Electronic Supporting Information for

Following the Aggregation of Human Prion Protein on Au (111) Surface in Real-Time

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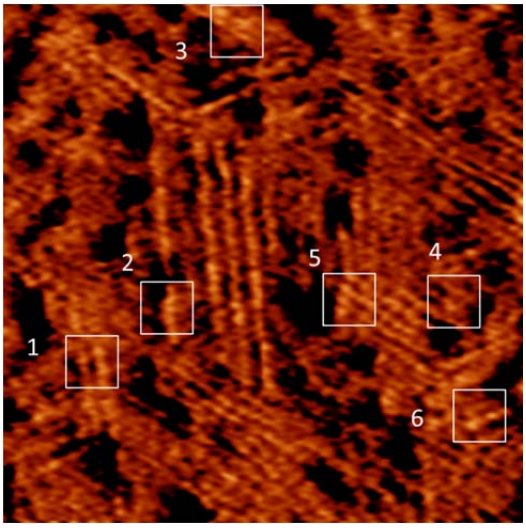

Fig. S1. Representative areas from Fig. 1A to show different PrP trimer conformations and orientations on Au(111) surface. Each area is 40 nm x 40 nm. Area 1 is shown in Fig. 2C. Area 2 to area 6 are shown in Fig. S2.

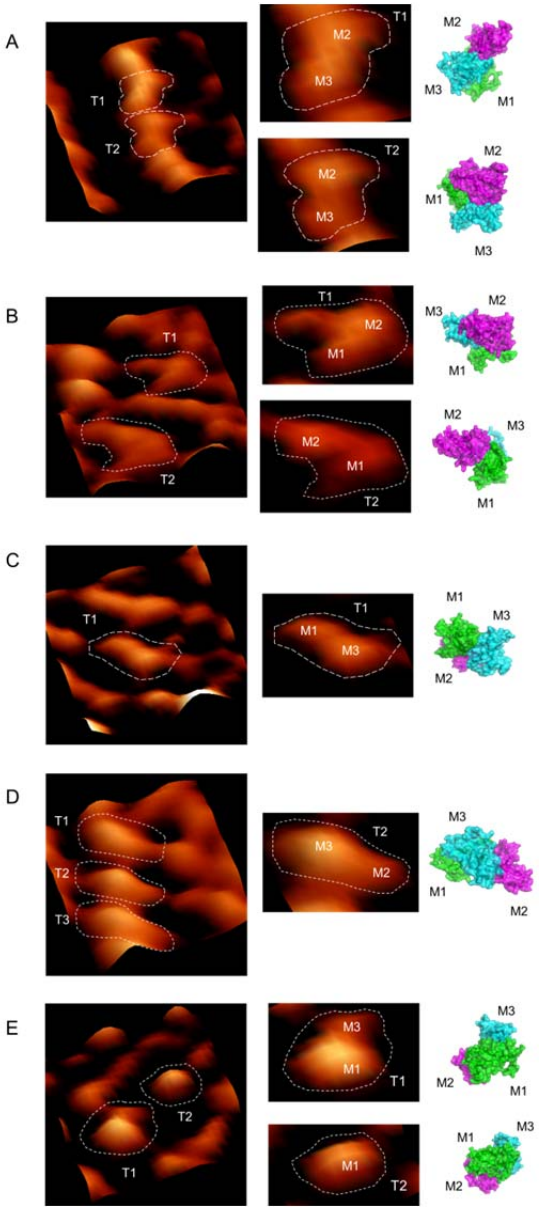

Fig. S2. Enlarged AFM 3D images for area 2 to area 6 in Fig. S1. The trimer conformation in each area is outlined and compared with simulated trimer structures. (A) corresponds to area 2, where two trimers showed different orientations. Both T1 and T2 bound to Au(111) surface with their monomer M1. (B) corresponds to area 3, where two trimers bound to Au(111) surface with different monomers. T1 bound to Au(111) surface with M1, while T2 with M3. (C) corresponds to area 4, where T1 bound to Au(111) surface with M2. (D) corresponds to area 5, where all T1, T2, and T3 bound to Au(111) surface with M1, but T2 showed higher resolutions due to thermal noise during the scanning. (E) corresponds to area 6, where both T1 and T2 bound to Au(111) surface with the M2, but T1 showed higher resolution, T2 didn't show M3 in the AFM image because of the fluctuations of M1 and M3 in the solution. All simulated structures are shown in top-view in order to be comparable to AFM images.

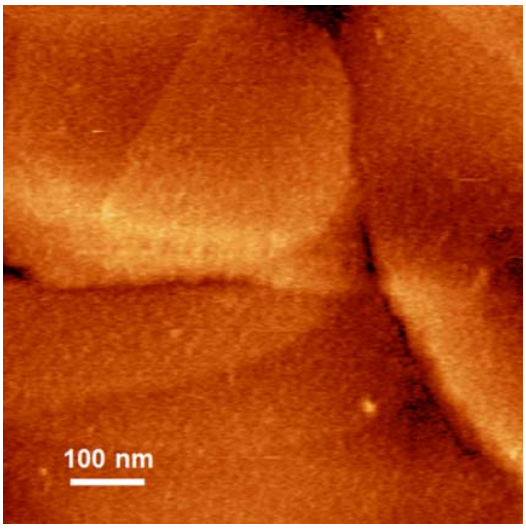

Fig. S3 Representative AFM topography image of Au(111) surface with 100 ng/mL PrP in pH 7 PBS buffer. The surface was continuously scanned after 3 hours. Some aggregates showed on the surface, but no special pattern could be observed.

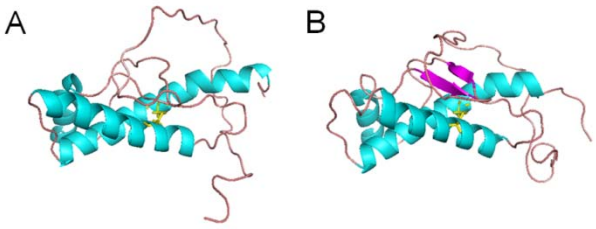

Fig. S4 The molecular dynamics simulations of PrP monomer under (A) pH 7 and (B) pH 4. The simulations were conducted by Amber 11, with 60 ns equilibration for each structure. For each structure, the three α-helices are in blue, β-sheets in purple, and the two cysteine residues are highlighted in stick representation and in yellow. The residues involved in those two β-sheet structures include Met129, Leu130, Gly131, Ser132, Gln160, Val161, Tyr162, and Tyr163.

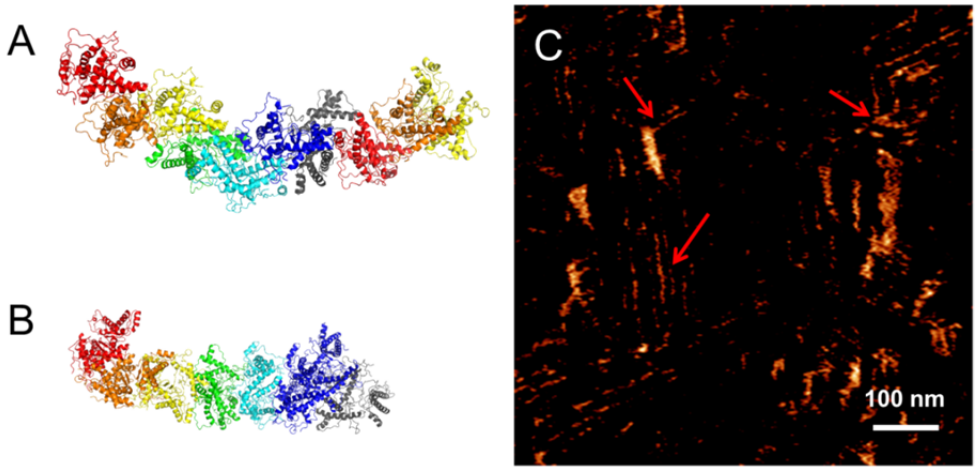

Fig. S5. The docking simulations for PrP long filaments on the second layer. (A) Docking result of 10 dimers in the form of a long filament. (B) Docking result of 7 trimers in the form of a long filament. (C) AFM image adjusted from Fig. 1C to only show the second layer. Red arrows highlight some long filaments on the second layer.

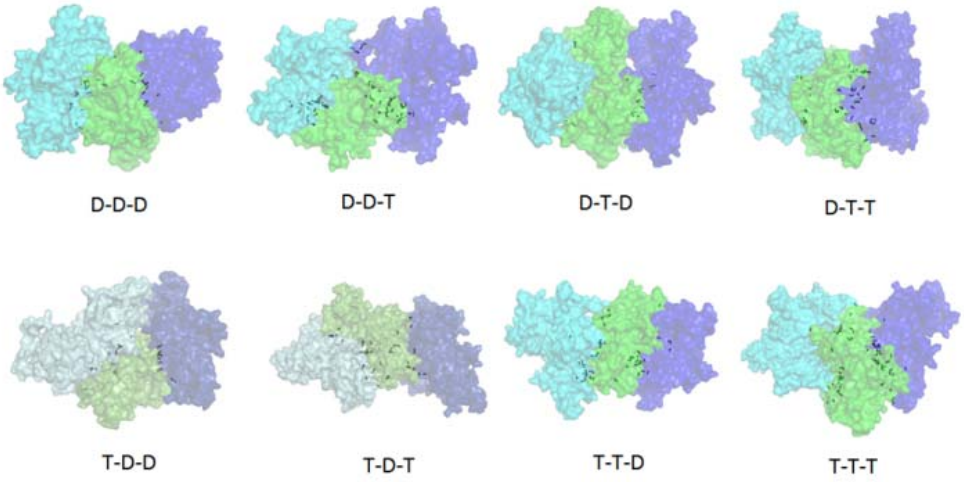

Fig. S6 The combinations of three basic units for PrP filaments on the second layer. Three different colors represent three different dimer or trimer in each aggregate. Here D and T stand for dimer and trimer, respectively. The black dash lines represent the hydrogen bonds formed on the interface of dimer and trimer. Some irregular and complex structures observed in Fig. 3B can be broken down into any of these 8 three- unit aggregates.

Table S1. Counting of different combinations of three-unit aggregates on the second layer in Fig. 3B, and comparison with simulations. Other smaller aggregates (individual dimer and trimer) on the second layer are not included. Here D represents the dimer unit, T the trimer unit.

Combination		D-D-D	D-D-T	D-T-D	D-T-T	T-D-D	T-D-T	T-T-D	T-T-T
Count in Fig.3B		5	7	7	3	5	3	4	1
Numbers of Hydrogen bonds predicted on the interfaces	Between unit A and unit B	13	18	6	6	19	12	18	15
	Between unit B and unit C	18	12	11	20	10	10	13	11
	Between unit A and unit C	0	3	0	0	0	0	0	0
	Total	31	33	17	26	29	22	31	26
Numbers of Hydrogen bonds predicted on the interfaces	Between unit A and unit B	57	52	51	52	71	71	60	65
	Between unit B and unit C	64	60	67	72	48	84	82	84
	Between unit A and unit C	0	10	0	0	0	0	0	0
	Total	120	122	118	124	119	155	142	149
Ratio of hydrogen bonds to binding residues	Between unit A and unit B	0.23	0.35	0.12	0.12	0.27	0.17	0.30	0.23
	Between unit B and unit C	0.28	0.2	0.16	0.28	0.21	0.12	0.16	0.13
	Between unit A and unit C	N/A	0.3	N/A	N/A	N/A	N/A	N/A	N/A

Table S2. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate D-D-D on the second layer in Fig. 3B. Here D represents the dimer unit. The residue numbers in PrP dimer start with 1 and end with 284, and kept same for all tables.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
D-D-D	Unit A	Chain A: Gly30, Ala31, Val32, Val33, Gly35, Leu36, Gly37, Gly38, Tyr39, Asn92, Ile93, Lys96, Val100, Thr104.	Unit A:Unit B Gly30:Ser142 Gly35:Gln213 Leu36:Asn212 Gly38:Arg189(2) Thr104:Lys247 Val175:Arg189 Gly176:Arg189(2) Leu178:Ser188 Arg217:Ser141(2) Asn227:Lys12 His230:Lys12 Asp231:Lys12 Lys238:Tyr137 Thr241:Lys17 Thr245:Lys163	Unit C	Chain A: Gly1, Gln2, Gln9, Gly34, Gly35, Leu36, Gly37, Gly38, Tyr39, Arg75, Tyr80, Asn85, Asp89, Ile93, Lys96, Thr99, Val100, Thr103, Thr104, Phe109.	Unit B:Unit C Val33:Lys238 Gly143:Thr104 Arg217:Leu320(2) Arg217:Gly35 His230:Asp89 Asp231:Gly38 Asn234:Asp89 Lys238:Gly38 Lys238:Val174 Gln239:Val175 Glu253:Gln9 Lys257:Asn85
		Chain B: Gly143, Gly145, Gln151, Val175, Gly176, Gly177, Leu178, Arg217, Tyr222, Asn224, Asn227, His230, Asp231, Ile237, Lys238, Thr241, Val242, Thr245, Thr246.			Chain B: Ala173, Val174, Val175, Gly176, Gly177, Leu178, Tyr181, Lys238, Val242, Thr246.	
	Unit B	Chain A: Gly5, His7, Ser8, Lys12, Lys17, Asp78, Tyr137, Gly140, Ser141, Ser142.		Unit B	Chain A: Ala31, Val32, Val33, Gly35, Gly37.	
		Chain B: Asn161, Lys163, His164, Met165, Ala166, Ala171, Ala186, Ser188, Arg189, His208, Asn212, Gln213, Thr244, Lys247.			Chain B: Gly143, Gly145, Thr148, Gln151, Trp152, Val175, Gly176, Gly177, Leu178, Gly180, Tyr181, Arg217, Asn224, Asn226, Asn227, His230, Asp231, Asn234, Ile235, Ile237, Lys238, Gln239, Thr241, Val242, Glu249, Phe251, Glu253, Lys257.	

Table S3. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate D-D-T on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit. The residue numbers in PrP trimer start with 1 and end with 426, and kept same for all tables.

Combination		Interface between unit A and unit B		Interface between unit B and unit C			Interface between unit A and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds		Predicted binding residues	Residues involved in hydrogen bonds		Predicted binding residues	Residues involved in hydrogen bonds
D-D-T	Unit A	Chain A: Gly1, Gln2, Gln9, Gly34, Gly35, Leu36, Gly37, Gly38, Arg75, Tyr80, Asn84, Asn85, His88, Asp89, Ile93, Lys96, Gln97, Thr99, Val100, Thr103, Thr104, Glu107, Phe109.	Unit A:Unit B Gln9:Glu253 Gly35:Arg217 Leu36:Arg217(2) Gly38:Asp231 Gly38:Lys238 Tyr80:Ile237 Asn84:Glu253 Asn85:Lys257 His88:Lys257 Asp89:His230 Asp89:Asn234 Lys96:Asn226 Lys96:His230 Gln97:Asn227 Thr104:Gly143 Val174:Lys238 Lys238:Val33	Unit C	Chain A: None.	Unit B:Unit C Gly1:Glu347 Tyr56:Asp231 Glu57:Asn234 Asp89:Arg331 Asn92:Ser330 Lys96:Sser330 Lys96:Arg331 Thr99:Ala308 Val100:Lys305 Thr104:Lys305 Glu122:Lys238	Unit C	Chain A: None.	Unit A:Unit C Glu253:Thr302(2) Lys257:Lys301
								Chain B: None.	
		Chain B: Ala173, Val174, Val175, Gly176, Gly177, Leu178, Tyr181, Lys238, Val242, Thr246.			Chain B: Gly145, Trp152, Gly177, Leu178, Gly179, Tyr181, Arg217, Tyr222, Asn227, His230, Asp231, Asn234, Ile235, Lys238, Val242, Thr245, Thr246, Gly248.			Chain C: Ser298, Lys301, Thr302, His335.	
					Chain C: Lys305, His306, Met307, Ala308, Met329, Ser330, Arg331, Arg346, Glu347, Met349, His350.				
	Unit B	Chain A: Ala31, Val32, Val33, Gly34, Gly35, Gly37,		Unit B	Chain A: Gly1, Gly3, Gln9, Trp10, Gly53, Ser54, Asp55, Tyr56, Glu57, Arg59, Tyr60, Arg75, Tyr80, Asn82, Asn84, Asn85, His88, Asp89, Asn92, Ile95, Lys96, Thr99, Val100, Thr104, Thr112, Lys115, Glu118, Arg119, Glu122, Gln123.		Unit A	Chain A: None.	
		Chain B: Gly143, Gly145, Thr148, Gln151, Trp152, Gly176, Gly177, Leu178, Tyr181, Arg217, Asn224, Asn226, Asn227, His230, Asp231, Asn234, Ile235, Ile237, Lys238, Thr241, Val242, Asn250, Phe251, Glu253, Lys257.			Chain B: Val175.			Chain B: Thr246, Gly248, Glu253, Thr254, Val256, Lys257.	

Table S4. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate D-T-D on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
D-T-D	Unit A	Chain A: Gly1, Ala31, Val33, Gly34, Gly35, Leu36, Gly37, Gly38, Tyr80, Asn92, Lys96, Gln97, Thr99, Val100, Thr104, Lys105.	Unit A:Unit B Gly1:Asn226 Gly1:His230 Gln97:Val33 Lys96:Val100 Lys105:Gln422 Asn227:Lys305	Unit C	Chain A: Gly1, Gln2, Ala31, Val32, Val33, Gly34, Gly35, Tyr39, Tyr80, Asp89, Thr99, Val100, Thr103, Thr104, Glu107.	Unit B:Unit C Thr18:Tyr80 Met20:Tyr80 Lys21:Asp89(2) Gln138:Val242 Lys380:Lys238 Lys380:Thr241 Thr383:Lys238 Thr387:Arg217 Lys389:Val32 Phe393:Asn227
		Chain B: Gly143, Val174, Val175, Leu178, Arg217, Tyr222, Asn227, Thr246, Lys247.			Chain B: Val175, Gly176, Gly177, Leu178, Arg217, Tyr222, Asn224, Asn226, Asn227, His230, Asp231, Asn234, Ile237, Lys238, Thr241, Val242, Thr243, Thr246, Lys247.	
	Unit B	Chain A: Val32, Val33, Gly34, Gly35, Val100, Thr104.		Unit B	Chain A: Lys17, Thr18, Met20, Lys21, Gln134, Gln138, Arg139, Gly140.	
		Chain B: Gly179, Tyr222, Asn226, Asn227, His 230, Lys238, Val242, Phe251.			Chain B: Met165, Ala166, Ala169, Ala171, Gly172, Ala173, Met187, Ser188.	
		Chain C: Lys301, Thr302, Met304, Lys305, Ala308, Ala310, Ala311, Ala312, Ala313, Arg415, Gln418, Gln422.			Chain C: Val317, Gly319, Tyr323, Arg359, His372, Asn376, Ile379, Lys380, Thr383, Val384, Thr387, Thr388, Lys389, Glu391, Asn392, Phe393, Glu395.	

Table S5. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate D-T-T on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
D-T-T	Unit A	Chain A: Gly1, Ala31, Val32, Val33, Gly34, Gly35, Gly37, Gly38, Tyr80, Asn92, Lys96, Gln97, Thr99, Val100, Thr104, Gly143, Val174, Val175, Leu178, Tyr181, Arg217, Asn227, Tyr246, Lys247.	Unit A:Unit B Gly1:Asn226 Tyr80:Asn227 Lys96:Val100 Lys96:Thr104 Gln97:Val33 Asn227:Lys305	Unit C	Chain A: Val33, Gly34, Gly35, Asn52, Asp89, Asn92, Lys96, Val100, Thr103, Thr104, Lys105, Gly106, Glu107, Asn108, Lys115, Glu118.	Unit B:Unit C Lys15:Asp89 Lys15:Asn92 Lys21:Glu118 Gln138:Gln422 Ser141:Ser426 Ala168:Asn108 Ala170:Asn108 Ser188:Ser284 Arg189:Ser284(2) Asn368:Lys301 Asn369:Lys309 His372:Tyr421 Asn376:Gln418 Lys380:Gln418 Lys389:Thr104 Asn392:Gly180 Glu395:Ser330 Glu402:His306 Glu406:Lys305
		Chain B: None.			Chain B: Thr148, His149, Ser150, Gly180, Tyr181, Tyr222, Ser284.	
					Chain C: Lys299, Lys301, Thr302, Met304, Lys305, His306, Ala308, Gly309, Ala311, Ser330, Gln418, Tyr421, Gln422, Gly424, Ser426.	
	Unit B	Chain A: Val32, Val33, Gly34, Gly35, Val100, Thr104.		Unit B	Chain A: Lys15, Lys17, Met20, Lys21, Gln138, Gly140, Ser141.	
		Chain B: Gly179, Tyr222, Asn226, Asn227, His230, Lys238, Val242, Thr245, Asn250.			Chain B: Ala168, Ala169, Ala170, Ala171, Ser188, Arg189, His208.	
		Chain C: Lys301, Thr302, Met304, Lys305, His306, Ala308, Gly309, Ala310, Ala311, Ala312, Ala313, Arg415, Gln418.			Chain C: Gln293, Trp294, Asn366, Asn368, Asn369, His372, Asn376, Lys380, Thr383, Val384, Thr388, Lys389, Gly390, Asn392, Phe393, Glu395, Val398, Lys399, Glu402, Glu406.	

Table S6. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate T-D-D on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
T-D-D	Unit A	Chain A: Val32, Val33, Gly34, Gly35, Thr99, Val100, Thr104, Gly104.	Unit A:Unit B Val33:Gln97 Val100:Lys96 Thr104:Lys96 Tyr222:Arg75(2) Tyr222:Tyr80 Asn226:Gly1 Asn227:Tyr80 His230:Gly1 Asn231:Tyr80 Thr246:Thr246 Lys305:Asn227 Lys305:Asp231 His306:Arg217 Ala308:Tyr181 Ser330:Lys238 Arg331:Lys238 Tyr421:Lys105 Gln422:Lys105	Unit C	Chain A: Ala31, Val33, Gly34, Gly35, Gly37, Lys96, Val100.	Unit B:Unit C His7:Asn224 His7:Asn226 Lys12:Asn227 Lys12:Asp231 Pro13:Asn234 Lys17:Thr241 Lys17;Thr245 Tyr137:Lys238 Arg139:Tyr181 Arg139:Arg217
		Chain B: Gln151, Gly179, Tyr222, Asn226, Asn227, His230, Asp231, Asn234, Ile235, Lys238, Thr241, Val242, Thr245, Thr246.			Chain B: Trp152, Gly177, Tyr181, Arg217, Tyr222, Asn224, Asn226, Asn227, His230, Asp231, Asn234, Ile237, Lys238, Thr241, Val242, Thr245, Thr246, Phe251.	
		Chain C: Lys301, Met304, Lys305, His306, Met307, Ala308, Gly309, Ala310, Ala311, Ala312, Ser327, Ser330, Arg331, Tyr421, Gln422.				
	Unit B	Chain A: Gly1, Gln9, Ala31, Val32, Val33, Gly35, Leu36, Gly37, Gly38, Arg75, Tyr80, Ile95, Lys96, Gln97, Thr99, Val100, Thr104, Lys105, Phe109.		Unit B	Chain A: His7, Ser8, Asn11, Lys12, Pro13, Lys15, Lys17, Thr18, Tyr137, Gln138, Arg139, Gly140, Ser141, Ser142.	
		Chain B: Gly143, Val175, Gly177, Leu178, Tyr181, Arg217, Tyr222, Asn227, Asp231, Ile235, Lys238, Thr241, Val242, Thr246, Lys247.			Chain B: Asn161, Lys163, Met165, Ala166, Ala171, Ser188, Glu205, His208, Asn212.	

Table S7. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate T-D-T on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
T-D-T	Unit A	Chain A: Val 32, Val33, Gly34, Gly35, Val100, Thr104, Lys105.	Unit A:Unit B Val33:Gln97 Val100:Lys96 Asn226:Gly1 Asn227:Tyr80 His230:Gly1 Lys305:Asn227 His306:Arg217 Ser330:Lys238 Arg331:Thr241 Arg346:Glu253 Tyr421:Lys105 Gln422:Lys105	Unit C	Chain A: Val33, Gly35, Asn92, Lys96, Va100, Thr104, Glu111.	Unit B:Unit C Ala171:Lys301 Ser188:Gln422 His193:Thr104 Asp197:Tyr222 Glu205:Ala310 Glu205:Ala311 Asn212:Lys299(2) Lys247:Thr302(2) Gly248:Lys305 Glu249:Lys305
		Chain B: Gln151, Tyr222, Asn226, Asn227, His230, Asn234, Ile235, Thr241, Val242, Thr245, Thr246, Phe251.			Chain B: Gly143, Arg217, Tyr222.	
		Chain C: Lys301, Thr302, Met304, Lys305, His306, Met307, Ala308, Gly309, Ala310, Ala311, Ala312, Ser327, Ser330, Arg331, Arg346, Gln418, Tyr421, Gln422.			Chain C: His291, Lys296, Ser298, Lys299, Lys301, Thr302, Met304, Lys305, His306, Ala308, Gly309, Ala310, Ala311, Gln418, Ala419, Tyr421, Gln422, Gly424.	
	Unit B	Chain A: Gly1, Gln2, Gln9, Ala31, Val32, Val33, Gly35, Gly37, Tyr80, Asn92, Ile95, Lys96, Gln97, Thr99, Val100, Thr104, Lys105,		Unit B	Chain A: His7, Tyr137, Gln138, Gly140, Ser141, Ser142.	
		Chain B: Gly143, Val175, Gly177, Leu178, Tyr181, Arg217, Tyr222, Asn227, his230, Asp231, Ile235, Ile237, Lys238, Thr241, Thr246, Lys247, Glu253.			Chain B: Thr160, Lys163, Met165, Ala169, Ala171, Ala173, Ala186, Ser188, Arg189, Ile191, His193, Gly195, Asp197, Arg204, Glu205, His208, Asn212, Thr244, Lys247, Gly248, Glu249.	

Table S8. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate T-T-D on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
T-T-D	Unit A	Chain A: Val33, Val100, Thr104, Lys105.	Unit A:Unit B Gln151:Ser338 Asn226:Asp339 Asn227:Asp342 Asn227:Arg331 Asp231:Arg331(2) Lys238:His350 Lys305:Val100 Arg331:Asn227 Arg331:Asp231(2) Arg346:His230 Glu347:his230 Glu347:Asn234 His350:Lys238	Unit C	Chain A: Gly143, Gln144, Gly145, Gln151, Trp152, Gly172, Ala173, Val174, Val175, Gly176, Glu177, Leu178, Gly180, Tyr181, Arg217, Asp220, Tyr222, Asn224, Asn227, Asp231, Ile237, Lys238, Gln239, Thr241, Val242, Thr245, Thr246, Phe251, Thr252, Glu253.	Unit B:Unit C Lys21:Aasp373(2) His22:Tyr323 Ala171:Lys238 Ser188:Arg217 Ser188:Asp231 Arg189:Asn227(2) Gln213:Lys238 Gly319:Gln239 Lys380:Thr246
		Chain B: Gln151, Trp152, Arg217, Tyr222, Asn226, Asn227, His230, Asp231, Asn234, Lys238.			Chain B: Ala315, Val316, Val317, Gly319, Leu320, Gly322, Tyr323, Arg359, Tyr364, Asn369, Aasp373, Lys380, Thr387, Thr388, Lys389, Phe393.	
		Chain C: Thr302, Asn303, Met304, Lys305, His306, Ala308, Ala310, Arg331, Ile333, His335, Gly337, Asp339, Arg346, Glu347, His350.				
	Unit B	Chain A: Val33, Val100, Thr101, Thr104.		Unit B	Chain A: Met20, Lys21, His22, Met23, Ala24, Gly25, Ala26, Asp55, Arg62.	
		Chain B: Gly145, Gln151, Trp152, Arg217, Tyr222, Asn226, Asn227, His230, Asp231, Asn234, Lys238.			Chain B: Met162, Lys163, Met165, Ala166, Gly167, Ala168, Ala169, Ala170, Ala171, Met187, Ser188, Arg189, Ile191, Asn212, Gln213.	
		Chain C: Thr302, Met304, Lys305, Met307, Ala308, Ala310, Arg331, Ile333, His335, Gly337, Ser338, Asp339, Asp342, Arg346, Glu347, His350.			Chain C: Val317, Gly318, Gly319, Lys380, Gln381, Thr383, Val384, Thr387, Thr388, Glu391, Asn392, Phe393.	

Table S9. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces for three-unit aggregate T-T-T on the second layer in Fig. 3B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B		Interface between unit B and unit C		
		Predicted binding residues	Residues involved in hydrogen bonds	Predicted binding residues		Residues involved in hydrogen bonds
T-T-T	Unit A	Chain A: Val33, Val100, Thr101, Thr104,	Unit A:Unit B Glu151:Ser338 Asn227:Arg331 His230:Glu347 Asp231:Arg221(2) Lys238:His350 Thr302:Thr104 Lys305:Val100 Arg331:Asn227 Arg331(2):Asp231 Ser338:Gln151 Asp339:Asn226 Arg346:His230 Glu347:His230 His350:Lys238	Unit C	Chain A: Val33, Thr104, Lys105.	Unit B:Unit C Lys21:Tyr198 Lys21:Glu199 Ala24:Lys257 Gln134:Asn226 Gln138:Asn153 Arg139:Gln151 Glu205:Arg346 His208:Arg331(2) His208:Arg346 Lys247:Ala308 Glu249:Arg331 Tyr364:Gln151 His372:Gln144 Lys380:Tyr222 Lys380:Asn227 Gln381:His230 Thr383:Arg217 Val384:Lys238 Glu395:Thr104 Glu402:Gly143
		Chain B: Gly145, Gln151, Trp152, Gly180, Arg217, Tyr222, Asn226, Asn227, His230, Asp231, Asn234, Lys238.			Chain B: Gly143, Gln144, Gly145, Ser150, Gln251, Trp152, Asn153, Gly179, Gly180, Tyr181, His193, Phe194, Gly195, Tyr198, Glu199, Arg217, Tyr222, Gln225, Asn226, Asn227, His230, Asn234, Ile235, Lys238, Asn250, Phe251, Thr252, Glu253, Lys257, Arg263, Glu264, Gln265, Ile268.	
		Chain C: Thr302, Met304, Lys305, His306, Ala308, Ala310, Arg331, Ile333, His335, Gly337, Ser338, Asp339, Arg346, Glu347, His350.			Chain C: Met449, Ala450, Ala453, Ser472, Arg473, Arg488, Glu489, Met491, His492.	
	Unit B	Chain A: Val33, Val100, Thr104.		Unit B	Chain A: Lys15, Thr18, Met20, Lys21, His22, Ala24, Gln134, Ala135, Gln138, Arg139, Gly140.	
		Chain B: Gly145, Gln151, Trp152, Arg217, Tyr222, Asn226, Asn227, His230, Asp231, Asn234, Lys238, Phe251.			Chain B: Ala166, Ala168, Ala169, Gly172, Arg204, Glu205, Thr246, Lys247, Gly248, Glu249.	
		Chain C: Lys301, Thr302, Met304, Lys305, His306, Met307, Ala308, Gly309, Ala310, Arg311, Ile313, His335, Gly337, Ser338, Asp339, Asp342, Arg346, Glu347, His350.			Chain C: Gly319, Arg359, Tyr364, His372, Asn376, Ile379, Lys380, Gln381, Thr383, Val384, Thr387, Thr388, Glu391, Asn392, Phe393, Thr394, Glu395, Glu402.	

Table S10. The numbers of predicted binding residues and hydrogen bonds for the two-unit aggregate formed by dimers and trimmers in the first and second layers in Fig.4. Here D represents the dimer unit, T the trimer unit.

Combination		D-D	D-D	T-D	T-T
Numbers of Hydrogen bonds predicted on the interfaces	Between unit A in first layer and unit B in second layer	59	91	61	75
Numbers of hydrogen bonds predicted on the interfaces	Between unit A in first layer and unit B in second layer	25	29	26	19
Ratio of hydrogen bonds to binding residues	Between unit A in first layer and unit B in second layer	0.42	0.32	0.43	0.25

Table S11. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces between the first layer and the second layer in Fig. 4A. Here D represents the dimer unit.

<table>
<tr><td colspan="2" rowspan="2">Combination</td><td colspan="2">Interface between unit A and unit B</td></tr>
<tr><td>Predicted binding residues</td><td>Residues involved in hydrogen bonds</td></tr>
<tr><td rowspan="4">D-D</td><td rowspan="2">Unit A</td><td>Chain A:
Gly3, Gln9, Trp10, Gly35, Tyr39, Ser54, Tyr56, Glu57, Arg75, Tyr80, Ser81, Asn82, Gln83, Asn84, Asn85, Val87, His88, Val91, Asn92, Ile95, Lys96, Gln97, Glu111, Thr112, Lys115, Glu118, Arg119, Glu122, Gln123, Ile126.</td><td rowspan="4">Unit A:Unit B
Tyr39:Asn226
Arg75:Asn227
Tyr80:Asp231
Tyr80:Lys238
Ser81:His230
Asn82:Ile237
Asn84:Glu260
Asn85:His230(2)
Val87:Lys257
His88:Glu260
Asn92:Asn226
Lys96:Glu264
Tyr56:Asp197
Tyr56:Tyr198
Lys115:Glu199
Arg119(2):Glu199
Gln123:Glu253
Glu118:Arg261
Arg119(2):Thr254</td></tr>
<tr><td>Chain B:
None.</td></tr>
<tr><td rowspan="2">Unit B</td><td>Chain A:
None.</td></tr>
<tr><td>Chain B:
Gln151, Trp152, His193, Phe194, Gly195, Ser196, Asp197, Tyr198, Glu199, Asn226, Asn227, Val229, His230, Asp231, Val233, Asn234, Ile237, Lys238, His240, Thr241, Phe251, Glu253, Thr254, Lys257, Met258, Glu260, Arg261, Glu264, Ile268.</td></tr>
</table>

Table S12. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces between the first layer and the second layer in Fig. 4B. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B	
		Predicted binding residues	Residues involved in hydrogen bonds
D-T	Unit A	Chain A: Gly1, Thr6, Gln9, Trp10, Tyr39, His51, Phe52, Gly53, Ser54, Tyr56, Glu57, Arg59, Arg75, Tyr80, Asn84, His88, Asp89, Asn92, Ile93, Ile95, Lys96, Gln97, Thr99, Val100, Thr103, Thr104, Gly106, Glu107, Phe109, Thr110, Glu111, Thr112, Val114, Lys115, Glu118, Arg119, Glu122, Gln123, Ile126,	Unit A:Unit B Gln9:Gly35 Gln9:Gln97 Tyr39:Asn227 Ser54:Ile334 Tyr56:Asp342 Glu57:Arg331(2) Glu57:Ile334 Glu57:Ile335 Tyr80:Asp220 Asp84:Ala310(2) His88:Gly180 Asp89:Arg217(2) Asn92:Lys238 Lys96:Tyr181 Lys96:Asp231(2) Thr99:Asn234 Thr99:Lys257 Glu111:Thr241 Thr112:Glu347 Lys115:Glu177 Lys115:Gln239 Glu118:Gln239 Arg119:Ser330 Glu122:Gly309 Gln123:Ala308
		Chain B: Ala173, Val175.	
	Unit B	Chain A: Val33, Gly34, Gly35, Gln97, Val100, Thr104, Lys105.	
		Chain B: Gly143, Gln144, Gly145, Thr148, Gly177, Gly180, Tyr181, Arg217, Asp220, Tyr222, Asn227, His230, Asp231, Asn234, Ile237, Lys238, Gln239, Thr241, Val242, Thr245, Thr246, Phe251, Glu253, Val256, Lys257, Glu260.	
		Chain C: Met307, Ala308, Gly309, Ala310, Ala311, Ser330, Arg331, Pro332, Ile333, Ile334, His335, Asp342, Tyr345, Agrg346, Glu347, Met349, His350.	

Table S13. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces between the first layer and the second layer in Fig. 4C. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B	
		Predicted binding residues	Residues involved in hydrogen bonds
T-D	Unit A	Chain A: Arg59, Tyr60, Glu63, His66, Asn108, Thr110.	Unit A:Unit B Tyr60:Gln151 Glu63:Trp152 Asn108:His149 Thr110:Ser150 His149:Thr269 Ser150:Glu272 Gln151:Gln265 Trp152:Thr269 Asn153:Glu264 Lys154:Gln225 Ser156:Glu264 Lys159:Asn227 Thr160:His230 His193:Thr254 Glu199:Arg201(2) Gln225:Glu199 His230:Gly195 Arg261:Asp197 Arg261:Tyr198 Glu264:Asp197 Glu272:Lys257 Tyr279:Asn226 Ser283:Asn153 Ser284:Ser156(2)
		Chain B: His149, Ser150, Gln151, Trp152, Asn153, Lys154, Ser156, lys157, Lys159, Thr160, Ile191, Ile192, His193, Glu199, Gln225, Asn226, Val229, His230, Arg261, Glu264, Ile268, Glu272, Tyr279, Gly282, Ser283, Ser284.	
		Chain C: None.	
	Unit B	Chain A: None.	
		Chain B: Thr148, His149, Ser150, Gln151, Trp152, Asn153, Ser156, Ile191, his193, Gly195, Ser196, Asp197, Tyr198, Glu199, Arg201, Gln225, Asn226, Asn227, His230, Asn234, Glu253, Thr254, Lys257, Arg261, Glu264, Gln265, Ile268, Thr269, Glu272.	

Table S14. Docking simulations of the interface residues and hydrogen bonds formed on the interfaces between the first layer and the second layer in Fig. 4D. Here D represents the dimer unit, T the trimer unit.

Combination		Interface between unit A and unit B	
		Predicted binding residues	Residues involved in hydrogen bonds
T-T	Unit A	Chain A: None.	Unit A:Unit B Asn226:Asp55 Lys238:Glu63 Lys238:Lys159 Thr245:Lys154 Glu253:Thr110(2) Glu253:Thr112 Glu260:Arg59 Ser330:Thr160 Arg331:Glu272 Gly337:Glu199 Asp339:Lys257 Asp339:Arg261(2) Asp342:Arg261 Arg346:Asn153 Arg346:Glu264 Glu347:Asn153(2)
		Chain B: Gly177, Gly179, Asn226, His230, Asn234, Ile235, Ile237, Lys238, Thr241, Val242, Thr245, Thr246, Glu249, Asn250, Phe251, Thr252, Glu253, Thr254, Val256, Lys257, Glu260, Glu264.	
		Chain C: Lys305, Met307, Ala308, Ala311, Ser330, Arg331, Ile333, Ile334, His335, Gly337, Asp339, Asp342, Arg343, Tyr345, Arg346, Glu347, Met349, His350, Gln407.	
	Unit B	Chain A: Asp55, Arg59, Tyr60, Arg62, Glu63, Asn64, His66, Asn108, Thr110, Thr112.	
		Chain B: Asn153, Lys154, Ser156, Lys159, Thr160, Asn161, Lys163, Met165, Ile191, His193, Ph194, Glu199, Gln225, Asn226, Lys257, Arg261, Glu264, Gln265, Ile268, Glu272, Tyr279, Arg281, Gly282, Ser284.	
		Chain C: None.	