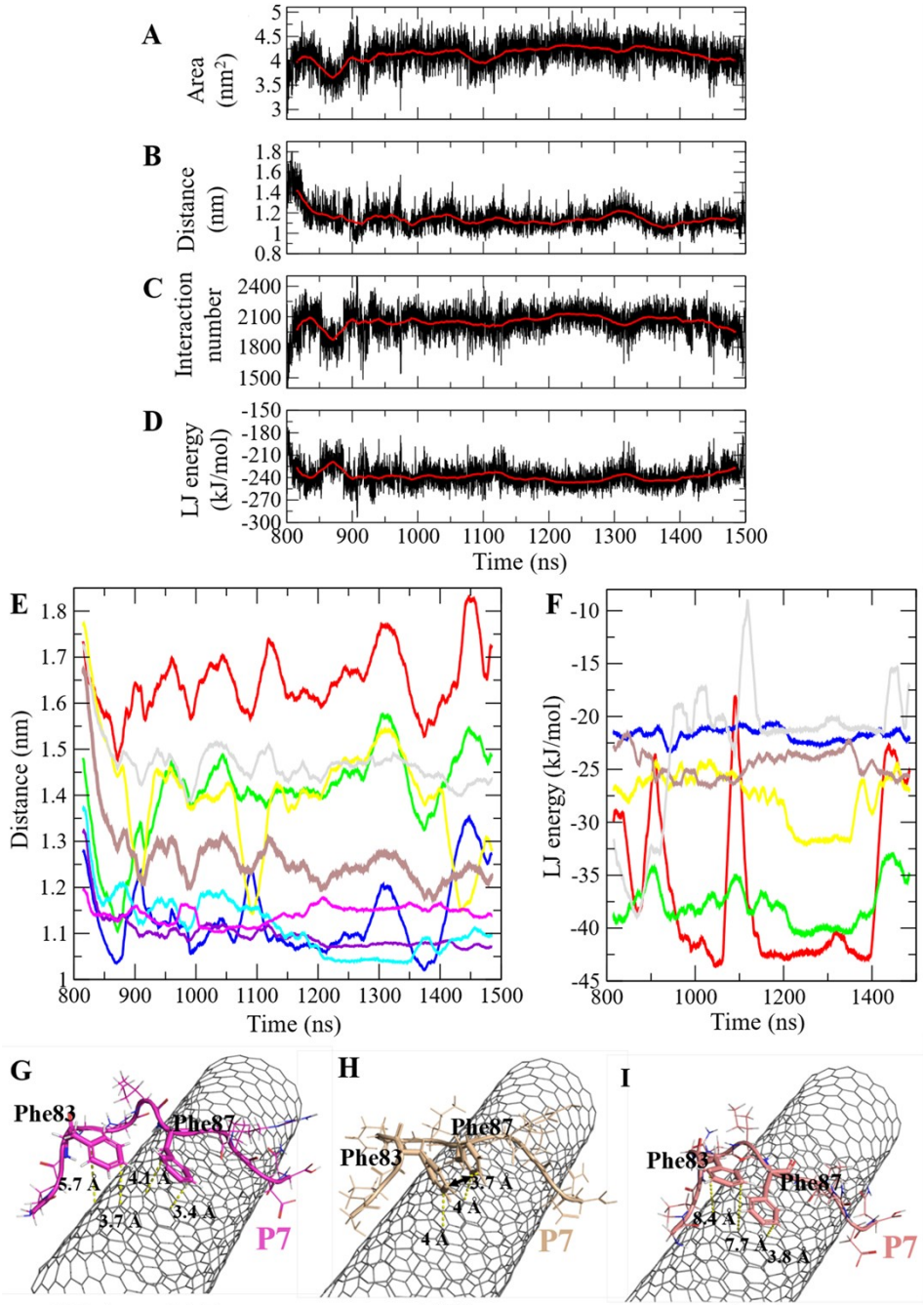

Figure S7: The time evolution of properties between the CNT and the P7 (β-H2-B3): (**A**) SAS area, (**B**) DCOM, (**C**) interaction frequency (< 6 Å), and (**D**) LJ energy. (**E**) The

average DCOM between the CNT and the P7 residues: Phe83 (red), Gly84 (green), Gln85 (blue), Ile86 (yellow), Phe87 (brown), Arg88 (gray), Pro89 (violet), Asp90 (cyan), Asn91 (magenta). (**F**) The average LJ energy of the CNT with the P7 residues: Gln85 (red), Phe87 (green), Asp90 (yellow), Asn91 (brown), Phe83 (gray), and Pro89 (blue). Graphs were generated with averaging every 300 frames of the 1.5 μs MD trajectory. (**G–I**) Phe83 and Phe87 (stick) of the P7 changes of orientation and distances to the CNT.

Figure S8

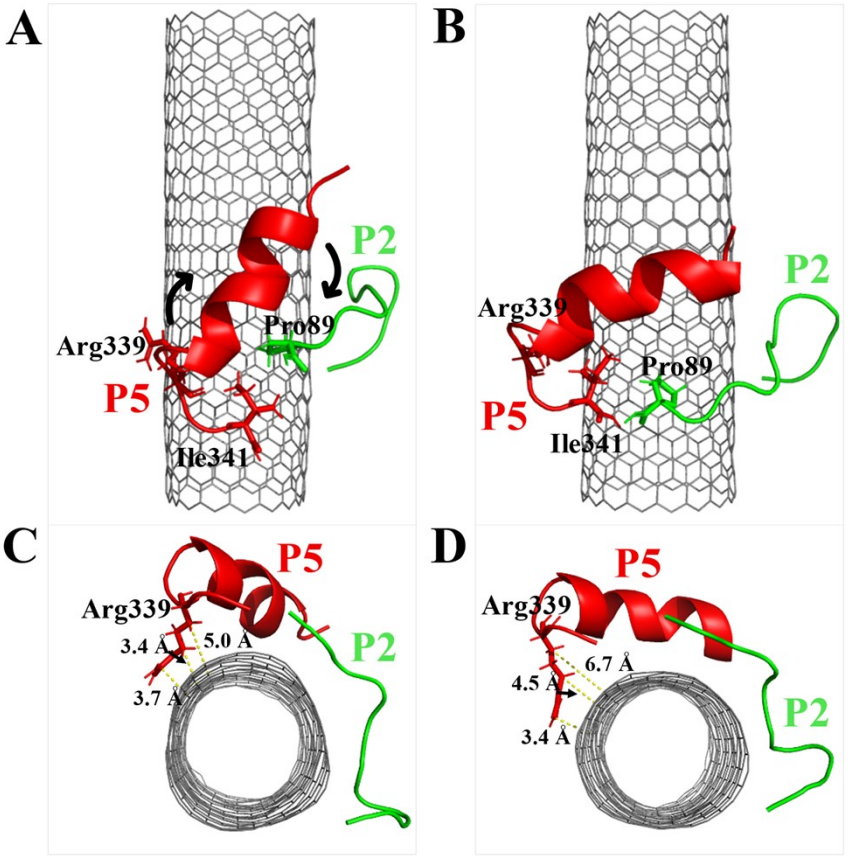

Figure S8: The binding profile of the P5 (red) moving from (**A**) diagonally positioned to (**B**) almost perpendicular to the CNT length axis while Pro89 f the P2 (green) approached Ile341 of the P5. The distance increase from the CNT of Arg339 (P5) from (**C**) ladder-shaped to (**D**) almost perpendicular to the CNT, weakening the P5 binding to the CNT.

Figure S9

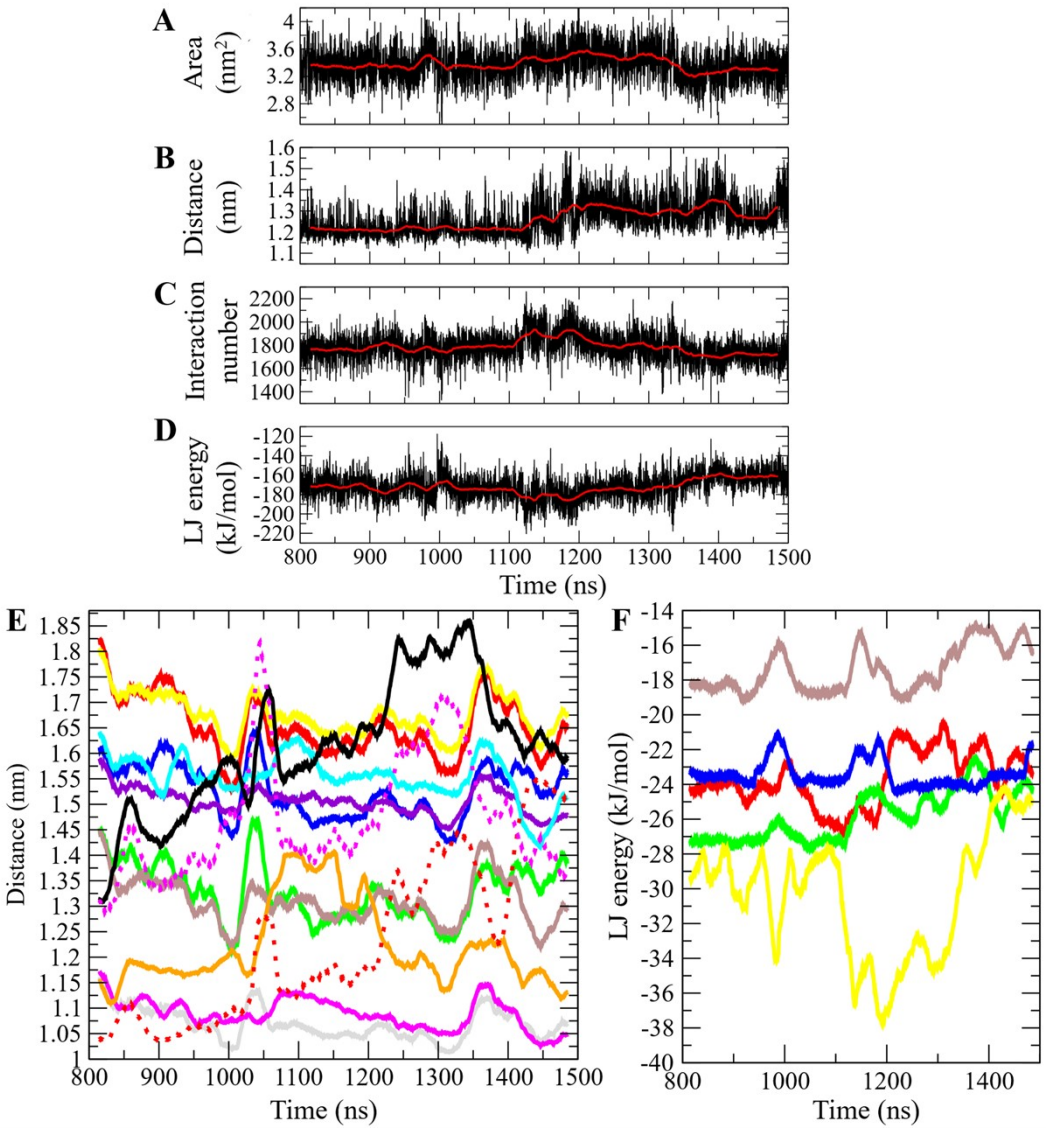

Figure S9: The time evolution of properties between the CNT and the P5 (α-H10): (**A**) SAS area, (**B**) DCOM, (**C**) interaction frequency (< 6 Å), and (**D**) LJ energy. (**E**) The average DCOM between the CNT and the P5 amino acids: Ile332 (cyan), Ile335 (violet), Val328 (magenta), Arg339 (blue), Ala330 (red), Ala331 (green), Thr334 (black), Asn329 (yellow), and Asp327 (brown). (**F**) The average LJ energy regarding the CNT with the P5 residues: Val328 (red), Ala331 (brown), Ile332 (green), Ile335 (blue), and Arg339

(yellow). Graphs were generated with averaging every 300 frames of the 1.5 μs MD trajectory.

Figure S10

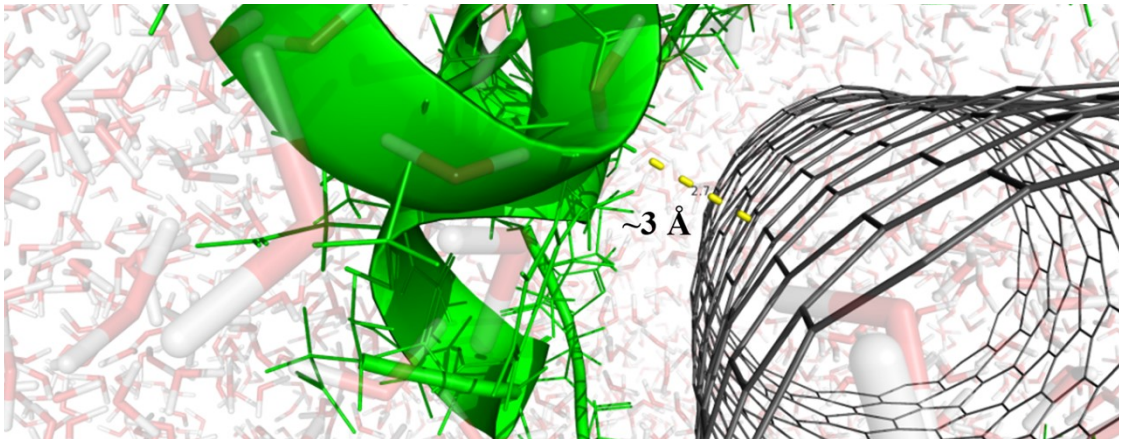

Figure S10: A dehydration gap of 3 Å between the exterior CNT shell and the peptides.

Figure S11

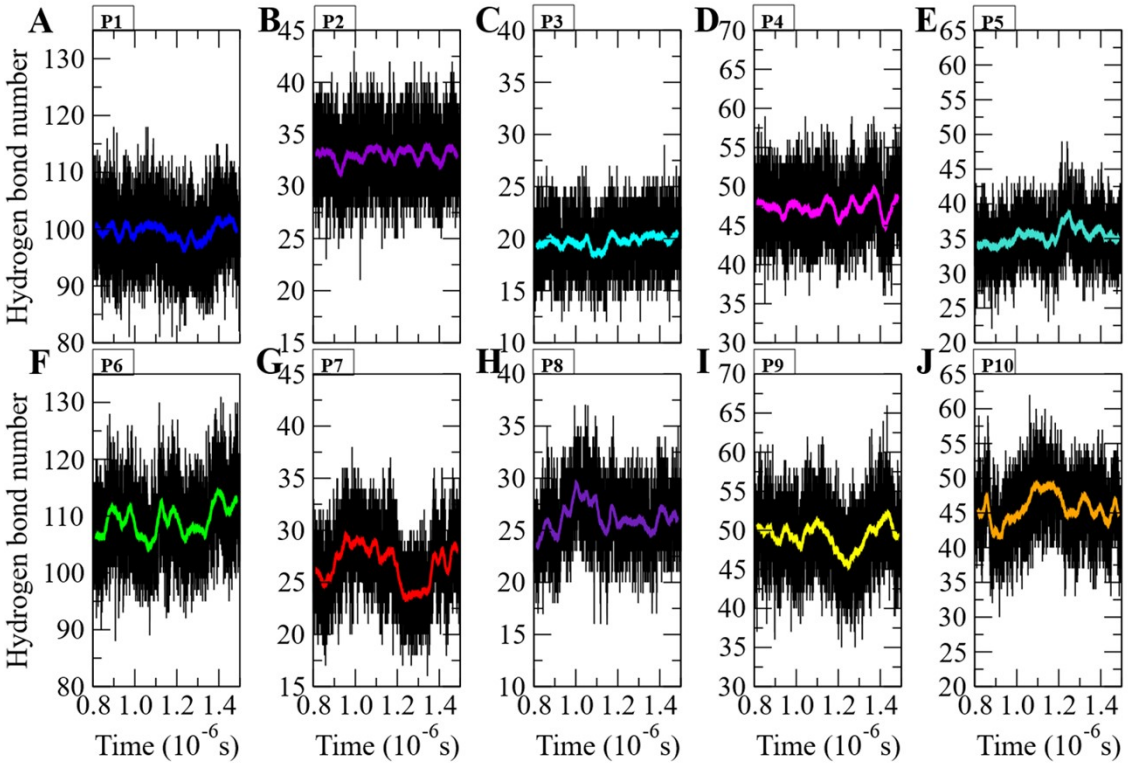

Figure S11: The time evolution of the intermolecular hydrogen bond number between water molecules and the peptides on the CNT (**A**) P1, (**B**) P2, (**C**) P3, (**D**) P4, (**E**) P5, (**F**) P6, (**G**) P7, (**H**) P8, (**I**) P9, and (**J**) P10.

Table S1

Free peptide	Segment in MT	Functional association in MT	Residue range (1JFF.pdb[1])	Sequence and amino acid (AA) number
P1'	α-H1-B2	Inter-subunits Lateral	Tyr24–Pro63	Y_{24}CLEHGIQPDGQMPSDKTIGGGDD SFNTFFSETGAGKHVP$_{63}$ (40 AA)
P2'	α-H2-B3	Inter-subunits Lateral	Arg79–Pro89	R_{79}TGTYRQLFHP$_{89}$ (11 AA)
P3'	α-H4-T5	Inter-subunits Lateral	Leu157–Tyr161	L_{157}SVDY$_{161}$ (5 AA)
P4'	α-M-loop	Inter-subunits Lateral	Tyr272–Val288	Y_{272}APVISAEKAYHEQLSV$_{288}$ (17 AA)
P5'	α-H10	Inter-subunits Lateral and Longitudinal	Asp327–Ile341	D_{327}VNAAIATIKTKRSI$_{341}$ (15 AA)
P6'	β-H1-B2	Inter-subunits Lateral	Ile24–Ala65	I_{24}SDEHGIDPTGSYHGDSDLQLERIN VYYNEAAGNKYVPRA$_{65}$ (40 AA)
P7'	β-H2-B3	Inter-subunits Lateral	Gly81–Asn91	G_{81}PFGQIFRPDN$_{91}$ (11 AA)
P8'	β-H4-T5	Inter-subunits Lateral	Glu159–Asp163	E_{159}EYPD$_{163}$ (5 AA)
P9'	β-M-loop	Inter-subunits Lateral	Pro274–Glu290	P_{274}LTSRGSQQYRALTVPE$_{290}$ (17 AA)
P10'	β-H10	Inter-subunits Lateral and Longitudinal	Asp329–Phe343	D_{329}EQMLNVQNKNSSYF$_{343}$ (15 AA)

Table S1: The tubulin-lateral peptides as control unbounded segments (the P1'–P10') with their assigned secondary structure on the tubulin heterodimer crystal structure (1JFF.pdb[1]) and location in the MT protofilaments. The amino acids are shown as single-letter codes. The letters "T", "B", and "H" refer to the loops, β-strand, and α-helix, respectively.

Table S2

Systems	№ of CNT carbon atoms	№ of water molecules	Water box dimensions (nm^3)
Pristine CNT (peptide free)	640	16726	8 x 8 x 8
C1 (the P1–P5 on the CNT)	640	16262	8 x 8 x 8
C2 (the P6–P10 on the CNT)	640	16269	8 x 8 x 8
P1'	-	4248	5.1 x 5.1 x 5.1
P2'	-	2135	4.2 x 4.2 x 4.2
P3'	-	1278	3.3 x 3.3 x 3.3
P4'	-	3363	4.8 x 4.8 x 4.8
P5'	-	2840	4.7 x 4.7 x 4.7
P6'	-	3797	5.0 x 5.0 x 5.0
P7'	-	2571	4.3 x 4.3 x 4.3
P8'	-	1443	3.6 x 3.6 x 3.6
P9'	-	3762	4.7 x 4.7 x 4.7
P10'	-	2919	4.5 x 4.5 x 4.5

Table S2: The number of CNT atoms, water molecules, and water box dimension of the pristine CNT (i.e., peptide-free), the tubulin peptides on the CNT systems (the C1 complex contains the P1–P5, and the C2 complex contains the P6–P10), and the unbounded peptides without the CNT (the P1'–P10').

Table S3

	EM parameters		EM output		
	Emtol (kJ mol^{-1} nm^{-1})	**Emstep (nm)**	**Potential Energy (kJ mol^{-1})**	**Maximum force (kJ mol^{-1} nm^{-1})**	**Normal of force (kJ mol^{-1} nm^{-1})**
Pristine CNT	100	0.01	−8.254E+05	99.97	13.52
C1 (the P1–P5)	100	0.01	−8.266E+05	99.73	10.10
C2 (the P6–P10)	65	0.005	−8.424E+05	64.37	5.37
P1'	1000	0.01	−2.095E+05	862.02	33.99
P2'	1000	0.01	−1.002E+05	901.58	51.65
P3'	1000	0.01	−5.899E+04	974.27	52.10
P4'	1000	0.01	−1.615E+05	953.49	33.02
P5'	1000	0.01	−1.337E+05	955.92	43.41
P6'	1000	0.01	−1.894E+05	900.33	30.13
P7'	1000	0.01	−1.203E+05	967.89	42.34
P8'	1000	0.01	−6.796E+04	801.96	53.04
P9'	1000	0.01	−1.805E+05	954.91	34.68
P10'	1000	0.01	−1.386E+05	869.27	41.16

Table S3: The energy minimization input parameters (i.e., emtol and emstep) and output data (i.e., potential energy, maximum force and normal of force) of the pristine CNT, the CNT-complexes C1 (the P1–P5) and C2 (the P6–P10), and each free peptide without the CNT (the P1'–P10').

Table S4

Peptides	Identity and similarity (%)	Alignment*
P1 vs. P6	32.4% and 75.7% (37 AA overlap of 4–40:4–37)	EHGIQPDGQMPSDKTIGGGDDSFNTFFSETGAGKHVP :::::.: :.. .:. . . .:.....:. ..:.:: EHGIDPTGSYHGDSDLQL--ERINVYYNEATGNKYVP
P2 vs. P7	44.4% and 77.8% (9 AA overlap of 3–11:1–9)	GTYRQLFHP : . :.:.: GPFGQIFRP
P4 vs. P9	26.7% and 60.0% (15 AA overlap of 3–17:1–15)	PVISAEKAYHEQLSV :. : . .. :.: PLTSRGSQQYRALTV
P5 vs. P10	16.7% and 66.7% (12 AA overlap of 3–14:1–12)	NAAIATIKTKRS . . ....: : DEQMLNVQNKNS

Table S4: The sequence similarities between pair of equivalent peptides from respective α- and β-tubulin subunits (i.e., the P1-P6; the P2-P7; the P3-P8; the P4-P9; and the P5-P10). In alignment, the colon (**:**) indicates conservation between groups of strongly similar properties, and the period (**.**) means conservation between groups of weakly similar properties.

Free peptides	Free peptides RMSF (Å)	Peptides on the CNT	C1 RMSF (Å)	C2 RMSF (Å)
P1'	3.94 ± 1.13	**P1**	2.25 ± 0.52	-
P2'	4.85 ± 0.50	**P2**	2.10 ± 0.31	-
P3'	2.83 ± 0.62	**P3**	5.87 ± 0.89	-
P4'	5.12 ± 0.92	**P4**	2.16 ± 0.44	-
P5'	4.39 ± 0.80	**P5**	1.96 ± 0.28	-
P6'	5.04 ± 1.02	**P6**	-	2.61 ± 0.53
P7'	4.70 ± 1.00	**P7**	-	3.10 ± 0.64
P8'	2.08 ± 0.35	**P8**	-	5.94 ± 1.08
P9'	4.72 ± 1.23	**P9**	-	3.48 ± 1.06
P10'	5.16 ± 0.58	**P10**	-	3.35 ± 0.46

Table S5

Table S5: The average root mean square fluctuation (RMSF) of the unbounded peptide systems without the CNT (the P1'–P10') and the peptides on the CNT of the C1 (containing the P1–P5) and the C2 (containing the P6–P10) complexes during 0.8–1.5 μs of MD trajectories.

Peptides	№ of intermolecular hydrogen bond with water molecules
P1	100 ± 4
P2	33 ± 2
P3	20 ± 2
P4	47 ± 3
P5	35 ± 3
P6	109 ± 5
P7	27 ± 3
P8	26 ± 2
P9	49 ± 3
P10	46 ± 3

Table S6

Table S6: The average hydrogen-bond number of each tubulin peptides with water of the C1 (the P1–P5) and the C2 (the P6–P10) on the CNT complexes during 0.8–1.5 μs simulation time.

Peptides	DCOM (nm)	SAS area (nm^2)	№ of Interactions	LJ energy (kJ/mol)	HYD, HILIC, and total SAS area (nm^2)
P1	1.85 ± 0.14	3.64 ± 0.32	1,840 ± 206	−219.69 ± 28.50	~17, ~15, 31.91 ± 0.79
P2	1.18 ± 0.13	4.27 ± 0.18	2,304 ± 83	−245.41 ± 8.92	~10, ~8, 17.55 ± 0.34
P3	1.32 ± 0.11	2.08 ± 0.25	975 ± 147	−101.51 ± 16.58	~5, ~4, 8.89 ± 0.29
P4	0.96 ± 0.04	6.05 ± 0.28	3,635 ± 139	−425.43 ± 16.21	~13, ~9, 21.97 ± 0.57
P5	1.26 ± 0.06	3.38 ± 0.19	1,783 ± 88	−172.03 ± 10.03	~9, ~8, 17.16 ± 0.44
P6	1.54 ± 0.09	5.56 ± 0.27	2,823 ± 113	−314.47 ± 12.18	~19, ~17.5, 36.46 ± 1.23
P7	1.15 ± 0.11	4.13 ± 0.22	2,046 ± 96	−238.11 ± 10.47	~9, ~8, 16.72 ± 0.44
P8	1.37 ± 0.23	1.97 ± 0.21	865 ± 101	−104.40 ± 12.33	~4, ~5, 9.02 ± 0.29
P9	1.11 ± 0.16	5.90 ± 0.43	3,373 ± 228	−375.84 ± 27.29	~13, ~11, 24.20 ± 0.61
10	1.25 ± 0.08	4. 40 ± 0.37	2,076 ± 180	−239.22 ± 20.56	~10, ~10, 19.89 ± 0.66

Table S7

Table S7: The average DCOM, SAS area, interaction frequency number (at a distance ≤ 6.0 Å), and LJ energy between each tubulin peptide and the CNT during 0.8–1.5 μs time interval. The approximation values of the hydrophobic (HYD) and hydrophilic (HILIC) SAS area, and the total average SAS area, of each peptide.