Supporting Information

Molecular Dynamics of Fibrinogen Adsorption onto Graphene, but not onto Poly(ethylene glycol) Surface, Increases Exposure of Recognition Sites that Trigger Immune Response

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Figure S1. Potential energy (kJ/mol) of fibrinogen D-domain as a function of simulation time. Here, unbound (Unbound-D), top (Top-D), side (Side-D), and perpendicular 1-3 (Perp1-D, Perp2-D, Perp3-D) are initial orientations of D-domain on graphene, and PEG-D is a perpendicular orientation of D-domain on a monolayer of PEG. For time plot, the 6,000 (or 3,000) data points were smoothed over 60 (30) points using a moving window average approach.

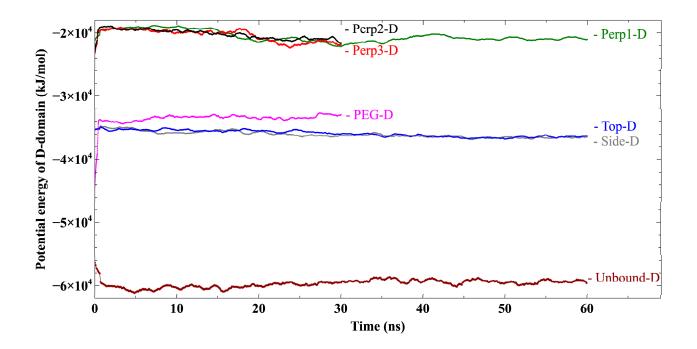


Figure S2. Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on graphene, for top orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

<mark>V S E D L R</mark> S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I <mark>V S E D L R S R I</mark> E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D <mark>I</mark> D I K I <mark>V S E D L R S</mark> R I E V <mark>L</mark> K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E <mark>V D</mark> I D I K I E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I R S b R G <mark>S a S R</mark> A L A R E V D L <mark>K D Y E D Q Q K Q L E Q V I A</mark> K D L L P K H <mark>Q L</mark> Y I D E T V N <mark>s b r g <mark>s</mark> a s r a l a r e v <mark>d</mark> l k d y e d q q k q l e q <mark>v l a</mark> k d l l p k h <mark>q l</mark> y i d e t v n</mark> R S b <mark>R G S a S</mark> R A L A R E V D <mark>L</mark> K D Y E D Q Q K Q L E Q V I <mark>A K D L</mark> L P K H <mark>Q</mark> L Y I D E T V N R S b R G S <mark>a</mark> S R A <mark>L</mark> A R E V <mark>D</mark> L K D Y <mark>E D</mark> Q Q K Q L E Q V I A <mark>K D L</mark> L P K H Q L Y I D E T V <mark>N</mark> S b R G S <mark>a</mark> S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K <mark>D L</mark> L P K H Q L Y I D E T V N <mark>NIP</mark>TNLRVLRSILENLRSKIQKLESDVSAQMEY<mark>CRT</mark>P NIPTNLRVLRSILENLRSKIQKLESDVSA<mark>Q</mark>MEYC<mark>RT</mark>P TVSANI v N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T</mark> P c <mark>T V</mark> S d N <mark>I</mark> v v PTNLRVLRSILENLRSKIQKLESDVS<mark>AQ</mark>MEYCR<mark>T</mark>Pc<mark>T</mark>V S d N I P V ENLRSKI v G K E E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y E D M N T E N G G W T V I Q N S G <mark>K E e E E I I R K G</mark> G E <mark>T S E M Y L I</mark> Q P <mark>D S S V K P Y R V Y e D</mark> M N T E N G G <mark>W T V I Q N</mark> SG<mark>KE eEEIIRKG</mark>GE<mark>TSEMYLI</mark>QP**DSSV**KP<mark>YRVYeDMNTEN</mark>GG<mark>WTV</mark> S <mark>G K E e E E I I R K G</mark> G <mark>E T S E</mark> MY L I Q P D <mark>S S V</mark> K P <mark>Y R</mark> V Y <mark>e D</mark> M N <mark>T E N</mark> G G W T EELL G G E T S E M Y L I Q P D S SVKPYRVYEDMN<mark>TEN</mark>GGWTVI . P G <mark>E Y W</mark>L G N D K I <mark>R Q D G S V D F G R K W D P Y K Q</mark> G <mark>F G N V A T</mark> N T <mark>D G K N Y</mark> d G I <mark>R Q D G </mark>S V D F G R K <mark>W D P Y K Q</mark> G <mark>F G</mark> N V A <mark>T</mark> N T **D G K N Y** d G I P G E Y W L G N D K Q D G S V D F G R K W D P Y K Q G F G N V A T N T D G K N Y d G L P G E Y W L G Q D G S V D F G R K W D P Y K Q G F G N <mark>V A T N T D G K N</mark> Y d G L P G E <mark>Y W</mark> L G N W D P Y K Q G <mark>F G N V A T N T</mark> DGKNYdG PGEYWLGN T <mark>R M G</mark> P T <mark>E L L I E M E</mark> D <mark>W K G</mark> D K V K A H Y <mark>G</mark> G F T V Q N E A N **K Y** Q I S V N K Y <mark>R G T A</mark> G M G P T E L L I E M E D <mark>W K</mark> G D K V K A H Y G <mark>G</mark> F T V Q N <mark>E A N K Y</mark> Q I S V N K Y R G T A G MG P T E L L I E ME D <mark>W K G</mark> D K V K A H Y G G F T V Q N E A N <mark>K Y</mark> Q I S V <mark>N</mark> K Y R G <mark>T A</mark> G T R M <mark>G</mark> P T E L L I E M E D <mark>W K G</mark> D K V K A H Y G G F T V Q N <mark>E A N K Y</mark> Q I S V N <mark>K Y R G T A</mark> G LIEME D <mark>WKG</mark> DK <mark>VKAHYGGFTV</mark>QN<mark>E</mark> ALMD G A <mark>S Q</mark> L M <mark>G E N R T M T I H N G M F F <mark>S T Y D R</mark> D N D G W L <mark>T S</mark> D P R K Q <mark>f S K E D</mark></mark> ALMD G A S Q L M <mark>G E N R T M T</mark> I H <mark>N G</mark> M F F <mark>S T</mark> Y D <mark>R</mark> D N D G W L T S D <mark>P R K Q F S K E D A L M D G A S Q L M G E N R T M T <mark>I</mark> H N G M F F <mark>S</mark> T Y D R D N D G W L T S D P R K Q F S K E D A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G W L T S D <mark>P R K Q F S K E</mark> D</mark> ALMD MGENRTMTIHNGMFFSTYDRDNDGWLTS GASOL G G G <mark>W</mark> W Y N R F H A <mark>A N P N G R</mark> Y Y W G G <mark>Q</mark> Y T <mark>W D M A K H G T D D </mark>G V V W M N W K G S W <mark>Y</mark> <mark>g</mark>gg<mark>w</mark>wy<mark>nrfha<mark>anpngr</mark>yy<mark>wggq</mark>ytwdmakhgtdd<mark>gv</mark>vwmnwk<mark>g</mark>sw<mark>y</mark>s</mark> G G G <mark>w</mark>wynrfh a <mark>an pngryywg g qytwd makhgt</mark>dd g v vw<mark>mnwk</mark>g sw<mark>y</mark>s G G G <mark>wwynr</mark>fh a <mark>an png</mark>ryy<mark>wg g q</mark>yt<mark>wd m</mark>ak<mark>hgtd</mark>d g vvwmnwk g sw<mark>y</mark>s NGGOYT<mark>WDM</mark>A кн<mark>дтр</mark>дд<mark></mark> G G G <mark>W W Y N R </mark>f H <mark>A</mark> GRYY

Figure S2. (Continued) Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on graphene, for top orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

M <mark>RKMSMKIR</mark> PFFPQK <mark>MLEE</mark> IMKYEASILTHDSSIRYLQEIYNSNNQKI
M <mark>R K M S M K I R P F F P Q K M L E E I</mark> M K YE A S I L T H D S S I R Y L Q E I Y N S N N Q K I
M <mark>R K M S M K I R P F F</mark> P Q K <mark>M L E E I</mark> M K Y E A S I L <mark>T H</mark> D S S I R Y L Q E I Y N S N N Q K I
M <mark>R K M S M K I R P</mark> F F P Q K <mark>M L E E I </mark> M K Y E A S I L T H D <mark>S</mark> S I R Y L Q E I Y N S N N Q K I
M <mark>R K M S M K I R P</mark> F F P Q K <mark>M L E E</mark> I M K Y E A S I L T H D S S I R Y L Q E I Y N S N N Q K I
VNLKEKVAQLEAQ <mark>bQE</mark> Pc <mark>KD</mark> TVQI <mark>HDITGKD</mark> gQDIANK <mark>G</mark> AK <mark>Q</mark> SGLYFI
VNLKEKVAQLE <mark>AQb</mark> Q <mark>E</mark> Pc <mark>KD</mark> TVQ <mark>IHDITGKDg</mark> QDIA <mark>NKG</mark> AKQS <mark>GLYFI</mark>
VNLKEKVAQLEAQЬ <mark>QEPC KD</mark> TVQI <mark>H</mark> DI <mark>TGKD</mark> g QDI ANK <mark>G</mark> AK QS <mark>GLYFI</mark>
VNLKEKVAQLEAQ b <mark>QE</mark> P <mark>CK</mark> D <mark>TVQIH</mark> DITG <mark>KD</mark> gQDIANK <mark>G</mark> AK <mark>Q</mark> S <mark>GLYFI</mark>
VNLKEKVAQLE <mark>AQbQE</mark> Pc <mark>K</mark> DTVQI <u>HDITG</u> KDgQDIANK <mark>G</mark> AKQSGLYFI
P1
KP <mark>lK</mark> A <mark>NQ</mark> QFLVYgEID <mark>GSGN</mark> GWTVFQKRLDGSVDFKKNWIQYKEGFGH
KP <mark>lK</mark> A <mark>NQ</mark> QFLVYgEID <mark>GSG</mark> N <mark>GWTVFQKRLDG</mark> S <mark>V</mark> DFKKNWIQYKEGFGH
KP <mark>lK</mark> A <mark>NQ</mark> QFLVYgEID <mark>GSG</mark> N <mark>GWTVFQKRLDG</mark> S <mark>V</mark> DFKKNWIQYKE <mark>G</mark> FGH
K P <mark>L K</mark> A <mark>N Q</mark> Q F L V Y g E I D <mark>G S G</mark> N <mark>G W T V F Q K R L D G S V</mark> D <mark>F K K</mark> N W I Q Y K E <mark>G</mark> F G H
K P <mark>L K</mark> A N <mark>Q</mark> Q F L V Y g E I D <mark>G S G</mark> N <mark>G W T V F Q K R L D G S V</mark> D F K K N WI Q Y <mark>K E</mark> G F G H
L S P T G T T E F W L G N E K I H L I S <mark>T</mark> Q S A I P YALR VELE D <mark>W N G</mark> R T S T A D YA M P L S P T G T T E F W L G N E K I H L I <mark>S T</mark> Q S A I P YALR VELE D <mark>W N G</mark> R T S T A D YA M F
L S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R T S I A D Y A M F L S P T G T T E F W L G <mark>N E</mark> K I H L <mark>I S T Q</mark> S A I P Y A L R V E L E D <mark>W N G</mark> R T S T A D Y A M F
L S P T G T T E F WL G N E K T H L I S T Q S A I P Y A L R V E L E D WN G R T S T A D Y A M F L S P T G T T E F WL G N E K I II L I S T Q S A I P Y A L R V E L E D WN G R T S T A D Y A M F
L S P T G T T E F WL G N E K I H L I S T Q S A I P Y A L R V E L E D WN G R T S T A D Y A M F
LO FIU TIEFWE <mark>NTEKITETOIQAATF</mark> TAEKYEEEU <mark>WINNE</mark> KIDIAUTAMF
<mark>K V</mark> G P <mark>E A D K Y</mark> R <mark>L T Y A Y F A G</mark> G <mark>D A </mark> G D <mark>A F D</mark> G F D F <mark>G D D P S D K F F T S H <mark>N G</mark> M Q <mark>F S</mark></mark>
K V G P E A D K Y R L T Y A Y F A G G D A G D A F D G F D F G D D P S D K F F T S H N G M Q F S
K V G P E A D K Y R L T Y A Y F A G G D A G D A F D G F D F G D D P S D K F F T S H N G M Q F S
K V G P E A D K Y R L T Y A Y F A G G <mark>D A </mark> G D <mark>A F D G F</mark> D F G D D P S D K F F <mark>T S H N G M</mark> Q F S
K V G P <mark>E A D K Y R L T Y A Y F A G G D A</mark> G D <mark>A F </mark> D G <mark>F D F G D D</mark> P S D K F F T S H N G M <mark>Q</mark> F S
T W D N D N D K F E G N h A E Q D <mark>G </mark> S G <mark>W W</mark> M N K h H A <mark>G H L N G V</mark> Y Y <mark>Q G G T</mark> Y S K A S T P N
T W D N D N D K F E G N h A E Q D G S G <mark>W</mark> W M N K h H A <mark>G H L N G V Y Y Q G G T</mark> Y S K A S T P N
<mark>t w d n</mark> d n d k f e g n h <mark>a e q d g s g w w</mark> m n k h <mark>h a</mark> g h l n g v y y q g g t y s k <mark>a s t</mark> p n
T <mark>w d n d n d k f e g n <mark>h</mark> a e q <mark>d</mark> g s g w <mark>w m</mark> n k h h a g h l n g v y y q g <mark>g t y s k a s t</mark> p n</mark>
T <mark>W D N D N D K F E G N h A E Q D</mark> G S G <mark>W W M N K h</mark> H A <mark>G H L N G V Y Y Q G G T Y</mark> S K <mark>A S T</mark> P N
P2
G Y <mark>D N <mark>G I I W A T W K</mark> T <mark>R W Y</mark> S M <mark>K K T T M K I I P F N R</mark> L T I G E</mark>
G Y D N <mark>G I I W A T W K</mark> T <mark>R W Y</mark> S M <mark>K K T T M K I I P F N R</mark> L <mark>T I</mark> G E
<mark>g y d n g</mark> i i w <mark>a t w k t r w y</mark> s <u>M k k t t M k i i p</u> f n r l t i g <mark>e</mark>
<mark>GYDN</mark> G <mark>I</mark> IW <mark>ATW</mark> KTRW <mark>Y</mark> S <mark>MKKTTMKIIP</mark> FNRLTIG <mark>E</mark>
<mark>g y d n g i </mark> i w <mark>a t w k t r w</mark> y s <mark>M k k t t M k i i p f n</mark> r l t i g <mark>e</mark>

Figure S3. Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on graphene, for side orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L <mark>R S R I</mark> E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I	D I K I D I K I D I K I
R S b R G S a S R A L A R E V D L K D Y E Q Q K Q L E Q V I A K D L K D Y E Q Q K Q L E Q V I A K D L K D Y I D R S b R G S a S R A L A R V D Q	E T V N E T V N E T V N
S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T P c T V </mark> S d N S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N	I P V V I P V I P V
S G K E E I I R K G G E I S F V	VIQN VIQN VIQN
R Q D G S V D F G P Y K Q G F G N T N T D G K N P G E Y N L G K N T N T D G K N P G E Y N L G N N T N T D G K N P G E Y N L G N N T N T D G K N D K N T T	I S Q L I S Q L I S Q L
T R M G P T E L I E M G D K V K A H Y G F T V N E A N K Y Q I S V N K Y R T R M G P T E L I E M G D K V K A H Y Q N E A N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N K Y N	G T A G G T A G G T A G
N A I M G E N T M T N G M F S T Y D N D D	S K E D S K E D
G G G <mark>W</mark> W Y N R f H A A N P N G R Y Y W G G Q Y T W D M A K H G T D D G V V W M N W K G G G G W W Y N R f H A A N P N G R Y Y W G G Q Y T W D M A K H G T D D G V V W M N W K G G G G W W Y N R f H A A N P N G R Y Y W G G Q Y T W D M A K H G T D D G V V W M N W K G G G G W W Y N R f H A A N P N G R Y Y W G G Q Y T W D M A K H G T D D G V V W M N W K G G G G W W Y N R f H A A N P N G R Y Y W G G Q Y T W D M A K H G T D D G V V W M N W K G	s w <mark>y</mark> s s w y s s w y s

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M <mark>R</mark> KMSMKIR <mark>PFFPQK<mark>MLEE</mark>IMKYEASILTHDSSIRYLQEIYNSNNQKI</mark>
M R K M S M K I R P F F P Q K M L E E I M K Y E A S I L T H D S S I R Y L Q E I Y N S N N Q K I
MRKMSMKIRP FFPQK <mark>MLEE</mark> IMKYEASILTHDSSIRYLQEIYNSNNQKI
MRKMSMKIRP <mark>FFPQK</mark> MLEEIMKYEASILTHDSSIRYLQEIYNSNNQKI
MR <mark>KMSMKIR</mark> PFFPQKM <mark>LEEI</mark> MKYEASILTHDSSIRYLQEIYNS <mark>N</mark> NQKI
VNLKEKVAQL <mark>EAQ<mark>bQE</mark>Pc<mark>KD</mark>TVQI<mark>HDITG<mark>KD</mark>gQDIANK<mark>G</mark>AK<mark>Q</mark>SGLYFI</mark></mark>
VNLKEKVAQL <mark>EAQbQE</mark> Pc <mark>KD</mark> TVQ <mark>IHDITGKDg</mark> QDIA <mark>NKG</mark> AKQSGLYFI
VNLKEKVAQLEAQ b <mark>q</mark> epc <mark>Kd</mark> TVQI <mark>HD</mark> I <mark>TGKD</mark> gQDIA <u>NK</u> GAK <mark>Q</mark> SGLYFI
VNLKEKVAQLEAQ <mark>b Q</mark> EP c <mark>KD TV</mark> Q <mark>I HDI TG KD</mark> g QDI A <mark>NKG</mark> AK <mark>QS</mark> GLYFI
VNLKEKVAQLEAQ <mark>bQ</mark> EPc <mark>KD</mark> TVQI <mark>HDI</mark> TGKDgQDIANKGAKQSGLYFI
P1
KP <mark>lKA</mark> NQQFLVYgEID <mark>GSGN</mark> GWTVFQKR <mark>LDG</mark> S <mark>V</mark> DFKKNWIQYKEG <mark>FGH</mark>
K P <mark>L K A N Q Q F L V Y g E I D <mark>G S G</mark> N <mark>G W T V F Q K R L D G</mark> S <mark>V</mark> D F K K N <mark>W I Q Y K E G F G H</mark></mark>
KP <mark>LKA</mark> NQQFLVYgEID <mark>GS</mark> GN <mark>GWTVFQKRLDGSV</mark> D <mark>F</mark> KKN <mark>WIQYKE</mark> GFGH
K P <mark>L K A N</mark> Q Q F L V Y g E I D <mark>G S G</mark> N G WT V F Q K R L D G S V D F K K N <mark>W I </mark> Q Y K E G F G H
K P <mark>L K A N</mark> Q Q F L V Y g E I D <mark>G S G N</mark> G WT V F Q K R <mark>L D G</mark> S <mark>V</mark> D F K K N WI Q Y <mark>K E</mark> G F G H
L S P T G T T E F W L G N E K I H L I S <mark>T</mark> Q S A I P Y A L R V E L E D <mark>W N G</mark> R T S T A D Y A M F
L S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R I S I A D Y A M F L S P T G T T E F W L G N E K I H L I <mark>S T</mark> Q S A I P Y A L R V E L E D W N G R T S T A D Y A M F
L S P T G T T E F WL G N E K I H L I S T Q S A I P Y A L R V E L E D WN G R T S T A D Y A M F
L S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R T S T A D Y A M F
L S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R T S T A D Y A M F
K V G P E A D K Y R L T Y A Y F A G G D A G D A F D G F D F G D D P S D K F F T S H N G M Q F S
<mark>K V</mark> G P <mark>E A D K Y</mark> R <mark>L T</mark> Y A <mark>Y F</mark> A <mark>G G D A</mark> G D <mark>A F D</mark> G F D F <mark>G D D P S D K F F T </mark> S H <mark>N G</mark> M Q F <mark>S</mark>
K V G P E A D K Y R L T Y A Y F A G G D A G D <mark>A F D</mark> G F D F <mark>G D</mark> D P S D K F F T S H N G M Q F S
K V G P <mark>E A D K Y</mark> R L T Y A <mark>Y F A G G D A</mark> G D <mark>A F D G</mark> F D F G D D <mark>P S D K F F T S H <mark>N G</mark> M Q <mark>F S</mark></mark>
K <mark>V</mark> G P E A D K Y R <mark>L</mark> T Y <mark>A Y F A G G D A G D A F D G</mark> F D F G D D <mark>P S</mark> D K F F T <mark>S H N G</mark> M Q <mark>F S</mark>
T W D N D N D K F E G N <mark>h A E Q D G</mark> S G <mark>W W</mark> M N K h H A <mark>G H </mark> L N G <mark>V</mark> Y Y <mark>Q G </mark> G <mark>T</mark> Y S K A S T P N
T W D N D N D K F E G N <mark>h A E Q D G S G W</mark> W M N K h H A <mark>G H </mark> L N G V Y Y <mark>Q G G T</mark> Y S <mark>K A S T P N</mark>
T W D N D N D K F E G N <mark>h A E Q D G</mark> S <mark>G W W</mark> M N K h H A <mark>G H L </mark> N G <mark>V</mark> Y Y Q <mark>G G T Y S K A S</mark> T P N
T W D N D N D K F E G N h A E Q D G S G <mark>W W</mark> M N K h H A G <mark>H</mark> L N G <mark>V</mark> Y Y Q G <mark>G T Y S K A S</mark> T P N
<mark>T W D N</mark> D N D K F E G N <mark>h</mark> A E Q D G S G <mark>W W</mark> M N K h H A <mark>G H</mark> L N G V Y Y Q G G T Y S K A S T P N
P2
GYDN <mark>GIIWATWK</mark> TRW <mark>Y</mark> SM <mark>KKTTMKIIPFNRLTI</mark> GE
G Y D N <mark>G I I W A T W K </mark> T <mark>R W</mark> Y S M <mark>K K T T M K I I P F N R</mark> L <mark>T I </mark> G E
G Y D N G I I W A T W K T R W Y S M K K T T M K I I P F N R I T I G E
G Y D N G I I W A T W K T R W Y S M K K T T M K I I P F N R L T I G E
GYDNGI <mark>IWATWKTRW</mark> YS <mark>MKKTTMKIIPFN</mark> RLT <mark>I</mark> G <mark>E</mark>

Figure S4. Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on graphene, for perpendicular orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S E DLR S RI E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I
R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N R S b R G S a S R A L A R E V D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N
S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T P</mark> c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T P</mark> c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N I P V V S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C R T P c T V S d N I P V V
S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N S G K E e E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y e D M N T E N G G W T V I Q N
R Q D G S V D F G N V A T N T D G N Y A T N T D G N Y A T N T D G N Y A T N T D G N Y A T N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N T D G N D
T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G T R M G P T E L L I E M E D W K G D K V K A H Y G G F T V Q N E A N K Y Q I S V N K Y R G T A G
N A L M D G A <mark>S Q L M G E N R T M T I H N G</mark> M F F <mark>S T Y D R</mark> D N D G WL T S D P R K Q f S K E D N A L M D G A <mark>S Q L M G E N R T M T</mark> I H N G M F F <mark>S T Y D R</mark> D N D G WL T S D P R K Q f S K E D N A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G WL T S D P R K Q f S K E D N A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G WL T S D P R K Q f S K E D N A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G WL T S D P R K Q f S K E D N A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G WL T S D P R K Q f S K E D
G G G <mark>W</mark> WY N R f H A A N P N G <mark>R</mark> Y Y WG G Q Y T <mark>WD M A K H G T</mark> D D <mark>G</mark> V V WM N WK G S WY S G G G <mark>W</mark> WY N R f H A A N P N G R Y Y WG G Q Y T WD M A K H G T D D G V V WM N WK G S WY G G G <mark>W WY N R f H A A N P N G R Y Y</mark> WG G Q Y T WD M A K H G T D D G V V WM N WK G S WY S G G G WWY N R f H A A N P N G R Y Y WG G Q Y T WD M A K H G T D D G V V WM N WK G S WY S

Figure S4. (Continued) Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on graphene, for perpendicular orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

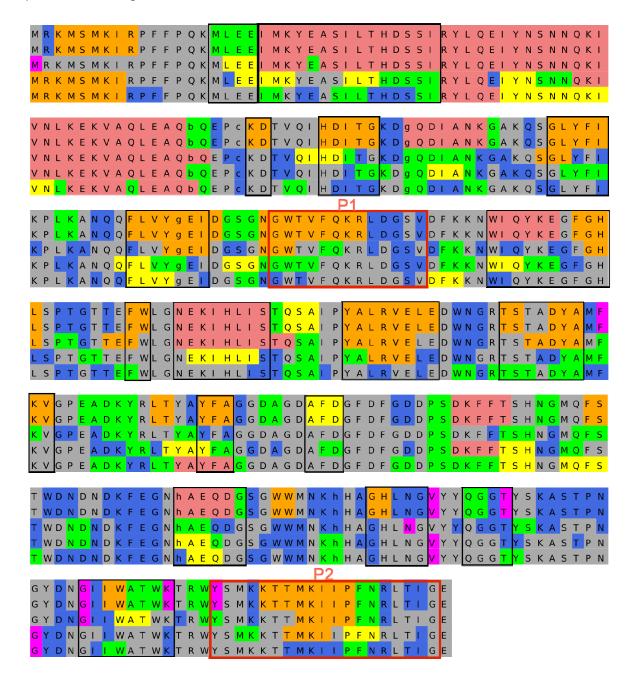


Figure S5. Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on PEG, for perpendicular orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns and 30 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

V S E <mark>D L R</mark> S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I V S <mark>E D L R S R I</mark> E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I DIKI V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K <mark>R L E V D I</mark> D I K I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I K I R S b R G <mark>S a </mark>S R A L A R E V D L K D Y E D Q Q K Q L E Q V I <mark>A</mark> K D L L P K H <mark>Q L</mark> Y I D E T V N TVN **R S** b **R G S** a **S R A L A R E V D L K D Y E D Q Q K Q L <mark>E Q</mark> V I A K D L** L P K H Q L <mark>Y I</mark> D E T V N RS b RGS a S RALA REV D L K D Y E D Q Q K Q L E Q V I A K D L L P K H Q L Y I D E T V N <mark>P</mark>TNLRVLRSILENLRSKIQKLESDVSAQMEY<mark>CRT</mark>P c T V SdN Ρ <mark>SN</mark>IPTNLRVLRSILENLRSKIQKLESDVSA<mark>Q</mark>MEYC<mark>RT</mark>PCTV<mark>S</mark>dN<mark>I</mark> ΡV V S NI P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C</mark> R <mark>T</mark> P C T V S d N I P V v S N I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y C **R T** P <mark>C T </mark>V <mark>S d N</mark> ΡV G K E E E I I R K G G E T S E M Y L I Q P D S S V K P Y R V Y E D M N T E N G G W T V I Q N S G <mark>K E e E E I I R K G</mark> G E T S <mark>E M Y L I</mark> Q P <mark>D S S V</mark> K P <mark>Y R V Y </mark>e D M <mark>N T E N G</mark> G <mark>W T V I Q N</mark> S G <mark>K E </mark> E E I I R K <mark>G</mark> G E T <mark>S E MY L I Q P D <mark>S S V</mark> K P <mark>Y R V Y</mark> E D M N T E N G G W T V I Q N</mark> <mark>R Q D G</mark> S <mark>V</mark> D F G R K W D P Y K Q G <mark>F G </mark>N <mark>V</mark> A T N T <mark>D G K N Y</mark> d G <mark>L P G E Y W</mark> L G N D K I S Q L R Q D G S V D F G R K W D P Y K Q G <mark>F G N V A T N T D G K N Y</mark> d G <mark>L P G E Y W</mark> L G N D K I S Q L R Q D G S V D F G <mark>R</mark> K W D P Y <mark>K Q</mark> G <mark>F G N V A T N T D G K N Y d G L P G E Y W</mark> L G N D K I S Q L G N <mark>V A</mark> T N T D <mark>G K N Y </mark>d G L <mark>P</mark> G E <mark>Y W</mark> L G N D K I S Q L Q D G S V D F G R K W D P Y K Q G T <mark>R M G</mark> P T <mark>E L L I E M E D W K G D K V K A H Y G</mark> G F T V Q N <mark>E A N K Y</mark> Q I S V N K Y R G <mark>T A</mark> G T **R M G** P T E L L I E M E D <mark>W K G</mark> D K V K A H Y G <mark>G</mark> F T V Q N E A N **K Y** Q I S V N K Y R G T A G T R M **G** P T E L L I E M E D <mark>W K</mark> G D K V K A H Y G G F T V O N <mark>E A N K</mark> Y O I S V N K Y R G T A <mark>G</mark> <mark>A L M D</mark> G A <mark>S Q L M G E N R T M T</mark> I H <mark>N G</mark> M F F <mark>S T Y D R</mark> D N D G W L T S D <mark>P R K</mark> Q f S K E D N A L M D G A S Q L M <mark>G E N R T M T</mark> I H <mark>N G</mark> M F F <mark>S T Y D R</mark> D N D <mark>G W L T S </mark>D P R K Q F S K <mark>E D</mark> N A L M D G A S Q L M G E N R T M T I H N G M F F S T Y D R D N D G W L T S D P R K Q F S K E D N A L M D G A S Q L M G E N R T M T I H N G M F <mark>F S T Y D R D</mark> N D G W L T <mark>S</mark> D P R K Q F S K E D G G G <mark>W</mark> W Y N R f H A <mark>A N P N G R</mark> Y Y W G G <mark>Q</mark> Y T <mark>W D M A K H G T</mark> D D <mark>G</mark> V V W M N W K G S W <mark>Y</mark> S G G G <mark>W</mark> W Y N R f H A <mark>A N P N G R</mark> Y Y <mark>W G G Q</mark> Y T W D M A K H G T D D <mark>G V </mark>V W M N W K <mark>G S W Y</mark> S G G <mark>G W W Y N R f</mark> H A <mark>A N P N</mark> G R Y Y W <mark>G G Q Y T W D M</mark> A K H <mark>G T D D G </mark>V W M N W K <mark>G S W Y S</mark> g g <mark>g w w</mark> y n r f h a a n p n g r y y w<mark>g g </mark> q y t w d m a k h g t d d g v v w m n w k g s w y

Figure S5. (Continued) Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD on PEG, for perpendicular orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns and 30 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

M <mark>R K M S M K I R </mark> P F F P Q K <mark>M L E E</mark> I M K Y E A S I L T H D S S I R Y L Q E I Y N : M R K M S M K I R P F F P Q K M L E E I M K Y E A S I L T H D S S I R Y L Q E I Y N :	-							
M <mark>R </mark> K M S M K I R <mark>P F F P Q K M L</mark> E E I M K Y E A S I L T H D S S I R Y L Q E I Y N S	S N N Q K I							
M <mark>R</mark> KMSMKIRPFFPQKM <mark>L</mark> EEIMKYEASILTHDSSIRYLQEIYN								
V N L K E K V A Q L E A Q <mark>b Q E</mark> P c <mark>K D</mark> T V Q I <mark>H D I T G K D</mark> g Q D I A N K <mark>G</mark> A K <mark>Q</mark> V N L K E K V A Q L <mark>E A Q b Q E</mark> P c <mark>K D T</mark> V Q <mark>I H D I T G K D</mark> g Q D I A <mark>N K G</mark> A K Q S	S <mark>G L Y F I</mark>							
V N L K E K V A Q L E <mark>A Q</mark> b <mark>Q E P c <mark>K D T</mark> V <mark>Q I H</mark> D I T G K D g Q D I A N K <mark>G</mark> A K <mark>Q</mark> V N L K E K V A Q L E <mark>A Q b Q E P c K D</mark>T V Q <mark>I H D I T G K D</mark> g Q D I A <mark>N K G</mark> A K Q</mark>								
<u>P1</u>								
K P <mark>L K </mark> A N Q Q <mark>F L V Y g E I D G S G N </mark> G W T V F Q K R L D G S <mark>V</mark> D F K K N WI Q Y I K P <mark>L K </mark> A N Q Q <mark>F L V Y g E I</mark> D <mark>G S</mark> G N <mark>G W T V F Q K R L D G</mark> S <mark>V</mark> D F K K N WI Q Y I	K E G <mark>F G H</mark>							
K P L K A N Q Q F L V Y G E I D G S G N G W I V F Q K K L D G S V D F K K N W I Q Y K P L K A N Q Q F L V Y G E I D G S G N G W T V F Q K R L D G S V D F K K N W I Q Y								
K P L K A N Q Q F L V Y g E I D G S G N G W T V F Q K R L D G S V D F K K N WI Q Y I								
L S P T G T T E F W L G N E K I H L I S <mark>T</mark> Q S A I P <mark>Y A L R V E L E</mark> D <mark>W N G R T S</mark> T .								
L S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R I S I . L S P T G T T E F W L G N E K I H L I <mark>S T</mark> Q S A I P Y A L R V E L E D <mark>W N G</mark> R T S T .								
L S <mark>P T G </mark> T T E F W L G N E K I H L I S <mark>T Q</mark> S A L P Y A L R V E L E D <mark>W N G</mark> R T S T .	A D Y A <mark>M</mark> F							
L S <mark>P T</mark> G T T E <mark>F W L</mark> G <mark>N E K I H L I S <mark>T Q</mark> S A I P <mark>Y A L R V E L E</mark> D <mark>W N</mark> G R <mark>T S T .</mark></mark>	A D Y A M F							
K V G P E A D K Y R L T Y A Y F A G G D A G D A F D G F D F G D D P S D K F F T S H	N G M Q <mark>F S</mark>							
<mark>ĸ v</mark> g p <mark>e a d k y</mark> r <mark>l т</mark> y <mark>a y f a g g d a</mark> g d <mark>a f d g f d f g d d p s d k f f t</mark> s h								
K V G P E A D K Y R L T Y A <mark>Y F A G G D A</mark> G D <mark>A F D G</mark> F D F <mark>G D D P S D K F F</mark> T S H								
K V G P E A D K Y R L T Y A Y F A G G D A G D <mark>A F D</mark> G F D F <mark>G D D P S D K F F T</mark> S H	N G <mark>M</mark> Q F S							
T W D N D N D K F E G N <mark>h A E Q D G S</mark> G <mark>W W</mark> M N K h H A <mark>G H L N G V</mark> Y Y <mark>Q G G T</mark> Y S I								
T W D N D K F E G N <mark>h A E Q D G</mark> S G <mark>W</mark> W M N K h H A <mark>G H L N G V Y Y Q G G T</mark> Y S I								
<mark>T W D N</mark> D N D K F E G N <mark>h A E Q D</mark> G S G <mark>W W</mark> M N K h H A <mark>G H L N G </mark> V Y <mark>Q G G T </mark> Y S T W D N D N D K F E G N <u>h A E O D</u> G S G W W M N K h H A G H L N G V Y Y <u>Q G G T</u> Y S								
G Y <mark>D</mark> N <mark>G I I W A T W </mark> K T <mark>R W</mark> Y S M K K T T M K I I P F N R L T I G E								
G Y D N <mark>G I I W A T W K</mark> T R W <mark>Y</mark> S M K K T T M K I I P F N R L T I G E								
G Y D N <mark>G</mark> I <mark>I W A T W K</mark> T <mark>R W</mark> Y S M K K T T M K I I P F N R L T I G E G Y D N G I I W A T W K T R W <mark>Y</mark> S M K K T T M K I I P F N R L T I G E								

Figure S6. Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD, for unbound orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

<mark>V S E D L R</mark> S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I V S E D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I κı SEDLRSRIEVLKRKVIEKVQHIQLLQKNVRAQLVDMKRLEVDIDI ĸι **V S E** D L R S R I E V L K R K V I E K V Q H I Q L L Q K N V R A Q L V D M K R L E V D I D I κı DI R S RI E VI K R K VI E K V O HI O I I O K N V R A O I V D M K R I E V D I D I R S b R G <mark>S a S R</mark> A L A R E V D L K D Y E D Q Q K Q L E Q V I <mark>A</mark> K D L L P K H <mark>Q L</mark> Y I D E T V N R <mark>S b R G <mark>S</mark> a <mark>S</mark> R A L A R E V <mark>D</mark> L K D Y E D Q Q K Q L E Q <mark>V I A</mark> K D L L P K H <mark>Q L</mark> Y I D E T V N</mark> R <mark>S b R G <mark>S</mark> a <mark>S</mark> R A L A R E V <mark>D</mark> L K D Y E D Q Q K Q L E Q <mark>V I A</mark> K D L L P K H <mark>Q L</mark> Y I D <mark>E T V N</mark></mark> R S b <mark>R G S a </mark>S R A L A R E V D <mark>L</mark> K D Y E D Q Q K Q L E Q V I <mark>A</mark> K D L L P K H Q <mark>L</mark> Y I <mark>D E</mark> T V N R S b <mark>R G S a S</mark> R A L A R E V D L K D Y E D Q Q K Q L E Q V I <mark>A</mark> K D L L P K H Q <mark>L</mark> Y I <mark>D E T</mark> V N <mark>S N I P</mark> T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T P</mark> c T V S d N <mark>I</mark> P NIPTNLRVLRSILENLRSKIQKLESDVSA<mark>Q</mark>MEYC<mark>RTP</mark>CTVSdN<mark>I</mark>P v v <mark>SN</mark>IPTNLRVLRSILENLRSKIQKLESDVSA<mark>Q</mark>MEYC**RTP**CTVSdN<mark>I</mark>P V V S <mark>N</mark> I P T N L R V L R S I L E N L R S K I Q K L E S D V S A Q M E Y <mark>C R T P</mark> C <mark>T V</mark> S d N <mark>I P</mark> v v TNLRVLRSILENLRSKI OKLESDVSAOMEYC<mark>RTP</mark>CTVSdNI S <mark>G K E</mark> E E E I I R <mark>K G</mark> G E **T** S E M Y L I <mark>Q P D S S V K P Y R V Y E D M N T E N G</mark> G <mark>W T V I Q N</mark> S G <mark>K E E E I I R K G</mark> G E T S <mark>E M Y L I</mark> Q P <mark>D S S V K P Y R V Y E D</mark> M N T E N G G <mark>W T V I Q N</mark> S G K E e E E I I <mark>R K G</mark> G E T S <mark>E M Y L I</mark> Q P **D S S V** K P <mark>Y R V Y e D M N T E N G</mark> G <mark>W T V I</mark> O N S <mark>G K E e E E I I R K G</mark> G E T S E M Y L I Q P D <mark>S S V</mark> K P <mark>Y R V Y e D</mark> M N <mark>T E N</mark> G G <mark>W T V I</mark> QN KE e E E I I R K <mark>G</mark> G E <mark>T S E MY L I Q P D S S V K P Y R V Y e D</mark> M N <mark>T E N</mark> G G <mark>W T V I Q N</mark> R Q D G S V D F G R K W D P Y K Q G F G N V A T N T D G K N Y d G L P G E Y W L G N D K I S Q L R Q D G S V D F G R K WD P Y K Q G F G N V A <mark>T</mark> N T **D G K N Y** d G <mark>L</mark> P G <mark>E Y W</mark> L G N D K I S Q L R Q D G S V D F G R K W D P Y K Q G F G N V A <mark>T</mark> N T <mark>D G K N Y</mark> d G <mark>L</mark> P G E <mark>Y W</mark> L G N D K I S Q L <mark>Q D G</mark> S <mark>V</mark> D F G R K W D P Y K Q G <mark>F G</mark> N V <mark>A T N</mark> T <mark>D G K N Y</mark> d G L P G E <mark>Y W</mark> L G N D K I S Q L <mark>Q D G</mark> S <mark>V</mark> D F G R K WD P Y K Q G <mark>F G </mark>N V <mark>A T</mark> N T <mark>D G</mark> K N Y d G L P G E <mark>Y W</mark> L G N D K I S O L T <mark>R M G</mark> P T <mark>E L L I E M E D W K G D K V K A H Y G</mark> G F T V Q N E A N <mark>K Y</mark> Q I S V N K Y <mark>R G T A</mark> G <mark>T R M G P</mark> T E L L I E M E D <mark>W K G</mark> D K V K A H Y G <mark>G</mark> F T V Q N <mark>E A N K Y</mark> Q I S V N K Y R G T A G <mark>T R M G P T E L L I E M E D <mark>W K G</mark> D K V K A H Y G <mark>G</mark> F T V Q N <mark>E A N K Y</mark> Q <mark>I S</mark> V N K Y R G T A G</mark> T R <mark>M G</mark> P <mark>T E L L I E M E D W K G </mark>D K V K A H Y G <mark>G</mark> F T V Q N <mark>E A N K Y</mark> Q I S V N K Y R G T A</mark> G T R <mark>M G</mark> P T E L L I E M E **D W K G D K V K A H Y G** G F T V O N **E A N K Y** O I S V N K Y RGT N A L M D G A S Q L M G E N R T M T I H <mark>N G</mark> M F F <mark>S T Y D R</mark> D N D G WL T S D P R K Q F S K E D A L M D G A S Q L M G E N R T M T I H N G M F F <mark>S T</mark> Y D <mark>R</mark> D N D G W L T S D P R K Q F S <mark>K</mark> E D N A L M D G A S Q L M G E N R T M T I H N G M F F <mark>S T</mark> Y D <mark>R</mark> D N D G W L T S D P R K Q F S <mark>K E D</mark> N A L M D G A <mark>S Q</mark> L M <mark>G E N R T M T</mark> I H <mark>N G</mark> M F F <mark>S T Y D R</mark> D N D G W L <mark>T S D P R K Q F S</mark> K **E D** G A S Q L M G E N R T M T I H N G M F F <mark>S T</mark> Y D R D N D G W L T SDPRKOfS<mark>K</mark> G G G <mark>W</mark> W Y N R f H A A N P N G <mark>R</mark> Y Y W G G <mark>Q</mark> Y T W D M A K H G T D D <mark>G</mark> V V W M N W K G S W <mark>Y</mark> S <mark>G</mark> G G <mark>W</mark> W Y N R F H A A N P N G <mark>R</mark> Y Y W G G Q Y T W D M A K H G T D D <mark>G </mark>V V M N W K <mark>G S</mark> W <mark>Y</mark> S G G <mark>W</mark> W Y N R f H A <mark>A N P N G R</mark> Y Y W G G <mark>Q</mark> Y T W D M A K H G T D D <mark>G</mark> V V W M N W K <mark>G S W Y</mark> S <mark>G G G W</mark> W Y N R F H A A N P N G R Y Y W G G Q Y T <mark>W D M A K H G</mark> T D D G V <mark>V W M N W K</mark> G <mark>S W</mark> Y S g <mark>g</mark> g <mark>w</mark> wy n r f h a a n p n g <mark>r</mark> y y wg g o y t wd m a k h g t d d <mark>g</mark> v <mark>v wm n wk</mark> g s wy s

Figure S6. (Continued) Secondary structure assignment per residue for the complete sequence of the D-domain of fibrinogen before and after MD, for unbound orientation simulated. The rows correspond to a D-domain crystal structure, its structure at 0 ns, 20 ns, 40 ns, and 60 ns of the simulation time, respectively. The outlined in black fragments correspond to the most significant changes in the secondary structure content of the D-domain such as unfolding of the α -helix and/or β -extended strand; while the outlined in red fragments are P1 γ 190-202 and P2 γ 377-395 binding sites.

M <mark>R K M S M K I R P F F P Q K <mark>M L E E</mark> I M K Y E A S I L T H D S S I R Y L Q E I Y N S N N Q K I</mark> MLEEI MKYEASILTHDSSIRYLQEIYNS MRKMSMKIRPF FPQK ΝΝΟΚΙ M <mark>R K M S M K I R P</mark> F F P Q K <mark>M L E E</mark> I M K Y E A S I L T H D S S I R Y L Q E I Y N S Ν NOKI M R K M S M K I R P F F P Q K M L E E I M K Y E A S I L T H D S S I R Y L Q E I Y N S N N Q K I M R K M S M K I R P F F P Q K M L E E I M K Y E A S I L T H D S S I R Y L Q E I Y N S N N Q K I V N L K E K V A Q L E A Q <mark>b Q E</mark> P C <mark>K D</mark> T V Q I <mark>H D I T G K D</mark> g Q D I A N K <mark>G</mark> A K <mark>Q</mark> S <mark>G L Y F I</mark> V N L K E K V A Q L E <mark>A Q </mark>b Q <mark>E</mark> P c <mark>K D T</mark> V Q <mark>I H D I T G K D g</mark> Q D I A <mark>N K G</mark> A K Q S <mark>G L</mark> V N L K E K V A Q L E <mark>A Q b</mark> Q <mark>E</mark> P C <mark>K D T</mark> V Q I H D I T G K D g Q D I A <mark>N K G</mark> A K Q S <mark>G L Y F I</mark> V N L K E K V A Q L E A Q <mark>b</mark> Q <mark>E</mark> P c K <mark>D T V</mark> Q I H D I T G <mark>K D</mark> g Q D I A N <mark>K G</mark> A K Q S <mark>G L Y F I</mark> V N L K E K V A <mark>O L E A O </mark>b O E P C <mark>K D T</mark> V O I H D I T G <mark>K D</mark> g O D I A N K <mark>G</mark> A K O S G L Y F I **P1** K P <mark>L K</mark> A N Q Q <mark>F L V Y g E I D G S G N <mark>G W T V F Q K R L D G S V</mark> D F K K N W I Q Y K E G F G H</mark> K P <mark>L K</mark> A N Q Q F L V Y g E I D <mark>G S G</mark> N <mark>G W T V F Q K R L D G S V</mark> D F K K N W I Q Y K E G F G H K P <mark>L K</mark> A N Q Q <mark>F L V Y g E I</mark> D <mark>G S G</mark> N <mark>G W T V F Q K R L D G S V</mark> D F K K N W I Q Y K E G F G H A N Q Q F L V Y g E I D <mark>G S G</mark> N <mark>G W T V F Q K R L D G S V</mark> D F K K N W I Q Y K E G F G H L S P T G T T E F W L G N E K I H L I S <mark>T</mark> Q S A I P Y A L R V E L E D <mark>W N G</mark> R T S T A D Y A M F L S <mark>P T G T T</mark> E F W L G N E K I H L I <mark>S T</mark> Q S A I P Y A L R V E L E D <mark>W N G</mark> R T S T A D Y A M F L S <mark>P T</mark> G T T E <mark>F W</mark> L G N E K I H L I S T <mark>Q S A I</mark> P Y A L R V E L E D <mark>W N G</mark> R T S T A D Y A M F S P T G T T E F W L G N E K I H L I S T Q S A I P Y A L R V E L E D W N G R T S T A D Y A M F K V G P <mark>E A D K Y</mark> R L T Y <mark>A Y F A G G D A</mark> G D A F D G F D F <mark>G D D P S</mark> D K F F T S H <mark>N G</mark> M Q <mark>F S</mark> <mark>K V </mark>G P <mark>E A D K Y</mark> R <mark>L T </mark>Y A <mark>Y F</mark> A <mark>G</mark> G D A G D A F D G F D F G D D P S D K F F T S H N G M Q F <mark>S</mark> <mark>K V </mark> G P <mark>E A D K Y</mark> R <mark>L T</mark> Y A <mark>Y F</mark> A <mark>G</mark> G D A G D A F D G F D F G D D P S D K F F T S H N G M Q F <mark>S</mark> K V G P <mark>E A D K Y</mark> R L T Y A Y F A G G **D A** G **D** A F D G F D F <mark>G D D P S D K F F T S</mark> H <mark>N G</mark> M Q F S K V G P E A D K Y R L T Y A Y F A G G D A G D A F D G F D F G D D P S D K F F T <mark>S</mark> H N G M Q F S T W D N D N D K F E G N h A E Q D <mark>G</mark> S G <mark>W W</mark> M N K h H A <mark>G H</mark> L N G <mark>V</mark> Y Y <mark>Q G G T</mark> Y S K A S T P N <mark>T W D N</mark> D N D K F E G N h A E Q D G S G <mark>W W</mark> M N K h H A <mark>G H L N G V</mark> Y Y Q G G T Y S K A S T P N . N G <mark>V</mark> Y Y <mark>Q G G T Y S K A S T P N</mark> P2 GYDN<mark>G</mark> W<mark>ATWK</mark>TRW<mark>Y</mark>SMKKTTMKIIPF NRLTI GΕ GYDN<mark>G</mark>I W<mark>ATWK</mark>TRW<mark>Y</mark>SMKKTTMKIIPFNRLTI GΕ GYDN<mark>GIIWATWK</mark>TRW<mark>Y</mark>SMKKTTMKI I P F N R L T I G E W A T W K T R W Y <mark>S</mark> M K K T T M K I I P F N R L T I GYDN<mark>G</mark>II GΕ GYDNG W WY S М

KEY:

	H-Bonded					Extended	
A-Helix	Turn	Bend	G-Helix	Beta Bridge	P-Helix	strand	Undetermined

Figure S7. Percent of secondary structure (α -helix, β -stand) relative to native (initial) state. Here, unbound (Unbound-D), top (Top-D), side (Side-D), and perpendicular 1-3 (Perp1-D, Perp2-D, Perp3-D) are initial orientations of D-domain on graphene, and PEG-D is a perpendicular orientation of D-domain on a monolayer of PEG. For time plots, the 6,000 (or 3,000) data points were smoothed over 60 (30) points using a moving window average approach.

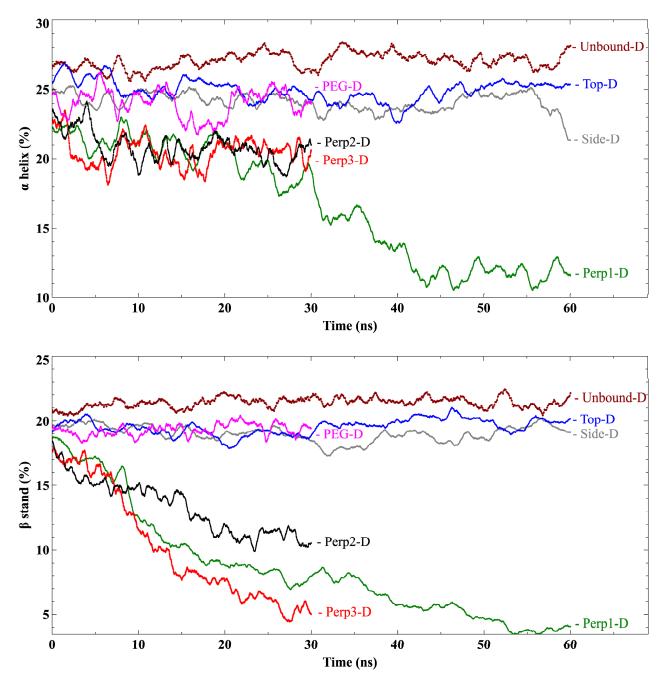


Figure S8. Number of hydrogen bonds (HBs) for initial and final orientations. Here, unbound (Unbound-D), top (Top-D), side (Side-D), and perpendicular 1-3 (Perp1-D, Perp2-D, Perp3-D) are initial orientations of D-domain on graphene, and PEG-D is a perpendicular orientation of D-domain on a monolayer of PEG.

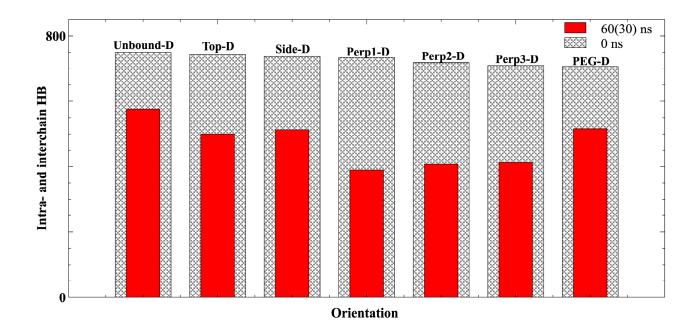


Figure S9. Radius of gyration as a function of simulation time. Here, unbound (Unbound-D), top (Top-D), side (Side-D), and perpendicular 1-3 (Perp1-D, Perp2-D, Perp3-D) are initial orientations of D-domain on graphene, and PEG-D is a perpendicular orientation of D-domain on a monolayer of PEG.

