Electronic Supplementary Material (ESI) for Environmental Science: Nano.

Supplementary Information

Extracellular Interactions Between Graphene Nanosheets and E-cadherin

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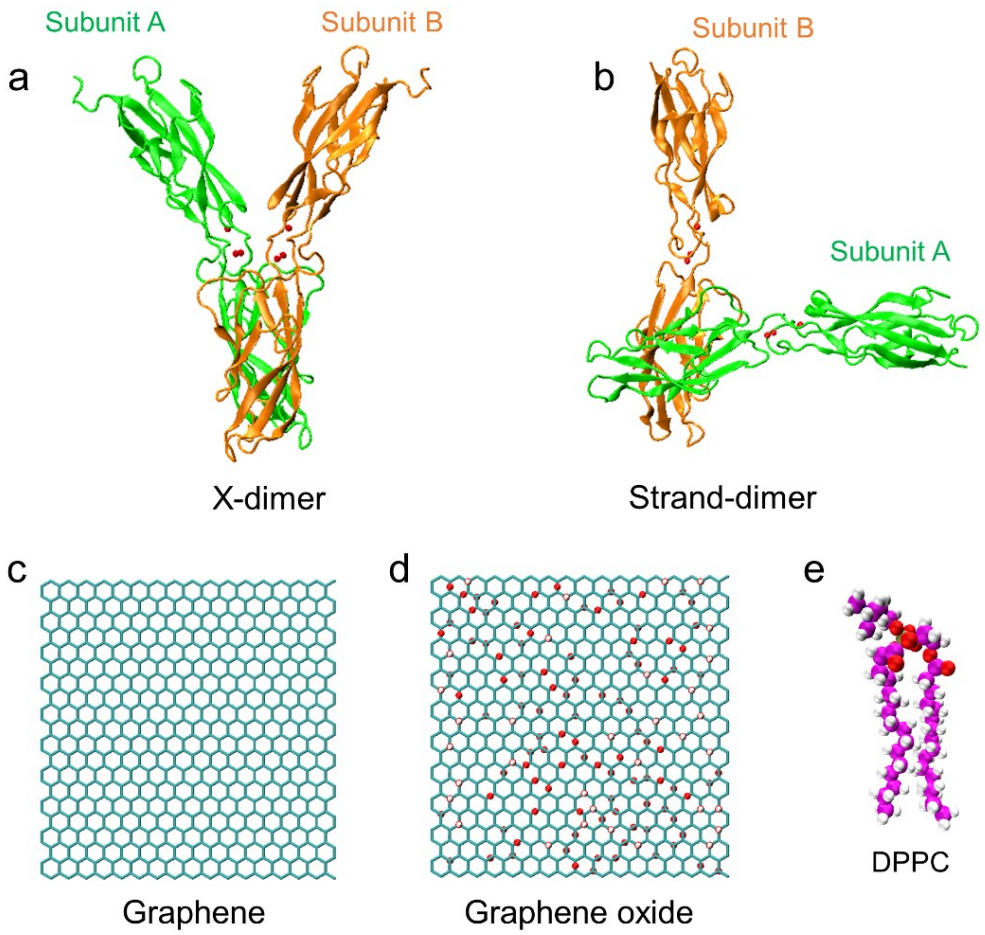

Figure S1. Atomistic models of different components used in our simulations. (a) X-dimer of E-cadherin. (b) Strand-dimer of E-cadherin. Two subunits were shown in different colors for clarity and Ca^{2+} ions were displayed as red points between two domains in each subunit. (c, d) Graphene and graphene oxide nanosheets. (e) DPPC molecule.

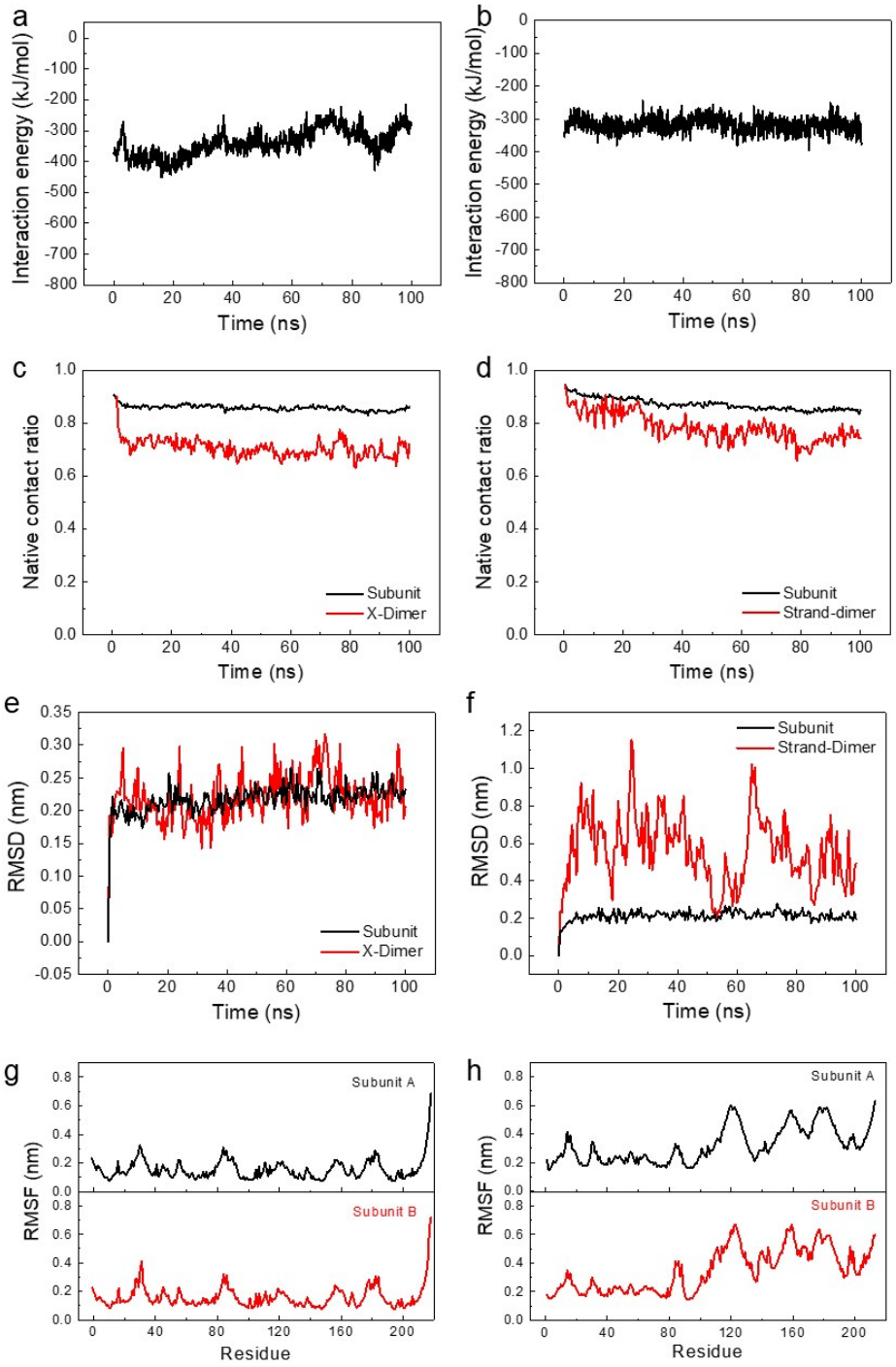

Figure S2. Structural stability of both the X- and strand-dimers of E-cadherin. (a, b) Time evolutions of the interaction energy between two subunits in the X- (a) and strand-dimer (b). (c, d) Time evolutions of the native contact ration calculated for subunit and the whole dimer. (e, f) Time evolutions of the root-mean-square deviation (RMSD) for subunit and dimer. (g, h) Time evolutions of root-mean-square fluctuation (RMSF) for residues in each subunit of the X- (g) and strand-dimer (h).

Table S1. Resides in contact at the X-dimer interface.

Interaction form	Monomer A	Monomer B
Hydrophobic interaction	Val3	Val3
	Ile4	Ile4
	Pro5	Pro5
	Pro6	Pro6
	Ile7	Ile7
	Ser8	Ser8
	Pro10	Pro10
	Asn12	Asn140
	Asn12	Tyr142
	Asn12	Val139
	Glu13	Asn140
	Glu13	Tyr142
	Glu13	Val139
	Asn140	Asn12
	Tyr142	Asn12
	Val139	Asn12
	Asn140	Glu13
	Tyr142	Glu13
	Thr99	Thr99
	Asn102	Asn102
	Asn104	Asn104
	Pro106	Pro106
	Leu196	Leu196
	Leu201	Leu201
Salt bridge	Lys14	Asp138
	Arg105	Glu199
Hydrogen bond	Asp100	Gln101
	Asn102	Asn102
	Gln101	Asn143
	Thr99	Thr99

Table S2. Resides in contact at the strand-dimer interface.

Interaction form	Monomer A	Monomer B
Salt bridge	Asp1	Glu89
Polar interaction	Trp2	Glu89
	Trp2	Met92
Hydrophobic interaction	Trp2	Pro5
	Trp2	Val22
	Trp2	Ile24
	Trp2	Met92
	Ile24	Ile24
Hydrogen bond	Asp1	Asn27
	Trp2	Asp90
	Val3	Lys25

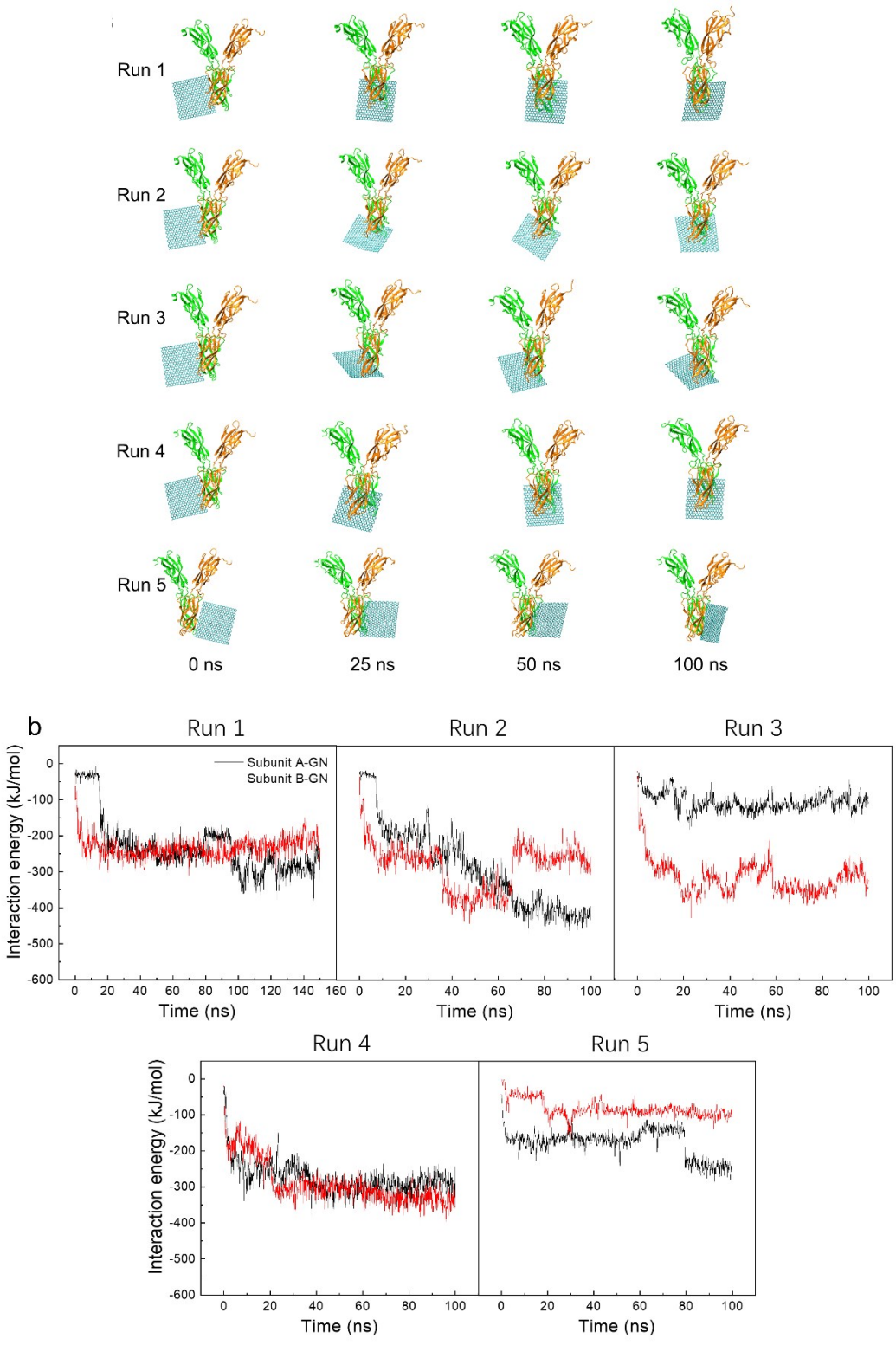

Figure S3. Five repeated simulations of GN intercalation in the X-dimer interface. (a) Time sequences of typical snapshots depicting GN interactions with X-dimer of E-cadherin. (b) Time evolutions of the energy of interactions between GN and two subunits of the X-dimer in five independent runs.

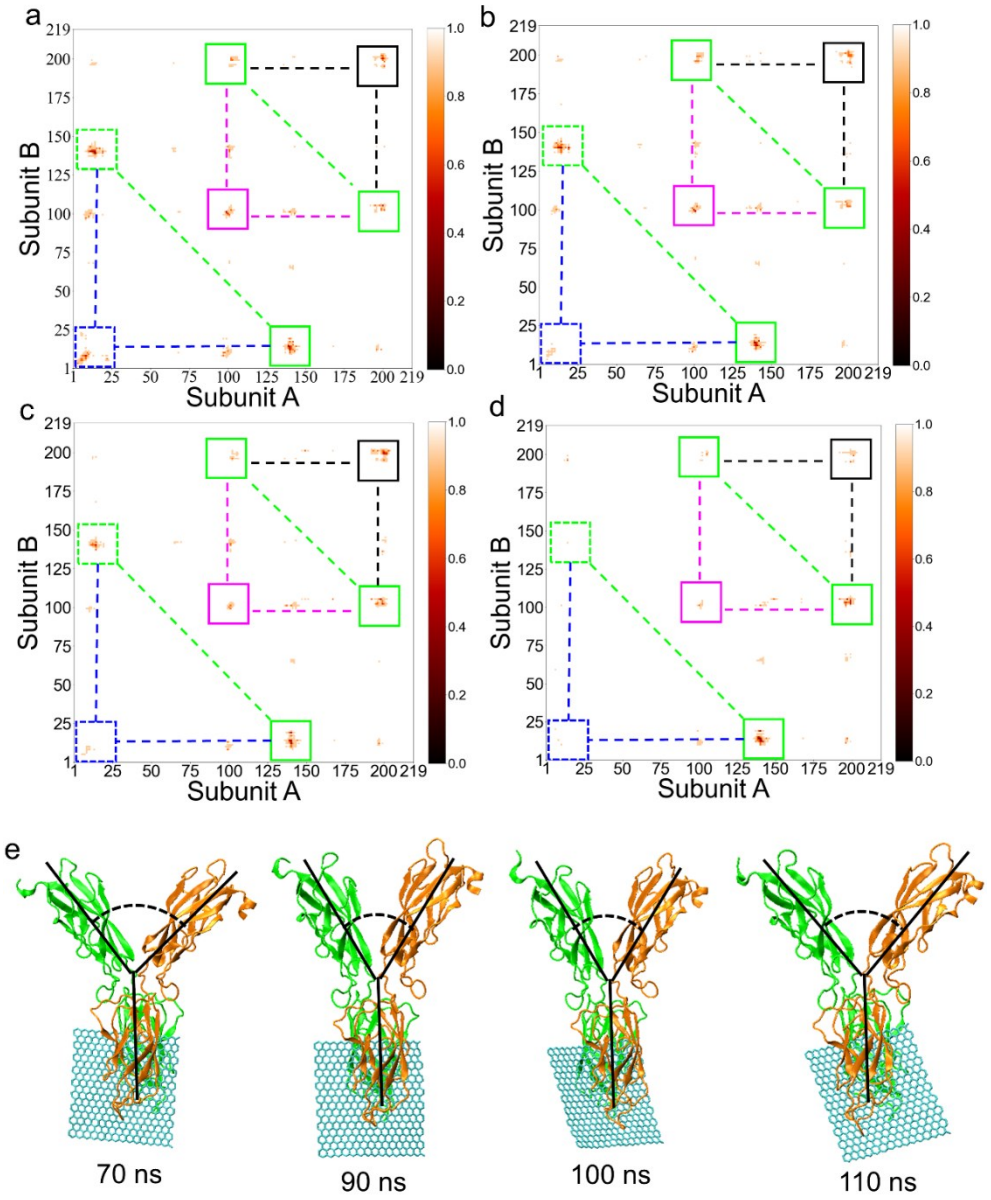

Figure S4. The structural change of X-dimer induced by GN intercalation. (a-d) The inter-subunit contact map at t = 0 ns, 15 ns, 80 ns and 150 ns, respectively. (e) Time sequence of typical snapshots depicting the change of cross angle between two subunits induced by GN intercalation.

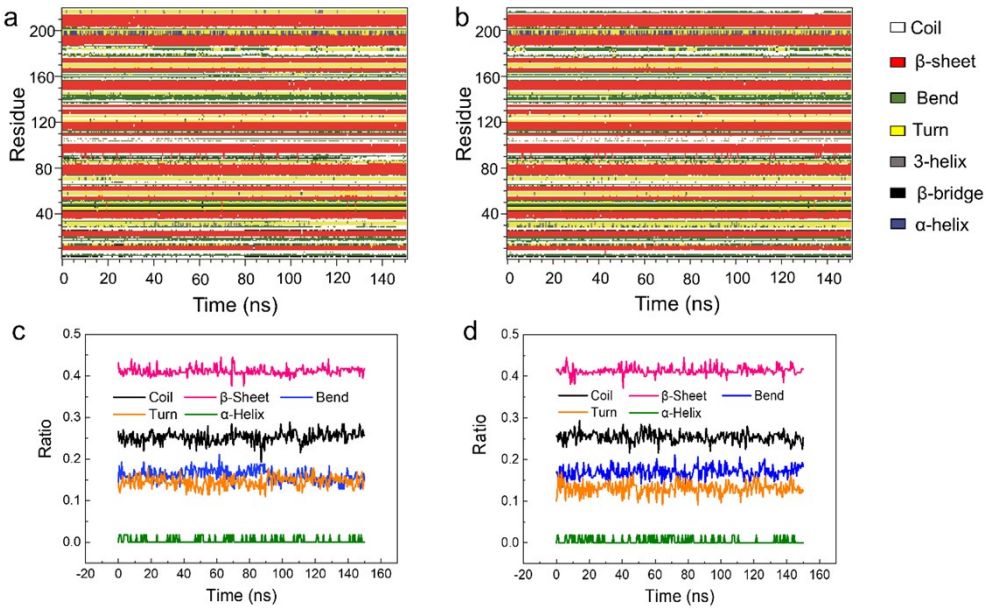

Figure S5. Time evolutions of the secondary structure change of two subunits during interactions with GN.

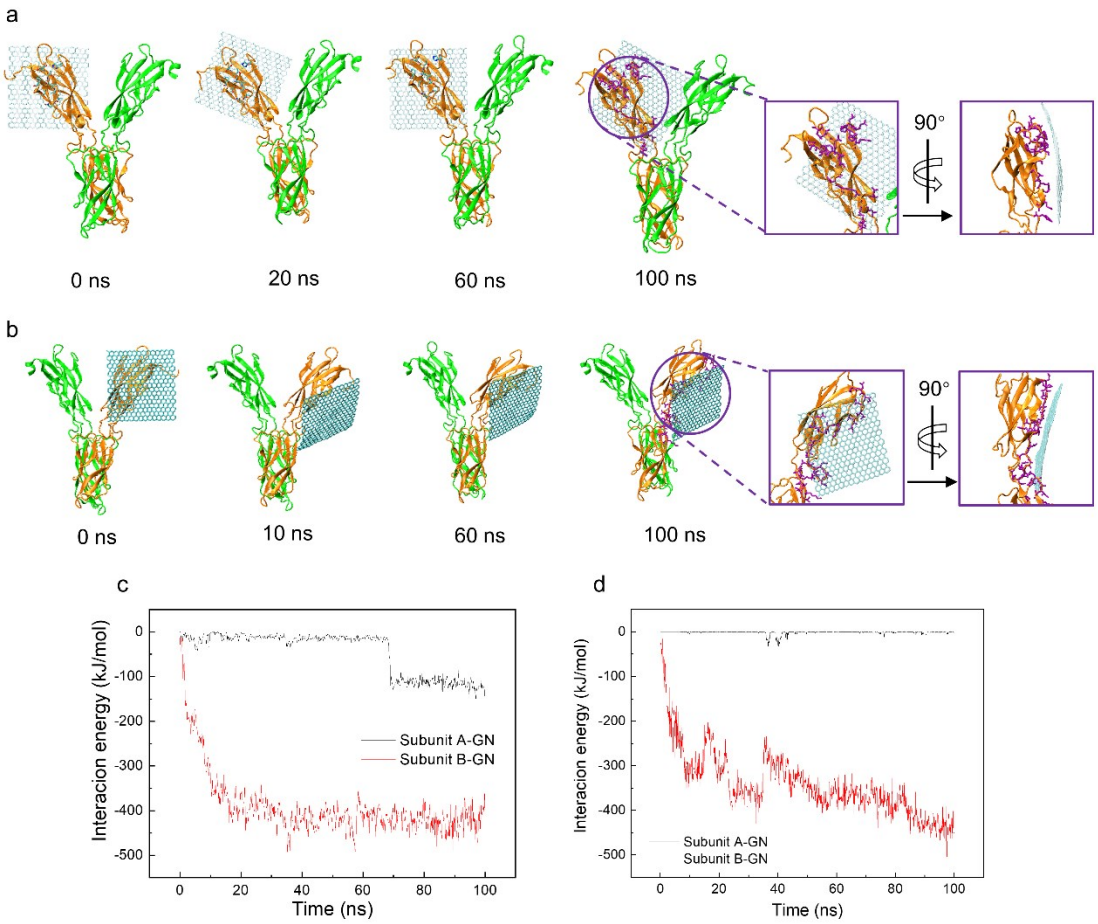

Figure S6. Interactions of GN with the second domain EC2 of E-cadherin. GN was initially placed at two different positions alongside EC2. Residues in final contact with GN were displayed in purple. (a, b) Time sequences of typical snapshots. (c, d) Time evolutions of the interaction energy between GN and two subunits in X-dimer.

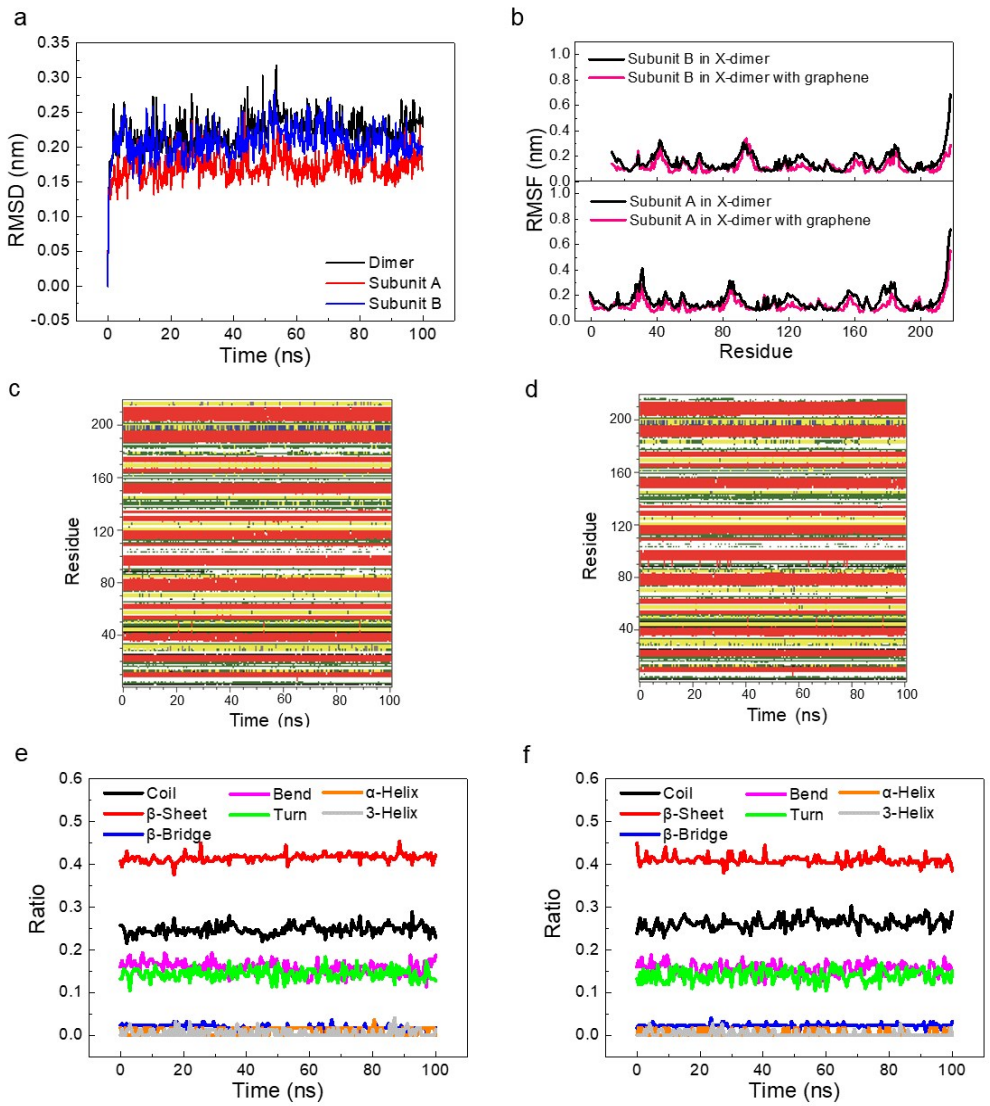

Figure S7. The structural change of X-dimer with the second domain EC2 interacted with GN. (a) Time evolutions of RMSD for each subunit and the whole dimer. (b) Time evolutions of RMSF for residues in each subunit before and after binding of GN to EC2. (c, d) Time evolutions of the secondary structure change for each subunit. (e, f) Time evolutions of the ratio of different secondary structures for both subunits.

Table S3. Cis structure contact sites

Interaction form	EC1	EC2
Hydrophobic interaction	Asn84	Val165
	Asn84	Asn166
	Val81	Pro123
	Val81	Leu175
	Phe35	Lue175
	Phe35	Pro123
Hydrogen bond	Asn84	Val165
	Asn84	Asn166
	Gly85	Leu175
	Arg55	Thr176

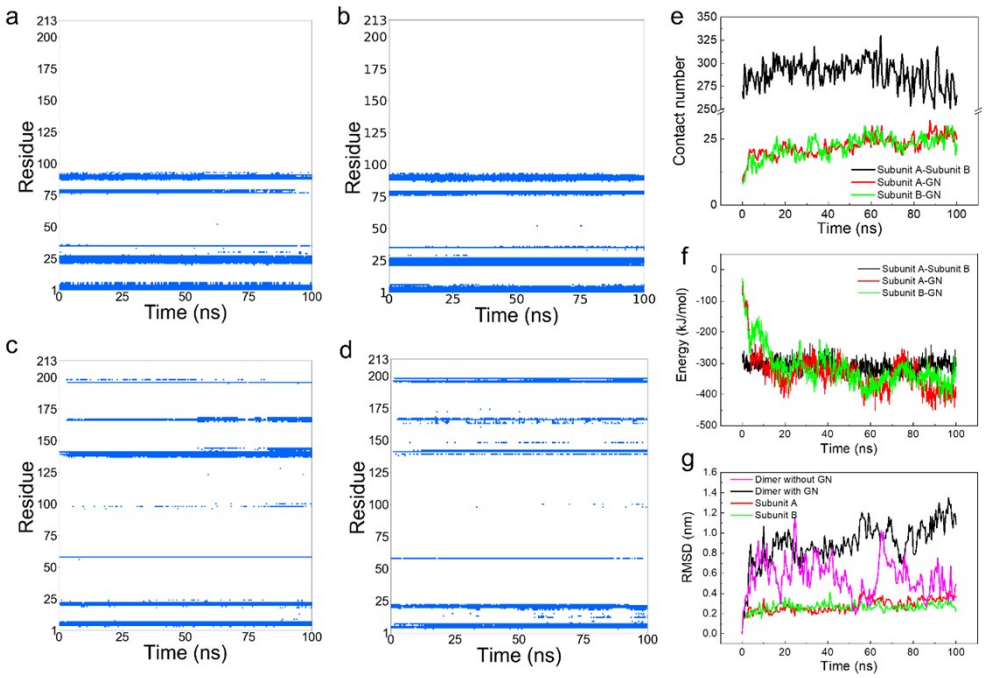

Figure S8. Interactions of GN with the strand-dimer of E-cadherin. (a, b) Time evolutions of the inter-subunit residue contact state. (c, d) Time evolutions of the GN contact with residues in each subunit. (e) Time evolutions of the inter-subunit contact number and the number of residues in each subunit in contact with GN. (f) Time evolutions of the inter-subunit and GN-subunit interaction energies. (g) Time evolution of the RMSD of each subunit and the dimer as affected by GN interactions.

Table S4. List of residues in each subunit of the strand-dimer in contact with GN.

Subunit A	Subunit B
Ile4	Ile4
Pro5	Pro5
Pro6	Pro6
Ile7	Ile7
Ser8	Ser8
Pro10	Pro10
Leu21	Lys19
Val22	Asn20
Gln23	Leu21
Trp59	Val22
Asp138	Gln23
Val139	Trp59
Asn140	Asn140
Thr141	Tyr142
Tyr142	Asn143
Asn143	Thr149
Ala144	Asn166
Ala145	Arg167
Ile146	Asp168
Asn166	Leu196
Arg167	Gln197
Asp168	Gly198
Thr169	Glu199
Gln197	

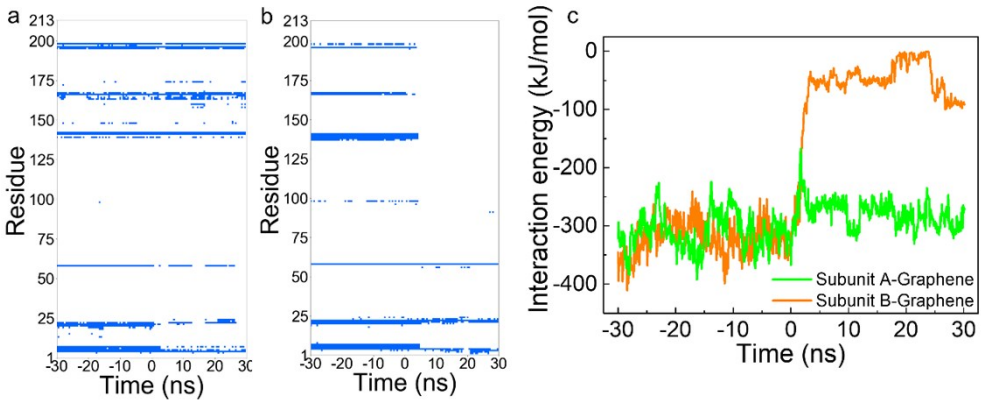

Figure S9. Mechanical separation of the X-dimer of E-cadherin influenced by GN intercalation. (a, b) Time evolutions of GN contacted residues in two subunits. The pulling operation was applied at t = 0 ns. (c) Time evolutions of the interaction energy between each subunit and GN.

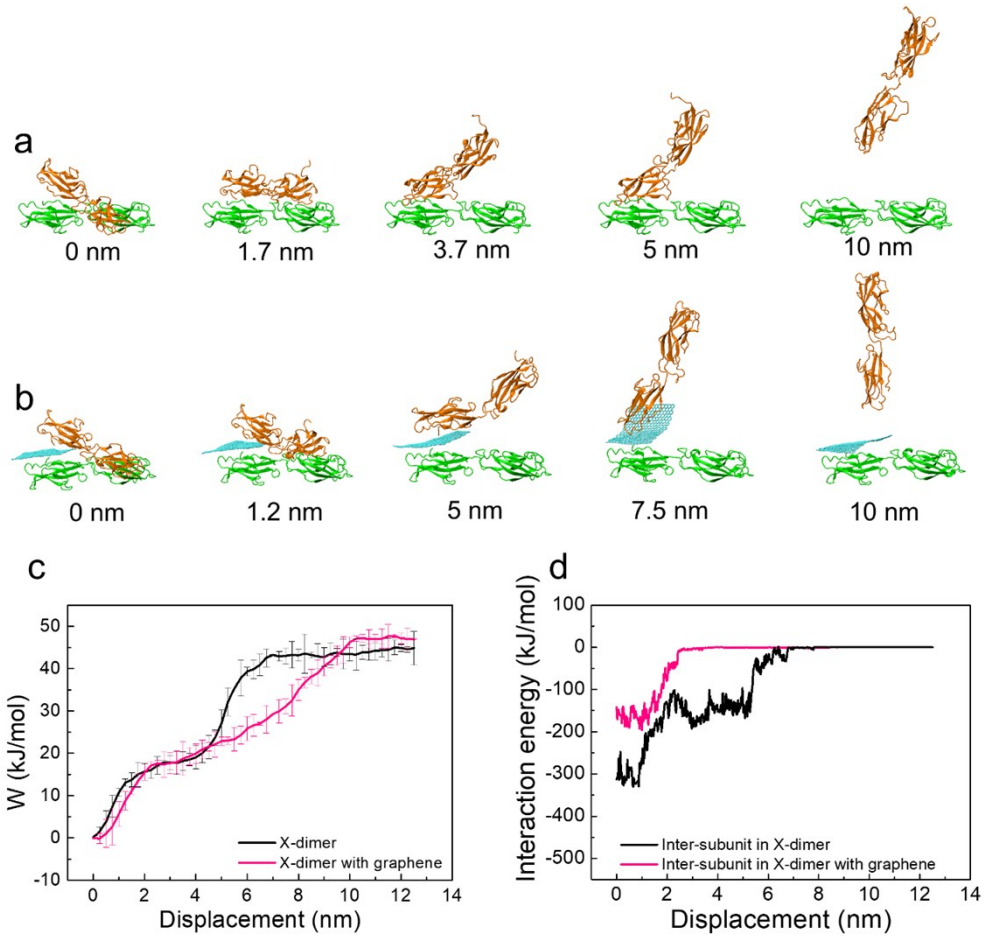

Figure S10. Mechanical separation of the X-dimer of E-cadherin by steered MD simulations using the constant pulling speed mode. (a, b) Time sequences of typical snapshots depicting separation of the X-dimer as affected by GN intercalation. (c) Time evolutions of the work separating two subunits. (d) Time evolutions of the interaction energy between two subunits during their mechanical separation.

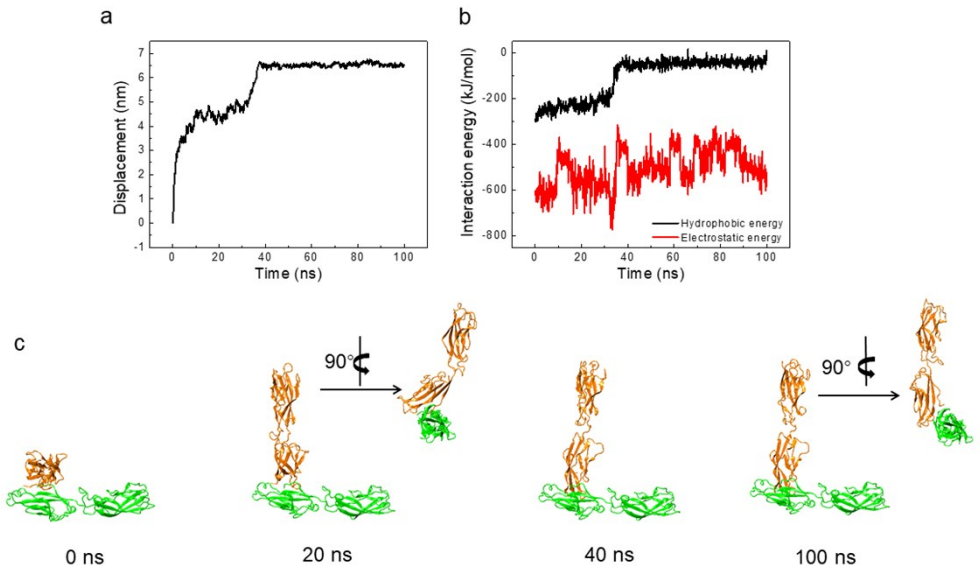

Figure S11. Mechanical response of the strand-dimer under a constant pulling force of 100 kJ/mol/nm. (a, b) Time evolutions of the displacement and interaction energy between two subunits. (c) Time sequence of typical snapshots depicting mechanical response of the strand-dimer to the constant force pulling.

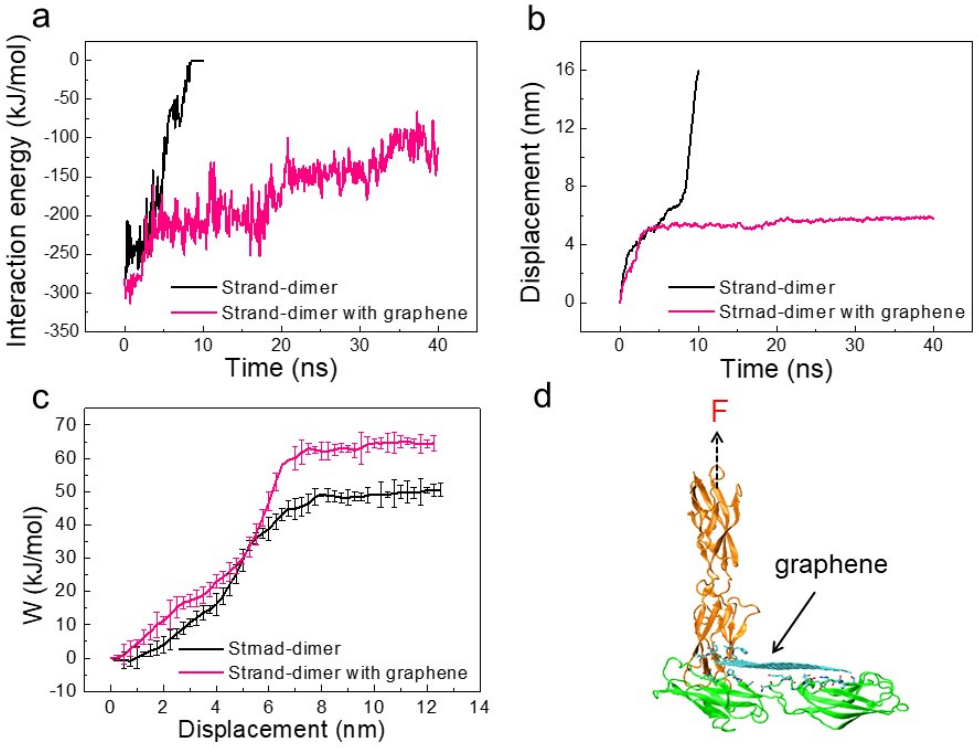

Figure S12. Mechanical separation of the strand-dimer of E-cadherin influenced by GN. (a-b) Time evolutions of the inter-subunit interaction energy, displacement during the pulling simulations. (c) Time evolutions of the work during the constant speed pulling simulation. (d) The final simulated snapshots of strand-dimer with graphene.

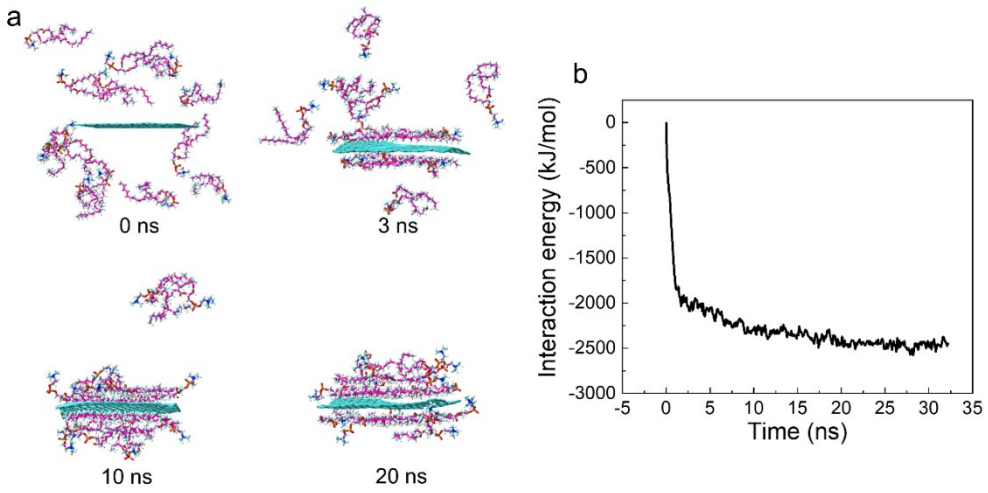

Figure S13. The adsorption of DPPC on graphene. (a) Time evolutions of the typical snapshots of DPPC and graphene. (b) Time of the interaction energy between DPPC and graphene.

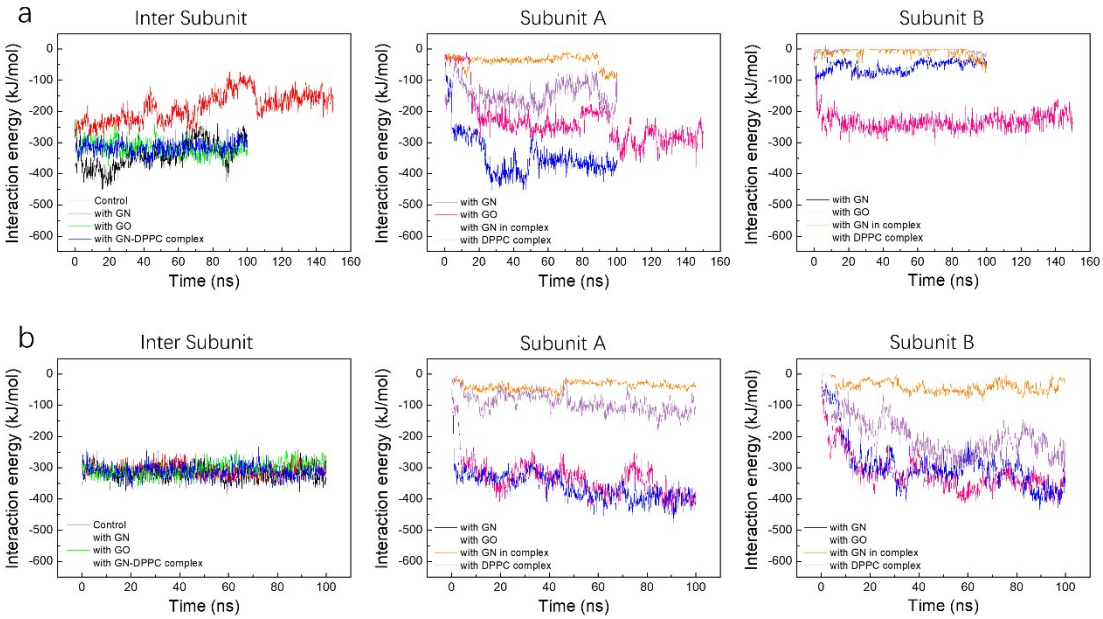

Figure S14. Time evolutions of the interaction energy between different components of E-cadherin (X-dimer (a) and strand-dimer (b)), GN, oxidized GN and DPPC-GN complex.