Supplementary materials for

Design principles of caveolins across metazoa and beyond

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Figure S1

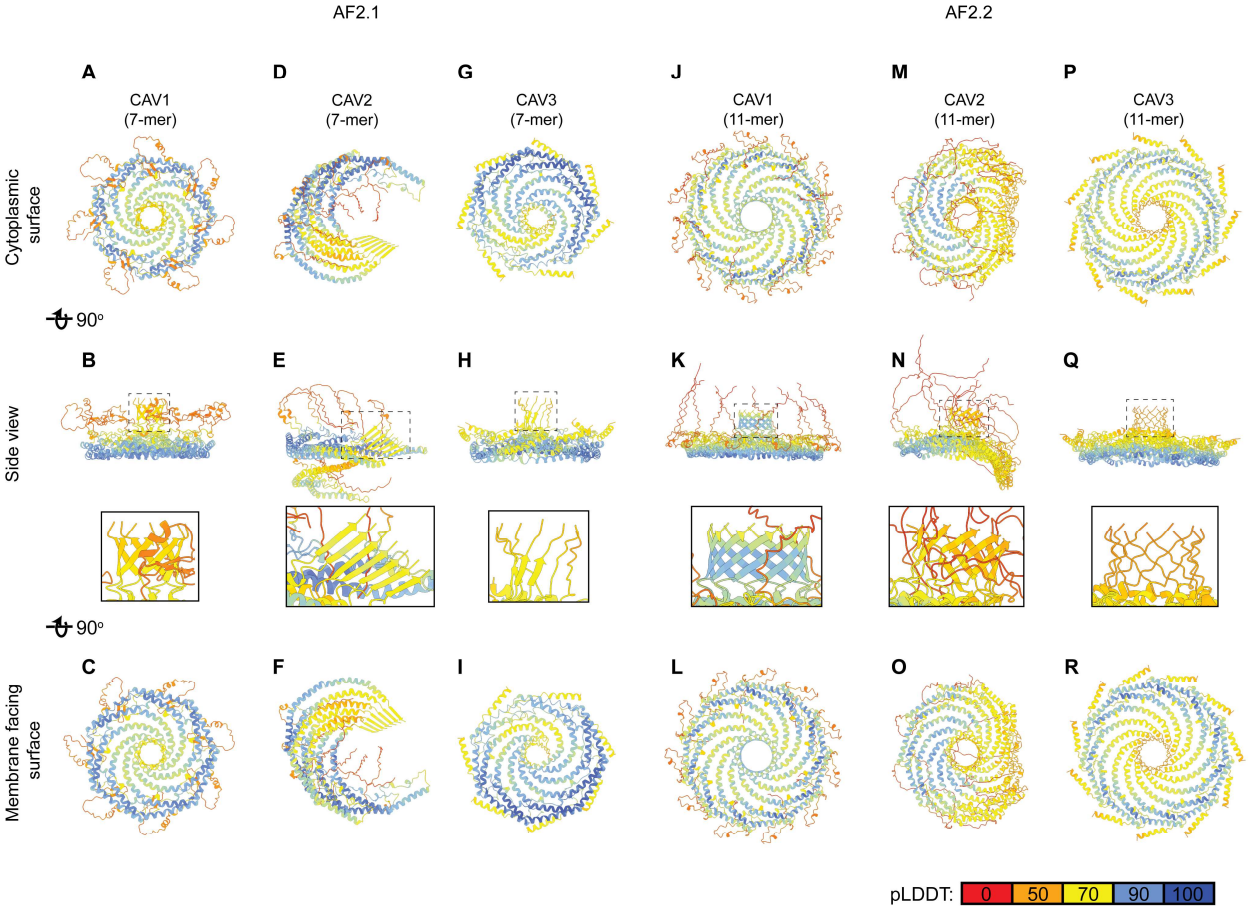

AF2.1
AF2.2
A
CAV1
(7-mer)
D
CAV2
(7-mer)
G
CAV3
(7-mer)
J
CAV1
(11-mer)
M
CAV2
(11-mer)
P
CAV3
(11-mer)
Cytoplasmic surface
90°
B
E
H
K
N
Q
Side view
90°
C
F
I
L
O
R
Membrane facing surface
pLDDT:
0
50
70
90
100

Figure S2

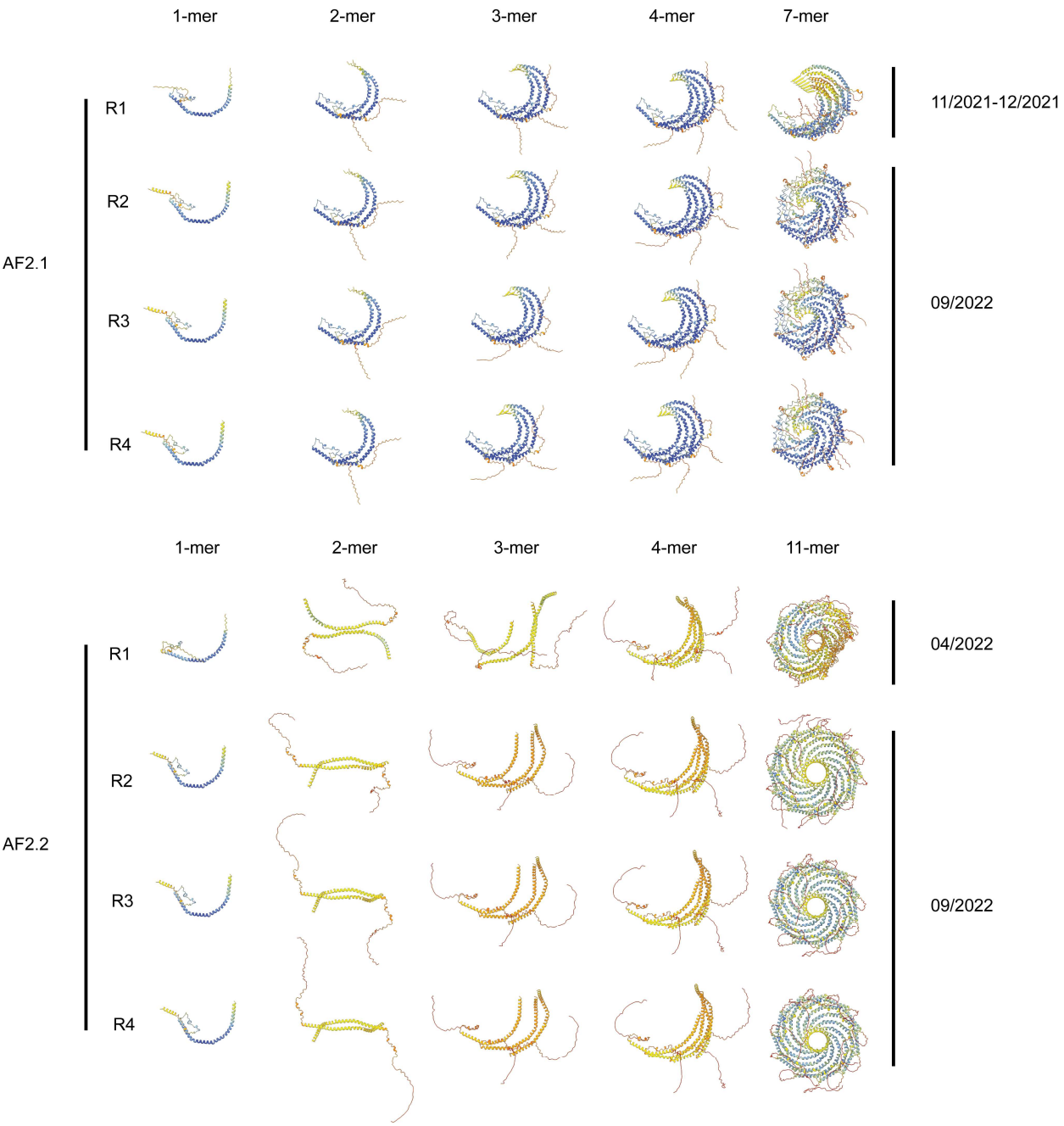

1-mer
2-mer
3-mer
4-mer
7-mer
AF2.1
R1
R2
R3
R4
11/2021-12/2021
09/2022
1-mer
2-mer
3-mer
4-mer
11-mer
AF2.2
R1
R2
R3
R4
04/2022
09/2022

Figure S3

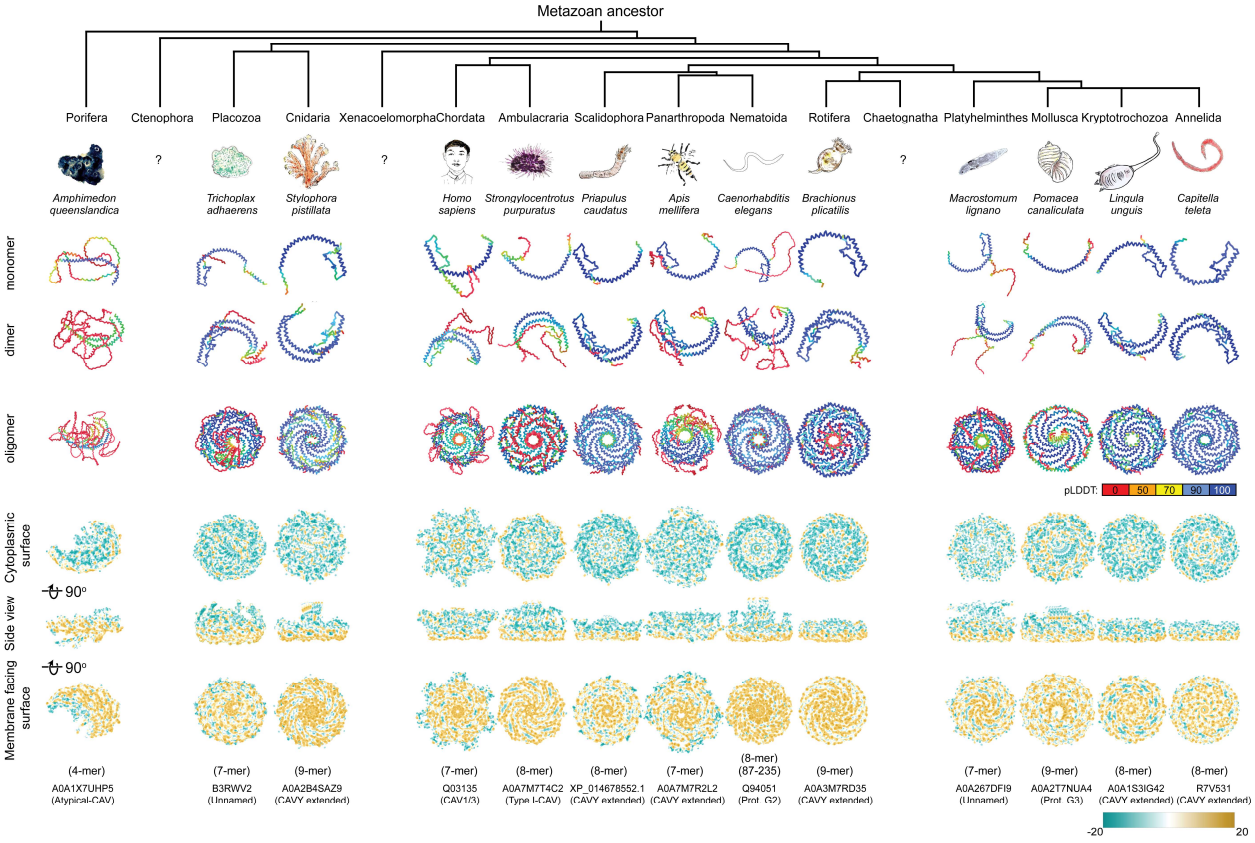

Metazoan ancestor
Porifera
Ctenophora
Placozoa
Cnidaria
Xenacoelomorpha
Chordata
Ambulacraria
Scalidophora
Panarthropoda
Nematoida
Rotifera
Chaetognatha
Platyhelminthes
Mollusca
Kryptotrochozoa
Annelida
Amphimedon queenslandica
Trichoplax adhaerens
Stylophora pistillata
Homo sapiens
Strongylocentrotus purpuratus
Priapulus caudatus
Apis mellifera
Caenorhabditis elegans
Brachionus plicatilis
Macrostomum lignano
Pomacea canaliculata
Lingula unguis
Capitella teleta
monomer
dimer
oligomer
pLDDT:
0
50
70
90
100
Cytoplasmic surface
Side view
90°
Membrane facing surface
(4-mer)
A0A1X7UHP5
(Atypical-CAV)
(7-mer)
B3RWV2
(Unnamed)
(9-mer)
A0A2B4SAZ9
(CAVY extended)
(7-mer)
Q03135
(CAV1/3)
(8-mer)
A0A7M7T4C2
(Type I-CAV)
(8-mer)
XP_014678552.1
(CAVY extended)
(7-mer)
A0A7M7R2L2
(CAVY extended)
(8-mer)
(87-235)
Q94051
(Prot. G2)
(9-mer)
A0A3M7RD35
(CAVY extended)
(7-mer)
A0A267DFI9
(Unnamed)
(9-mer)
A0A2T7NUA4
(Prot. G3)
(8-mer)
A0A1S3IG42
(CAVY extended)
(8-mer)
R7V531
(CAVY extended)
-20
20

Figure S4

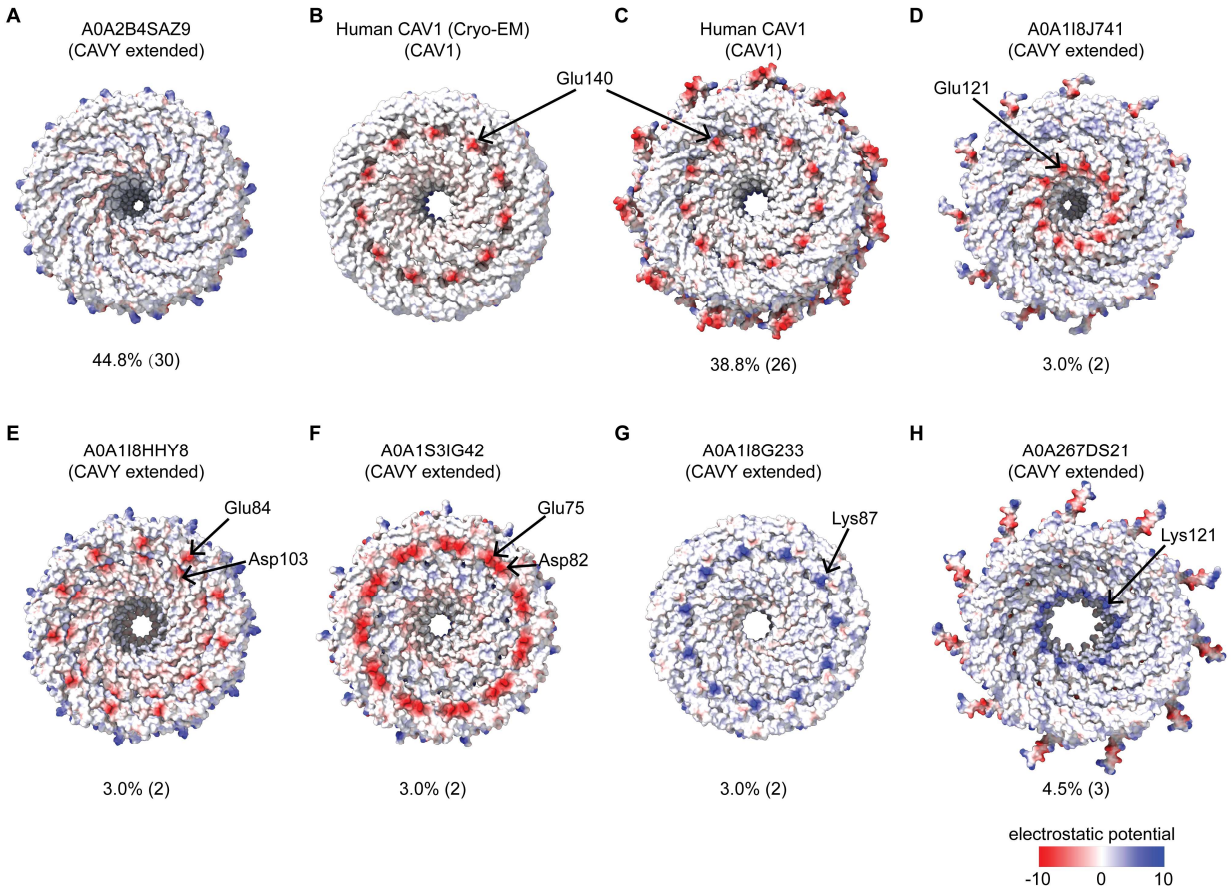

A
A0A2B4SAZ9
(CAVY extended)
44.8% (30)
B
Human CAV1 (Cryo-EM)
(CAV1)
Glu140
C
Human CAV1
(CAV1)
38.8% (26)
D
A0A1I8J741
(CAVY extended)
Glu121
3.0% (2)
E
A0A1I8HHY8
(CAVY extended)
Glu84
Asp103
3.0% (2)
F
A0A1S3IG42
(CAVY extended)
Glu75
Asp82
3.0% (2)
G
A0A1I8G233
(CAVY extended)
Lys87
3.0% (2)
H
A0A267DS21
(CAVY extended)
Lys121
4.5% (3)
electrostatic potential
-10
0
10

Figure S5

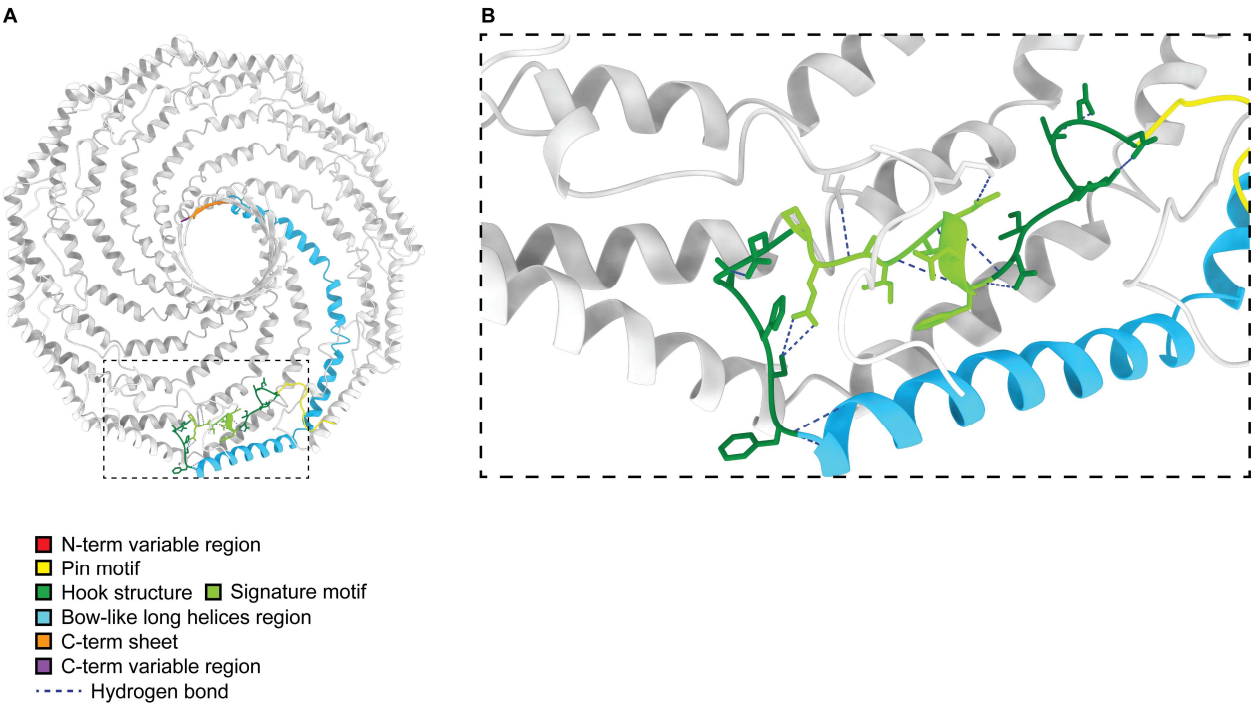

A
B
N-term variable region
Pin motif
Hook structure
Signature motif
Bow-like long helices region
C-term sheet
C-term variable region
Hydrogen bond

Figure S6

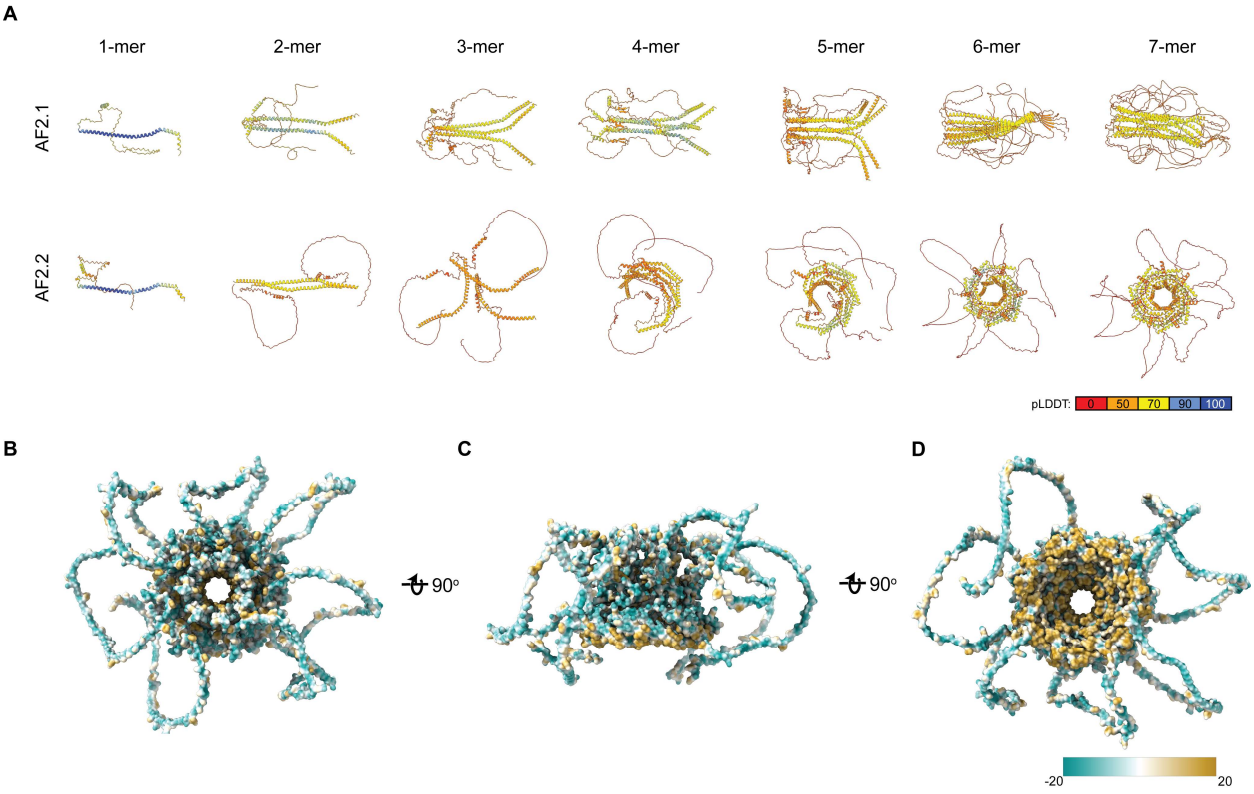

A
1-mer
2-mer
3-mer
4-mer
5-mer
6-mer
7-mer
AF2.1
AF2.2
pLDDT:
0
50
70
90
100
B
90°
C
90°
D
-20
20

Figure S7

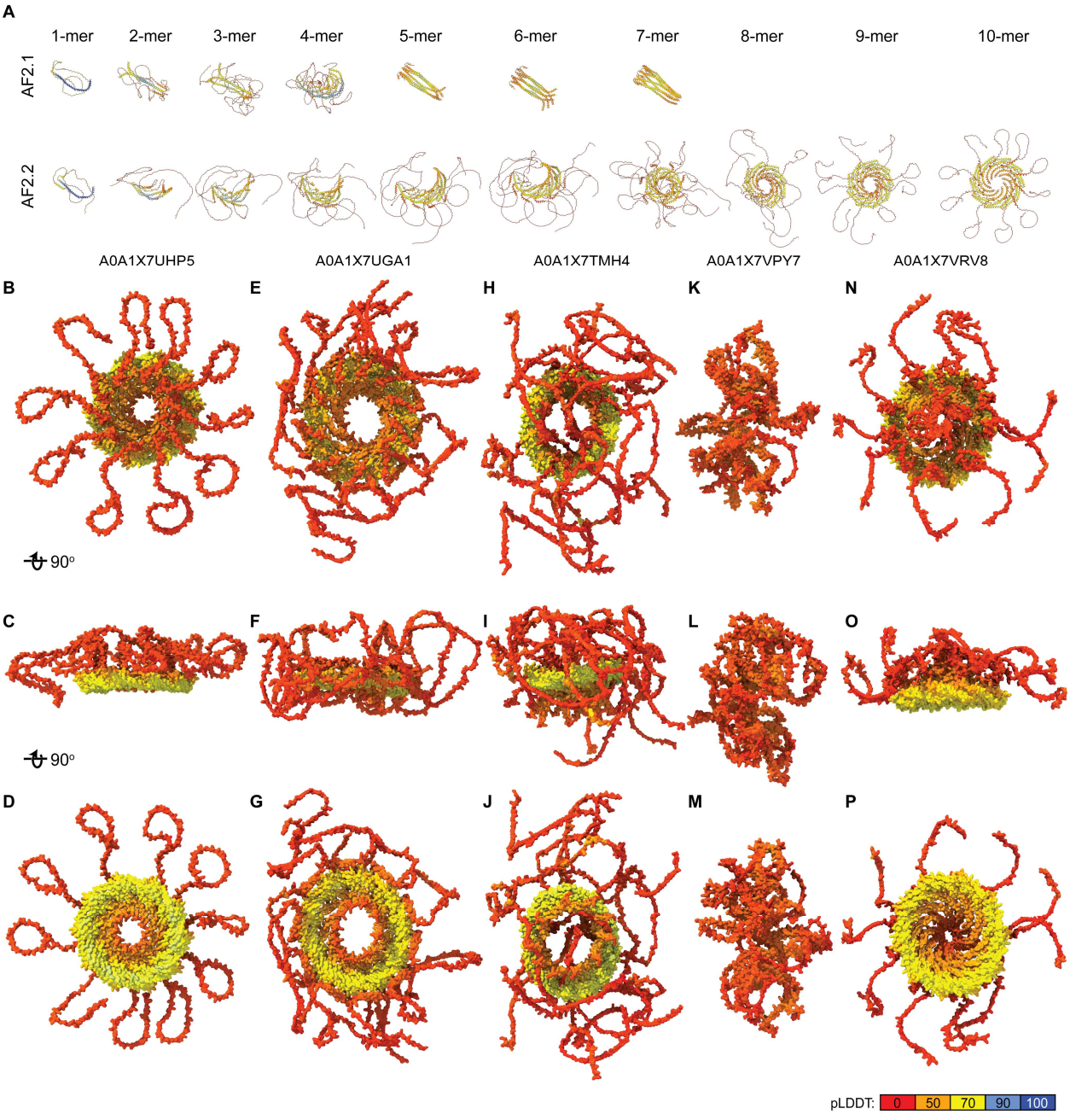

A
1-mer
2-mer
3-mer
4-mer
5-mer
6-mer
7-mer
8-mer
9-mer
10-mer
AF2.1
AF2.2
A0A1X7UHP5
A0A1X7UGA1
A0A1X7TMH4
A0A1X7VPY7
A0A1X7VRV8
B
E
H
K
N
90°
C
F
I
L
O
90°
D
G
J
M
P
pLDDT:
0
50
70
90
100

Figure S8

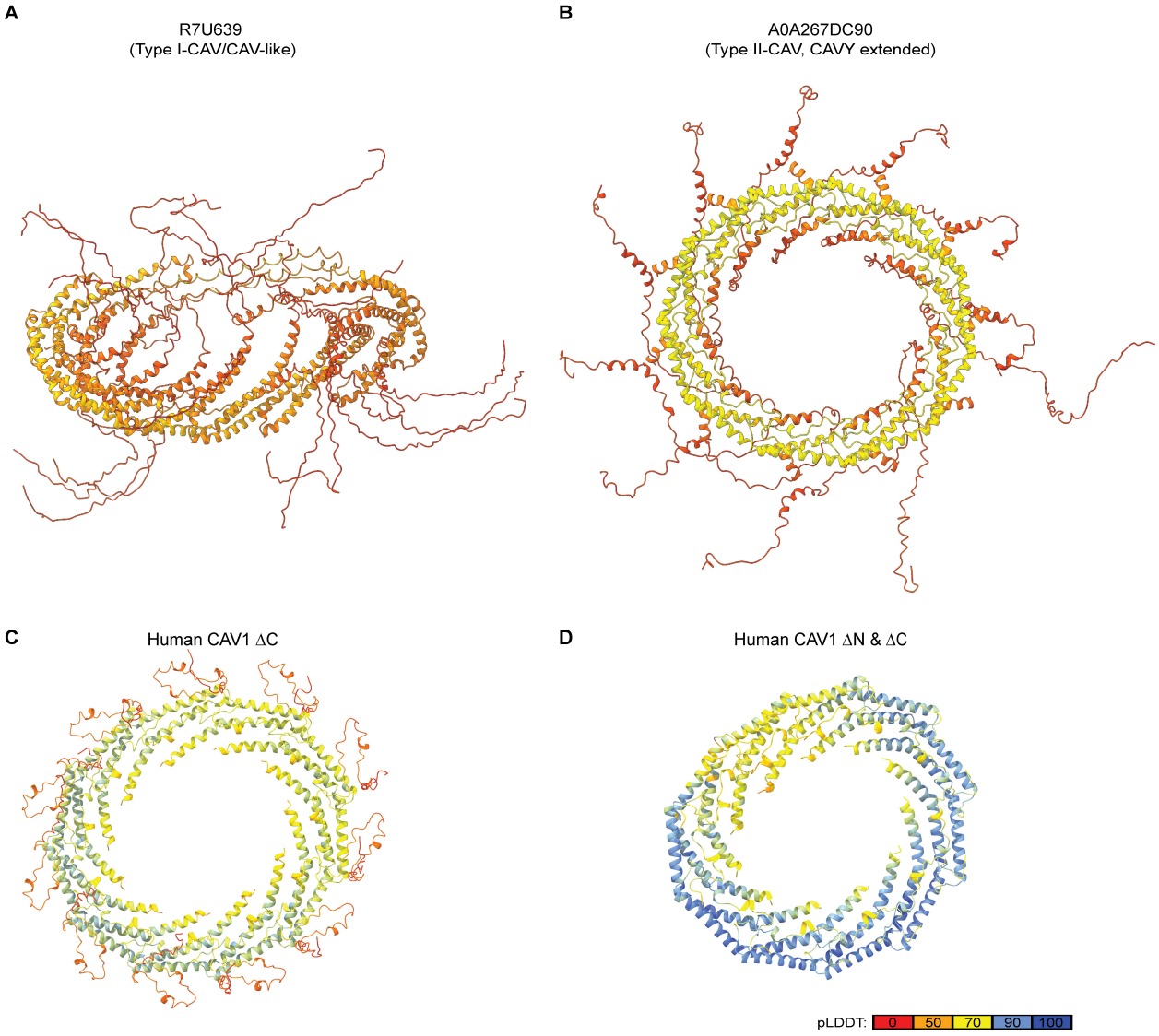

A
R7U639
(Type I-CAV/CAV-like)
B
A0A267DC90
(Type II-CAV, CAVY extended)
C
Human CAV1 ΔC
D
Human CAV1 ΔN & ΔC
pLDDT:
0
50
70
90
100

Figure S9

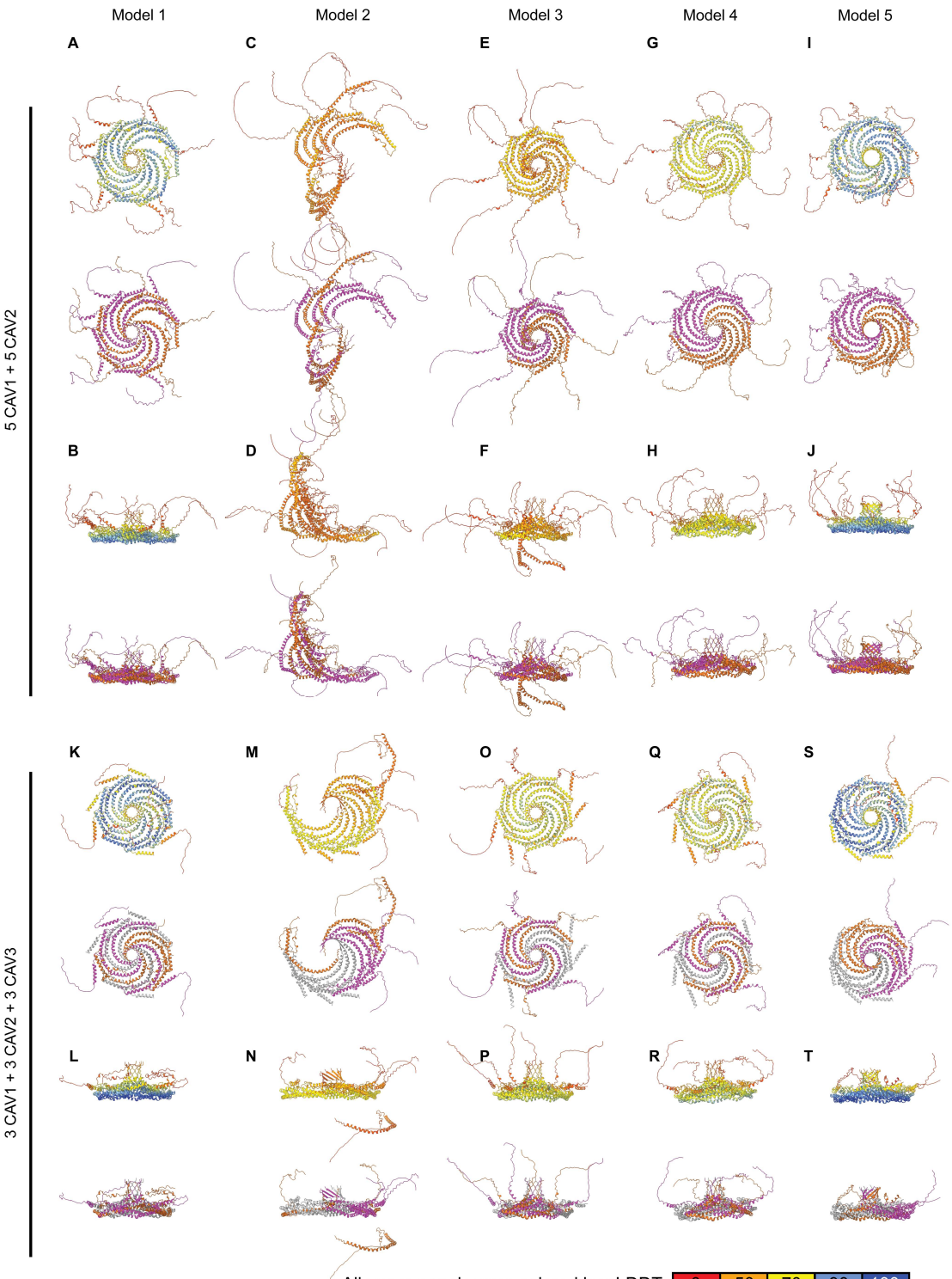
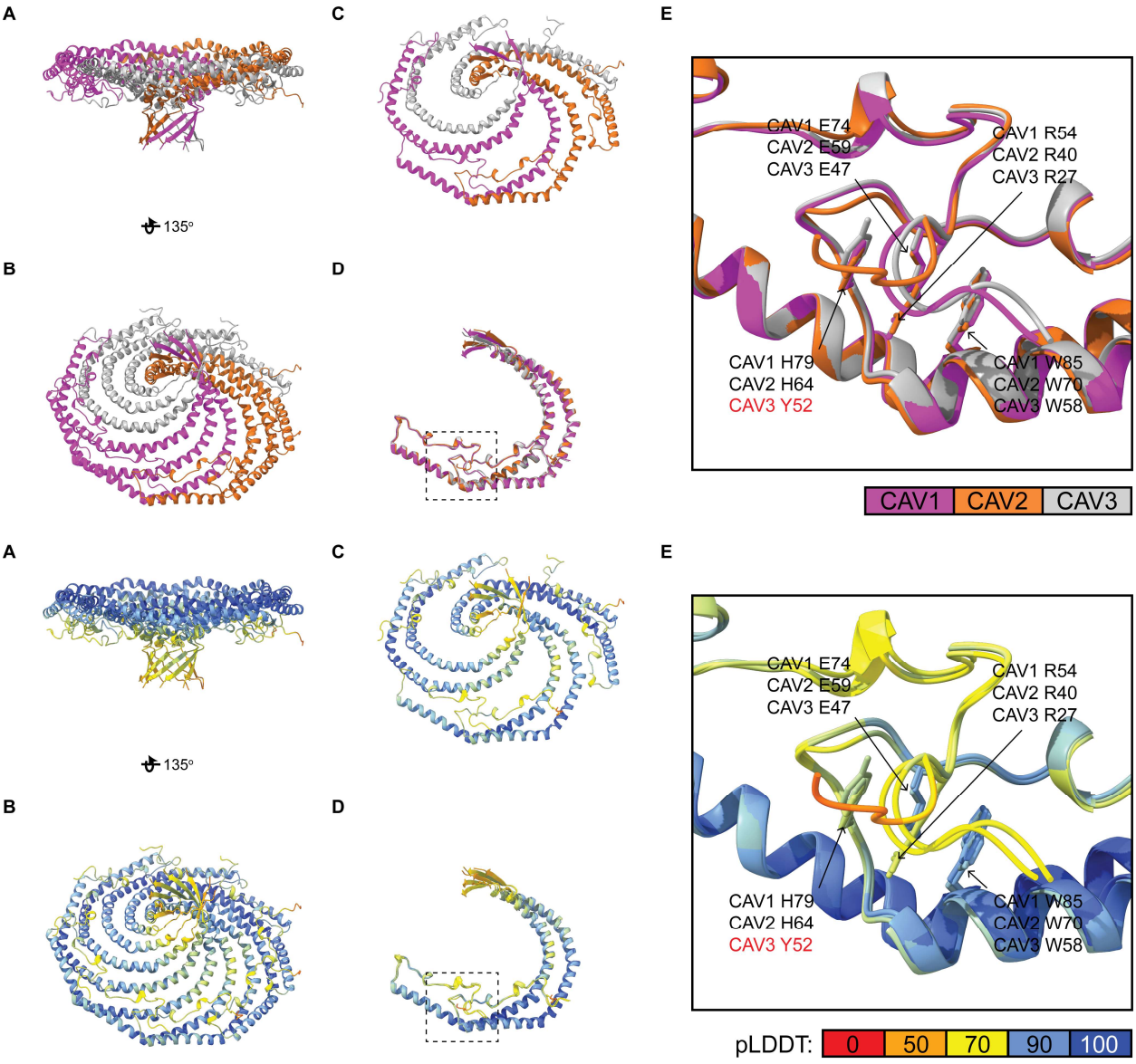

Model 1
Model 2
Model 3
Model 4
Model 5
A
C
E
G
I
B
D
F
H
J
5 CAV1 + 5 CAV2
K
M
O
Q
S
L
N
P
R
T
3 CAV1 + 3 CAV2 + 3 CAV3
All upper panels were colored by pLDDT:
0
50
70
90
100
All upper panels were colored by sequence:
CAV1
CAV2
CAV3

Figure S10


A
C
E
135°
B
D
CAV1 E74
CAV2 E59
CAV3 E47
CAV1 R54
CAV2 R40
CAV3 R27
CAV1 H79
CAV2 H64
CAV3 Y52
CAV1 W85
CAV2 W70
CAV3 W58
CAV1
CAV2
CAV3
A
C
E
135°
B
D
CAV1 E74
CAV2 E59
CAV3 E47
CAV1 R54
CAV2 R40
CAV3 R27
CAV1 H79
CAV2 H64
CAV3 Y52
CAV1 W85
CAV2 W70
CAV3 W58
pLDDT:
0
50
70
90
100

Conservation
Quality
Consensus
Occupancy

File S1. Prediction results of the structures of caveolins monomer or oligomers by AlphaFold2.1 with different protomer numbers.

Note:

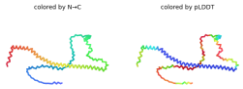
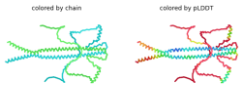
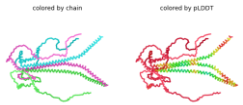
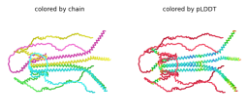
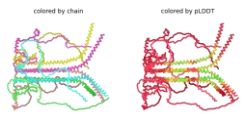
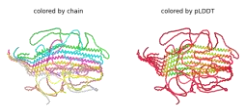
The 2D example color sketches were generated from the 3D model by AlphaFold2_advanced notebook.

The left panel of the monomers were colored by N → C; the left panel of the oligomers were colored by chain; the right panels were colored by pLDDT values as below color key indicated:

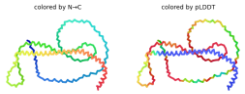
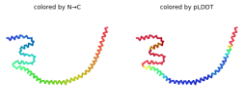
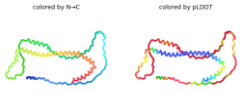
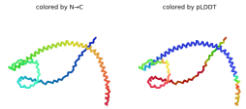
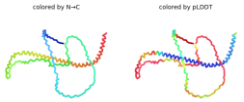
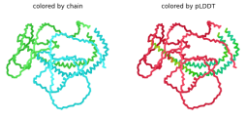
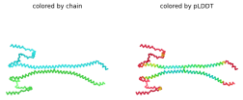
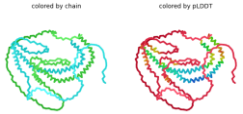
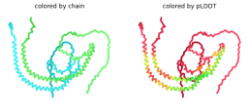
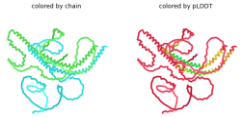
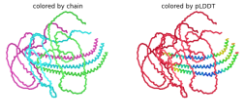
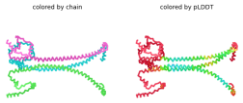
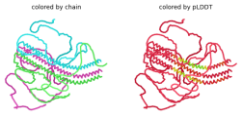
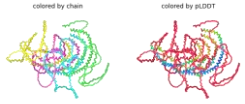
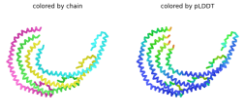
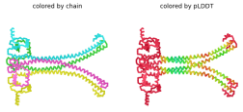
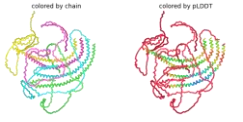
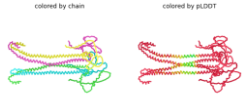
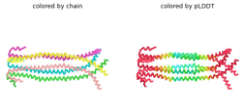
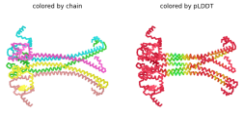
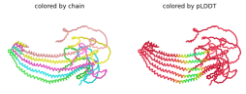
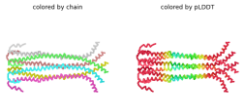
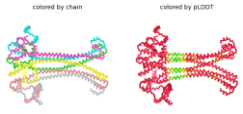
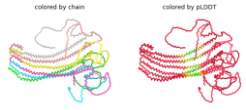
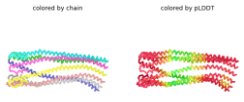
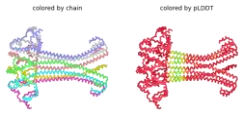
Five models were generated for each prediction. The 2D sketches were based on rank 1 models (R1) in this supplemental file if there is no special note was left under the pLDDT value.

Salpingoeca rosetta

F2U793

	pLDDT		
1-mer	73.91		
2-mer	59.81		
3-mer	47.29		
4-mer	57.45		
5-mer	42.52		
6-mer	42.05		
7-mer	45.02		

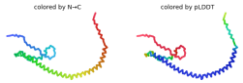
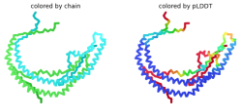
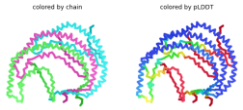
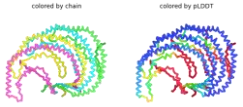
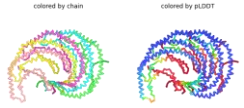
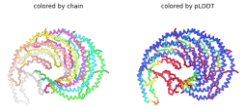
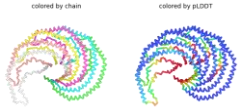
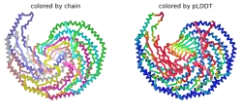
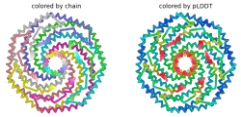
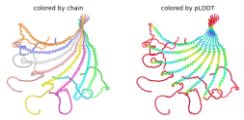
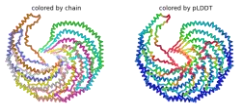
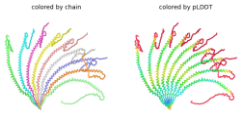
Amphimedon queenslandica

	A0A1X7UHP5	A0A1X7UGT7 A0A1X7UHP5 (182-285)	**A0A1X7VPY7**	**A0A1X7UGA1**	**A0A1X7VRV8**	**A0A1X7TMH4**
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	68.65 		69.28 	64.32 	73.34 	67.66 
2-mer	41.36 (R5) 		61.25 	50.96 	48.33 (R3) 	42.28 (R3) 
3-mer	40.06 (R2) 		54.53 	41.10 (R2)	46.90	38.45 (R2) 
4-mer	42.18 	82.77 	46.63 	40.04 	37.42 	36.54
5-mer		55.49 	41.76 	37.93	36.84 	
6-mer		53.68 	39.07 		35.60 	
7-mer		53.93 	37.63 			

Oscarella carmela

EC368417.1

EC368417.1
(22-160)

	pLDDT		*pLDDT*	
1-mer	75.60			
2-mer	73.64			
3-mer	73.41			
4-mer	72.32			
5-mer	71.13			
6-mer	69.85		78.14	
7-mer	68.87		70.80 (R3)	
8-mer	56.33		75.50	
9-mer			59.62	

Trichoplax adhaerens

B3RWV2

B3RWV2 (1-151)

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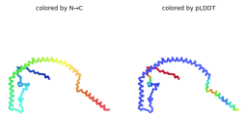
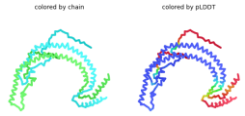
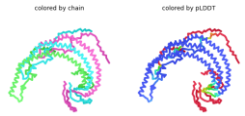
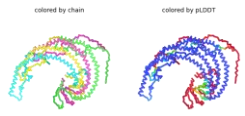
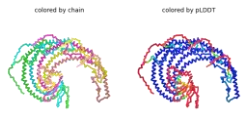
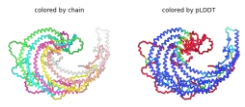
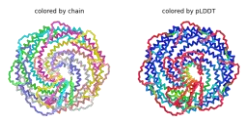
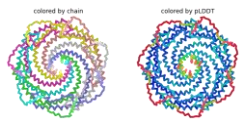
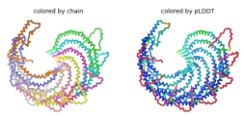
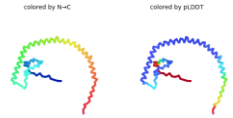
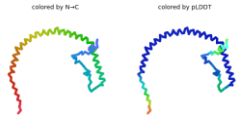
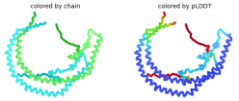
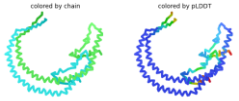
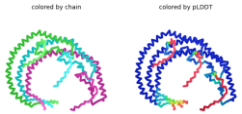
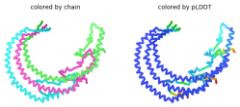
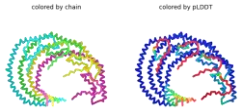
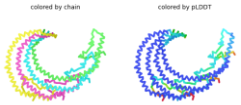
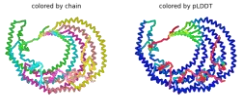
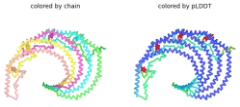
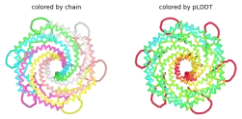
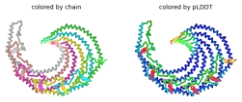
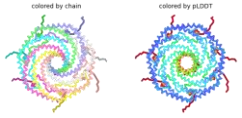
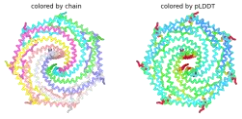
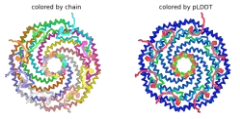
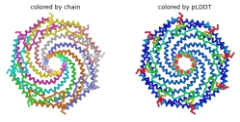
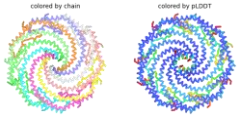
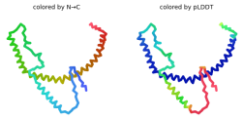
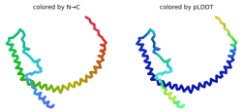
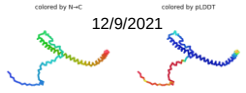
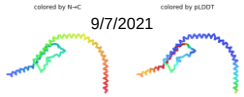
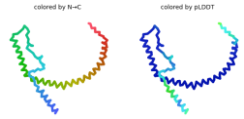
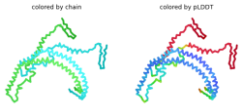
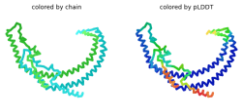
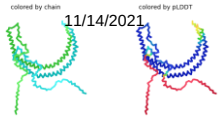
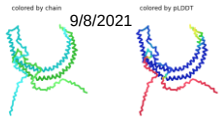
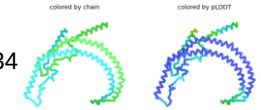
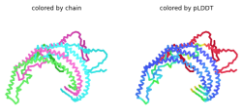
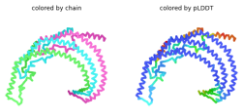
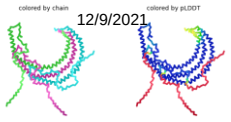
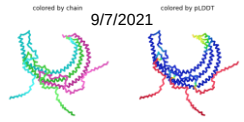
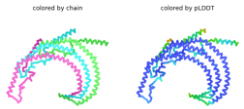
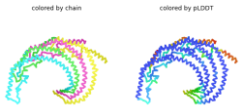
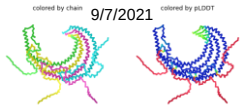
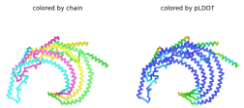
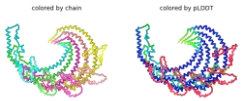
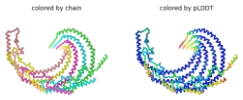
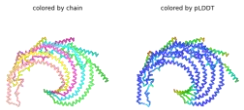
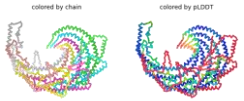
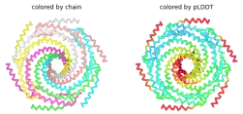
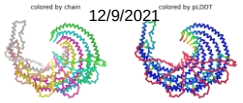
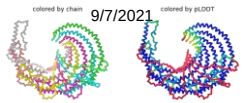
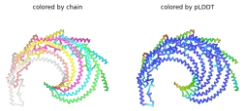
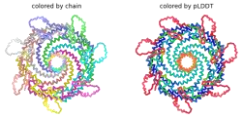
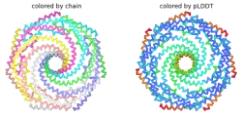
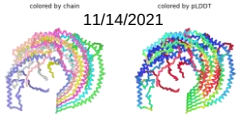
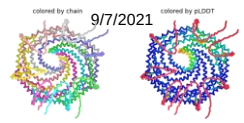
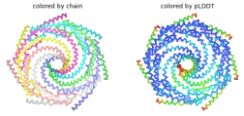
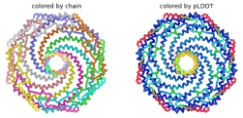
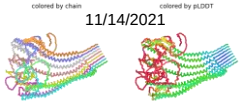
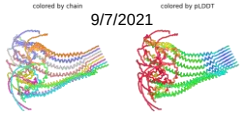
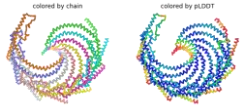
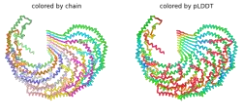
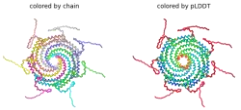
1-mer	84.57			
2-mer	77.88			
3-mer	75.07			
4-mer	74.30			
5-mer	73.37			
6-mer	70.10			
7-mer	69.58		75.76 (R2)	
8-mer			77.55	

Stylophora pistillata

	A0A2B4SEV1		A0A2B4SAZ9	
	pLDDT		*pLDDT*	
1-mer	80.64		88.47	
2-mer	79.69		87.52	
3-mer	82.25		87.38	
4-mer	80.80		85.36	
5-mer	80.20		83.95	
6-mer	60.22 (R5)		80.22	
7-mer	71.63 (R3)		71.44	
8-mer	76.17		78.22	
9-mer			79.52	

Homo sapiens

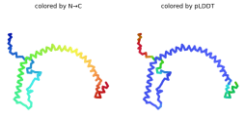
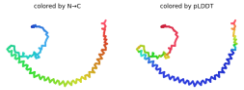
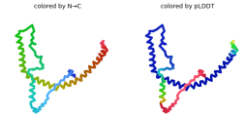
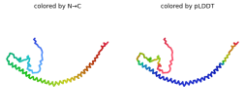
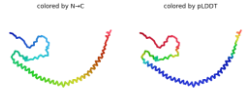
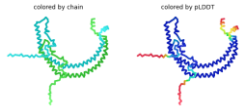
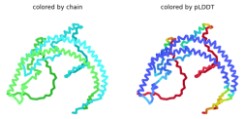
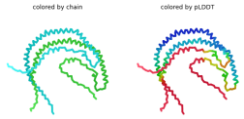
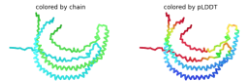
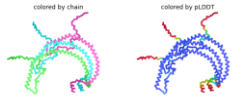
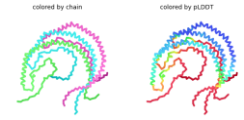
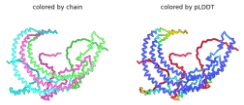
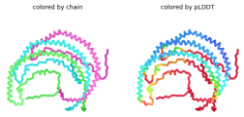
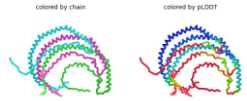
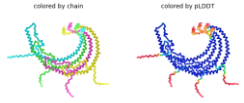
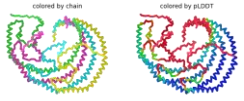
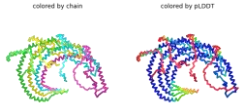
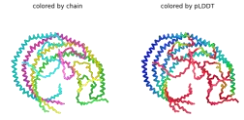
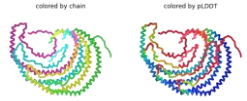
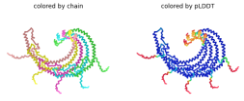
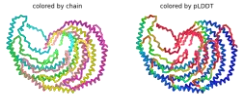
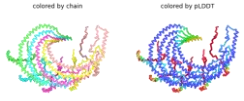
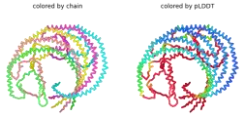
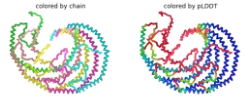
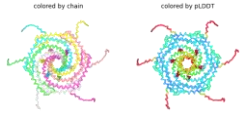
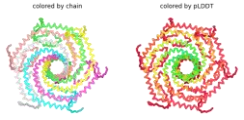
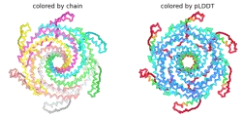
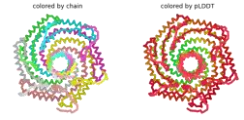
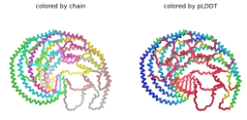
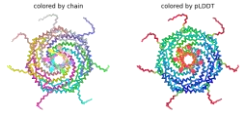
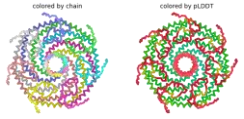
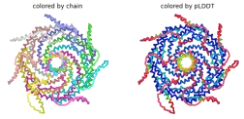
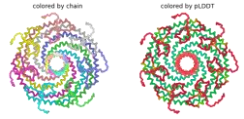
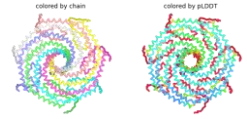
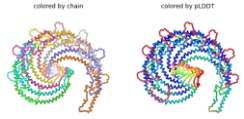
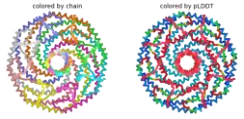
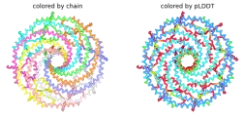
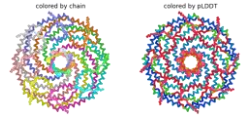
	Q03135（CAV1）		Q03135 32-178 (Beta-CAV1)		P51636 (CAV2)		P51636 (CAV2)		P56539 (CAV3)	
	pLDDT		*pLDDT*		*pLDDT*		*pLDDT*		*pLDDT*	
1-mer	78.74		85.84		78.75		78.42		89.43	
2-mer	71.65		80.75		77.96		78.05		86.34	
3-mer	72.78		83.56		78.13		78.22		86.93	
4-mer	72.63		83.92		77.83		78.28		86.56	
5-mer	73.18		83.13		77.62		76.36		86.01	
6-mer	69.58		67.52 (R4)		73.79		74.37		85.48	
7-mer	68.40 (R2)		77.40 (R2)		67.51		73.70		80.75 (R2)	
8-mer			80.60 (R2)		58.30		58.30		80.57	
8-mer			64.71							


65.78(R3)

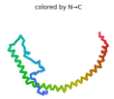
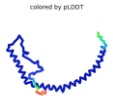
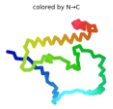
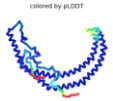
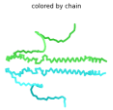
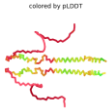
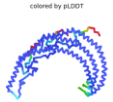
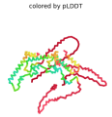
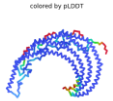
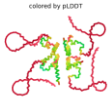
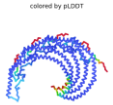
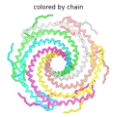
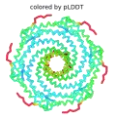
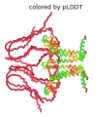
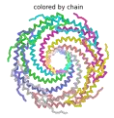
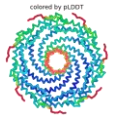
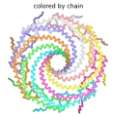
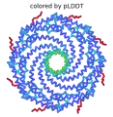
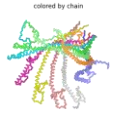
Strongylocentrotus purpuratus

	A0A7M7HEM1	A0A7M7HEM1 (40-192)	**A0A7M7GJ11**	A0A7M7GJ11 (48-196)	**A0A7M7HH57**	A0A7M7HH57 (53-218)
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	71.52		77.68		67.60	
2-mer	63.88		74.03		58.89	
3-mer	64.72		73.39		57.35	
4-mer	65.88		72.43		56.15	
5-mer	62.42		71.39		53.61	
6-mer	60.00		67.54		52.04	
7-mer		65.02 (R2)		80.10 (R2)		62.06
8-mer		70.13		81.94 (R2)		58.49

Strongylocentrotus purpuratus

	A0A7M7RAC4		A0A7M7T4C2		A0A7M7P0X0		A0A7M7G9F7		A0A7M7PLL3	
	pLDDT		*pLDDT*		*pLDDT*		*pLDDT*		*pLDDT*	
1-mer	86.56		75.62		77.44		74.60		76.79	
2-mer	84.35		66.51		75.56		66.39		69.26	
3-mer	85.09		65.39		75.46		64.79		68.09	
4-mer	84.47		64.73		74.73		62.76		67.23	
5-mer	83.58		67.18		74.92		62.72		66.90	
6-mer	68.55 (R4)		47.44 (R2)		67.05 (R2)		48.11 (R2)		62.18	
7-mer	72.61 (R2)		56.63 (R2)		70.19 (R2)		58.15 (R2)		59.98	
8-mer	75.00		63.56				61.97		64.18	

Priapulus caudatus

	XP_014678552.1			XP_014664738.1		
	pLDDT			*pLDDT*		
1-mer	92.04			63.94		
2-mer	87.97			51.44		
3-mer	88.48			52.25		
4-mer	87.26			48.50		
5-mer	86.68			47.72		
6-mer	72.19 (R3)			47.78		
7-mer	77.05 (R2)			45.26		
8-mer	83.06			41.55		
9-mer	48.14					

Apis mellifera

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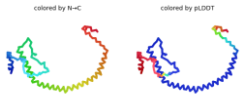
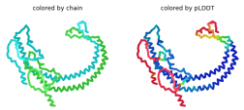
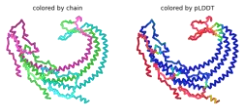
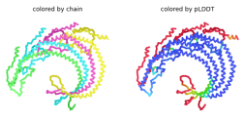
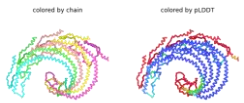
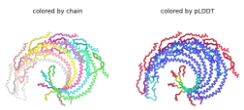
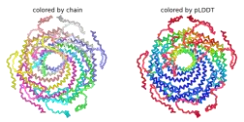
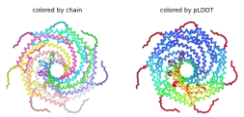
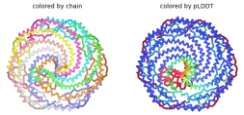
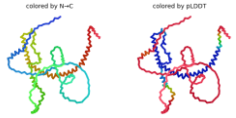
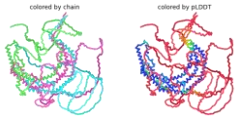
A0A7M7R2L2 (24-177)

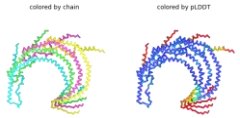
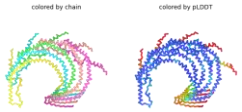
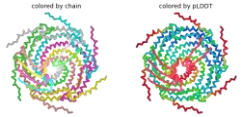
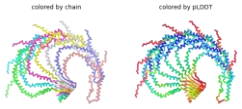
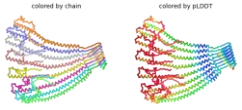
	pLDDT		*pLDDT*	
1-mer	80.39			
2-mer	72.87			
3-mer	74.73			
4-mer	74.72			
5-mer	74.02			
6-mer	73.72			
7-mer	65.85		70.61 (R2)	
8-mer			76.08	

Caenorhabditis elegans

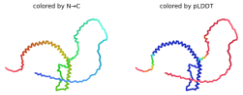
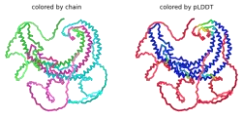
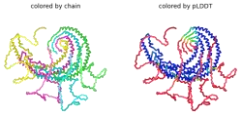
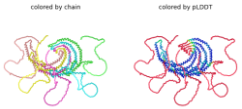
Q18879

	pLDDT	
1-mer	57.76	
2-mer	54.24	
3-mer	51.82	
4-mer		
5-mer		
6-mer		
7-mer		
8-mer		
9-mer		
10-mer		

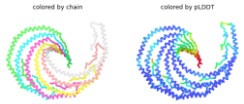
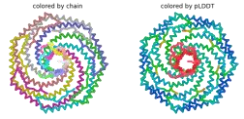
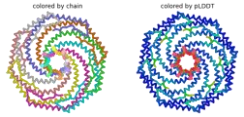
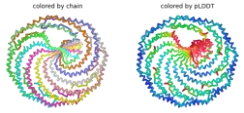
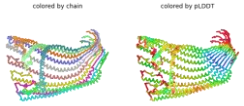
Q18879（192-351）

	pLDDT	
4-mer	79.74	
5-mer	80.34	
6-mer	67.27 (R4)	
7-mer	74.16	
8-mer	61.28	

Q94051

	pLDDT	
1-mer	68.02	
2-mer	63.28	
3-mer	63.32	
4-mer	61.95	
5-mer	59.08	

H2L2G6 Q94051（110-235）

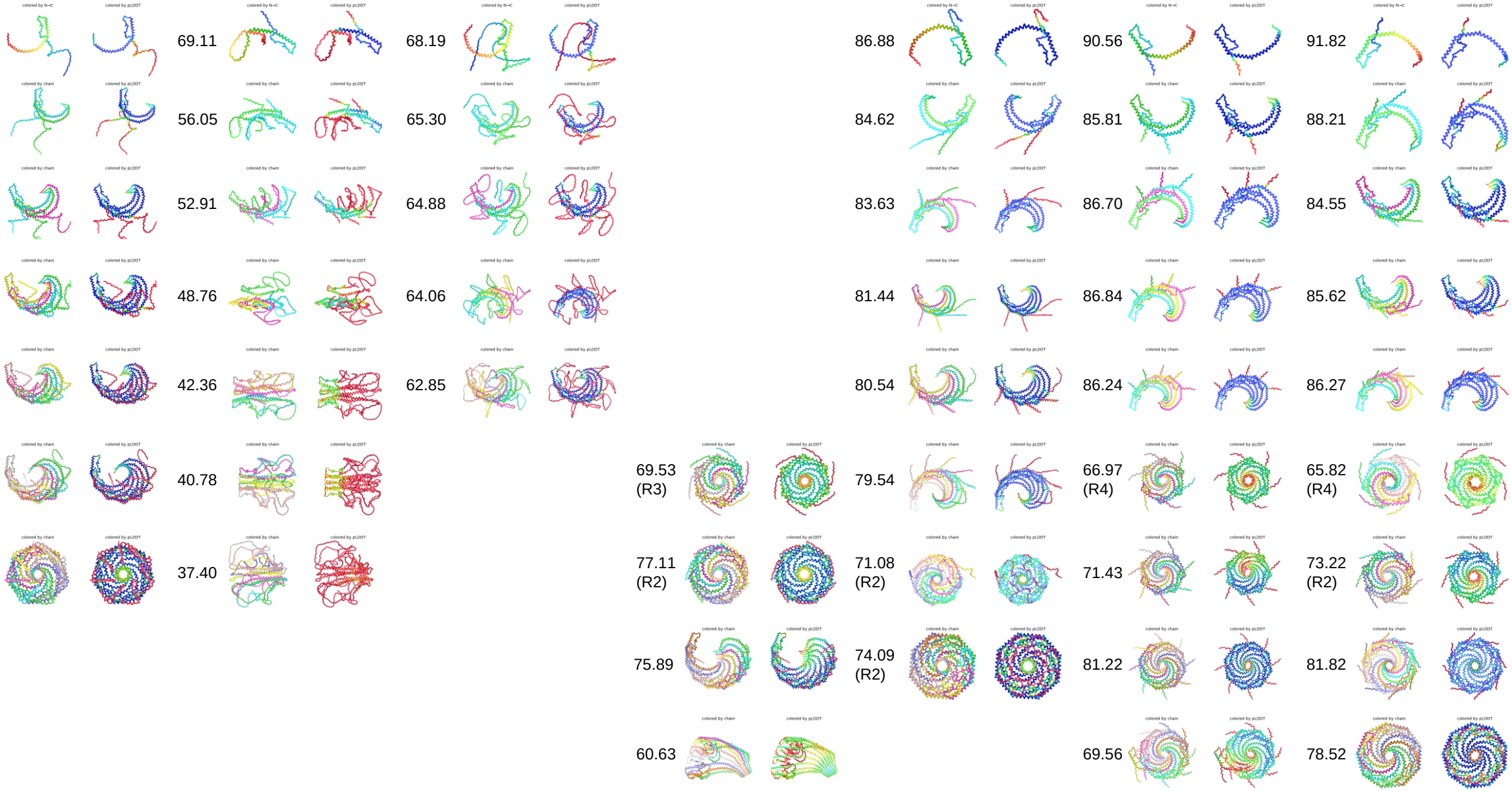
	pLDDT	
6-mer	83.91	
7-mer	73.61 (R4)	
8-mer	79.90 (R2)	
9-mer	74.55	
10-mer	64.11	

Brachionus plicatilis

	A0A3M7SAK0	A0A3M7SAF6	A0A3M7SAF6 (1-132)	A0A3M7RD35	A0A3M7RCJ9	A0A3M7SB10	A0A3M7Q0Q1
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	87.10	82.78		92.58	90.03	86.77	92.75
2-mer	82.46	76.09		87.69	85.27	80.28	85.81
3-mer	81.39	72.98		88.74	83.61	80.22	89.24
4-mer	80.98	71.70		87.76	83.17	79.85	87.42
5-mer	80.50	48.99 (R4)		84.76	82.73	79.84	86.84
6-mer	75.65	68.53		73.01 (R4)	69.33 (R4)	68.47 (R4)	75.12 (R2)
7-mer	74.14 (R2)	67.40	73.48 (R2)	78.86	75.24 (R2)	72.45 (R2)	79.72
8-mer	77.24		43.14	82.37	78.78	75.94	82.50
9-mer				82.97			83.19

Macrostomum lignano

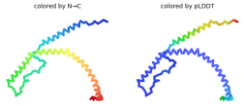
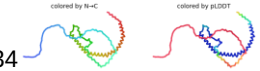
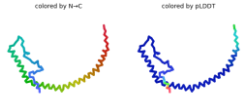
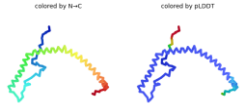
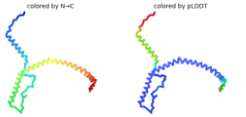
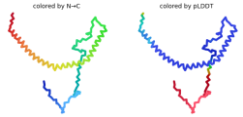
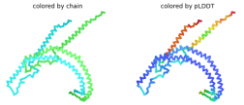
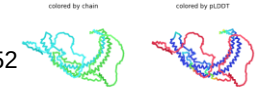
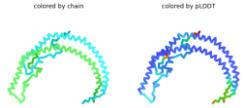
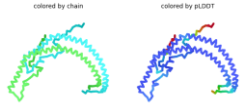
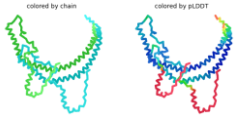
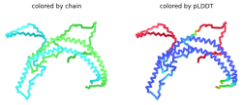
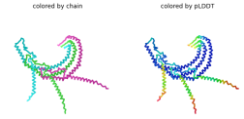
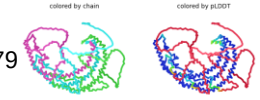
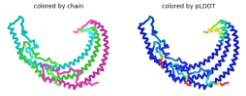
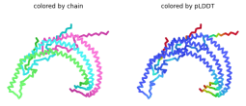
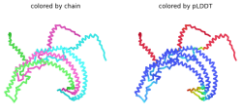
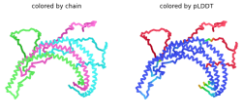
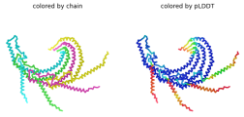
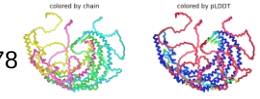
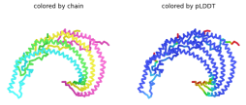
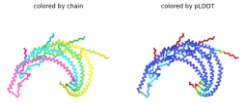
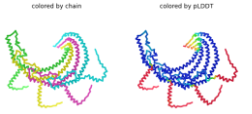
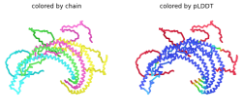
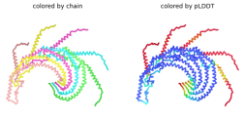
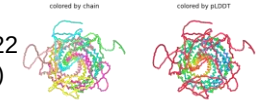
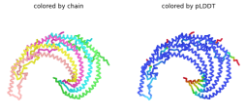
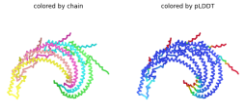
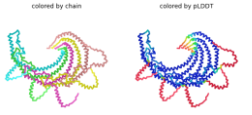
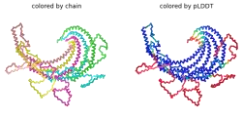
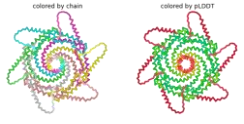
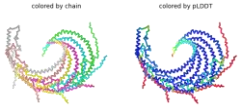
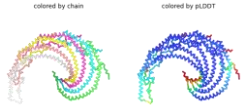
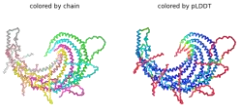
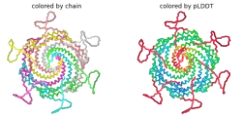
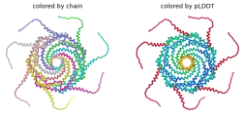
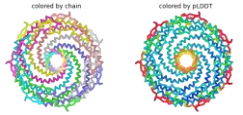
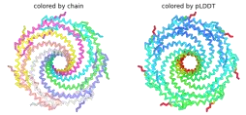
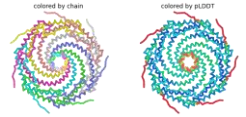
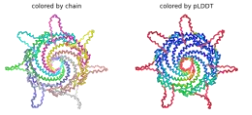
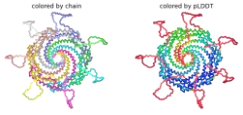
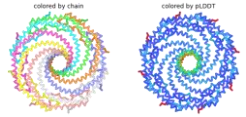
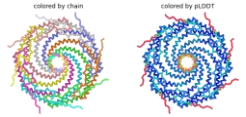
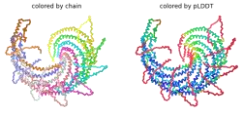
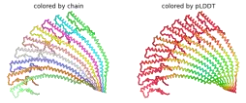
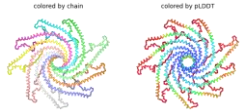
	A0A267DFI9	A0A267DC90	A0A267G3E9	A0A267G3E9 (94-239)	A0A267G387	A0A1I8H2T4	A0A1I8J741
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	81.25	69.11	68.19		86.88	90.56	91.82
2-mer	81.08	56.05	65.30		84.62	85.81	88.21
3-mer	77.90	52.91	64.88		83.63	86.70	84.55
4-mer	76.51	48.76	64.06		81.44	86.84	85.62
5-mer	75.70	42.36	62.85		80.54	86.24	86.27
6-mer	74.27	40.78		69.53 (R3)	79.54	66.97 (R4)	65.82 (R4)
7-mer	71.10	37.40		77.11 (R2)	71.08 (R2)	71.43	73.22 (R2)
8-mer				75.89	74.09 (R2)	81.22	81.82
9-mer				60.63		69.56	78.52



Macrostomum lignano

	A0A267G1N3	A0A267DS21	A0A267DU21	A0A267GQL3	A0A267GQL3 (70-221)	A0A267G3D8	A0A1I8GQY0
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	70.70	91.04	91.65	70.38		86.00	80.01
2-mer	67.66	84.34	83.53	67.77		81.41	78.32
3-mer	66.66	85.29	86.99	66.43		84.06	78.15
4-mer	65.65	87.02	87.12	65.99		82.84	78.03
5-mer	65.11	83.66	86.48	54.51 (R5)		80.31	61.93 R4
6-mer	57.02 (R2)	68.64 (R2)	68.27 (R4)		67.83 (R3)	67.54 (R4)	74.72
7-mer	62.07	73.78 (R2)	73.60 (R2)		73.09 (R2)	70.81 (R2)	72.76 (R2)
8-mer		81.20	82.23		79.09 (R2)	74.80 (R2)	
9-mer		80.80	81.09				

Macrostomum lignano

	A0A267EVV7	A0A267DNA3	A0A267DNA3 (69-221)	A0A267F6W6	A0A267FNG7	A0A1I8GFP4	A0A1I8J849
	pLDDT	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*	*pLDDT*
1-mer	86.25 	70.34 		92.13 	91.42 	84.58 	79.45 
2-mer	79.71 	67.52 		84.98 	86.06 	73.86 	74.12 
3-mer	81.58 	66.79 		87.18 	85.55 	78.40 	75.55 
4-mer	80.37 	65.78 		88.11 	85.58 	78.63 	75.04 
5-mer	78.45 	55.22 (R5) 		87.92 	86.07 	78.50 	73.65 
6-mer	60.77 		81.73 	84.67 	85.64	72.65 	61.99 (R3) 
7-mer	69.98 (R2) 		74.54 	75.53 (R2) 	76.64 (R2) 	70.79 (R2) 	65.26 
8-mer				83.80 	81.10 	67.84 	
9-mer				55.89 	65.07 (R2) 		

Macrostomum lignano

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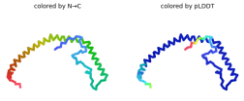
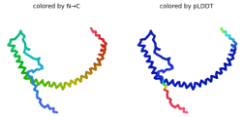
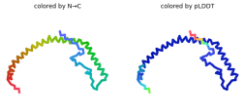
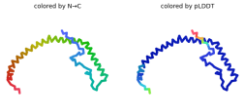
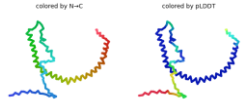
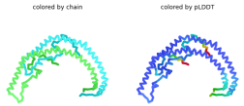
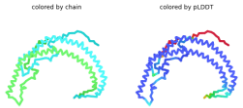
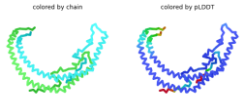
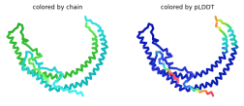
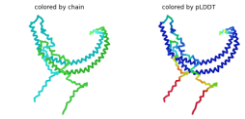
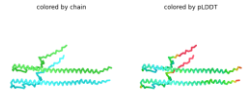
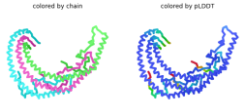
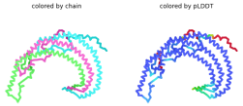
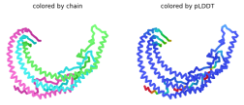
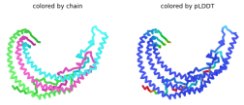
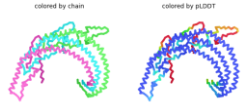
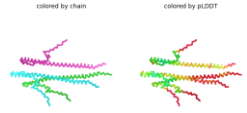
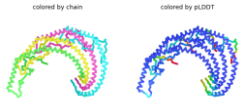
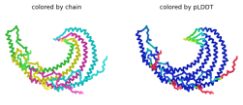
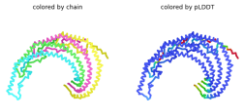
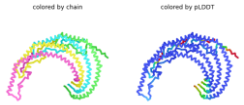
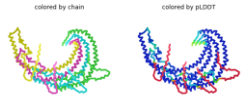
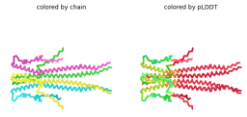
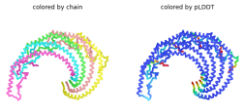
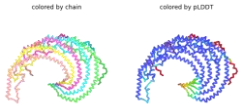
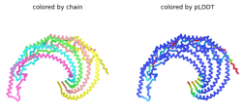
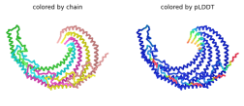
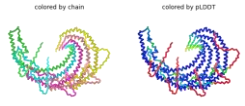
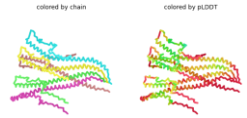
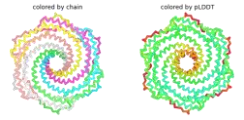
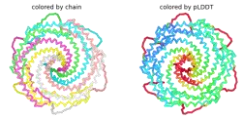
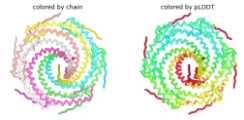
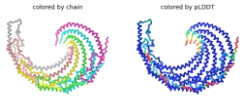
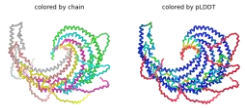
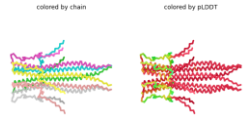
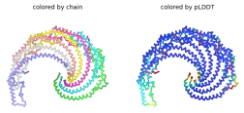
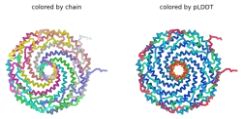
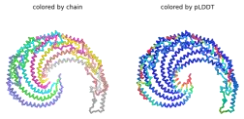
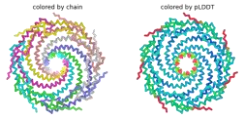
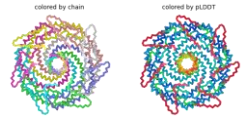
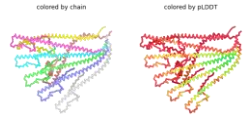
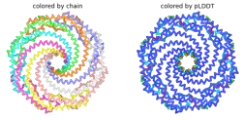
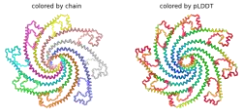
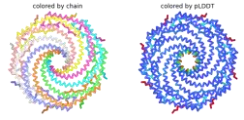
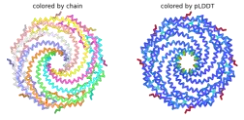
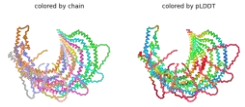
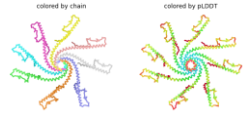
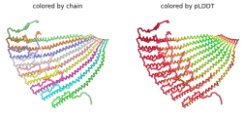
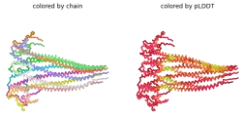
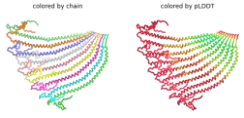
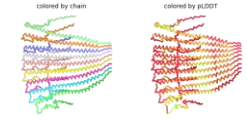
1-mer	91.05		89.47		91.97		92.13		85.04		87.80	
2-mer	87.07		84.92		87.83		89.62		83.07		72.48	
3-mer	88.45		85.73		89.22		88.17		82.25		61.33	
4-mer	87.04		85.42		88.29		88.27		79.79		56.07	
5-mer	87.59		84.51		87.82		88.48		78.59		57.23	
6-mer	66.71 (R3)		68.30 (R4)		65.06 (R3)		87.59		74.81		49.18	
7-mer	85.47		76.65 (R2)		84.93		77.34 (R2)		71.65 (R2)		51.47	
8-mer	84.65		62.06		83.89		83.62		62.40		62.52	
9-mer	51.78				48.53		50.50				51.88	

Macrostomum lignano

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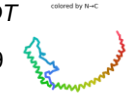
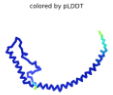
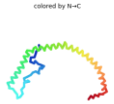
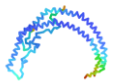
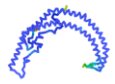
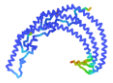
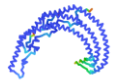
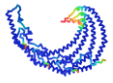
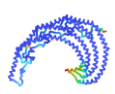
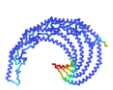
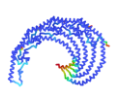
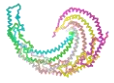
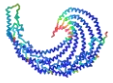
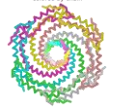
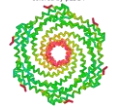
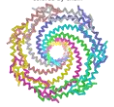
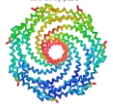
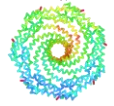
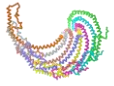
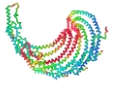
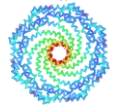
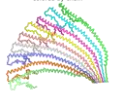
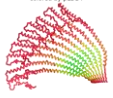
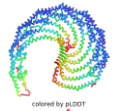
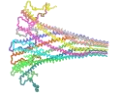
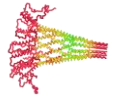
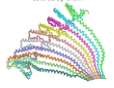
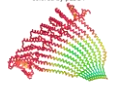
1-mer	93.29			93.09		
2-mer	83.86			91.90		
3-mer	88.69			89.88		
4-mer	88.52			89.12		
5-mer	88.54			89.29		
6-mer	85.04			66.35 (R4)		
7-mer	73.63 (R2)			72.50 (R2)		
8-mer	68.26			77.40 (R2)		
9-mer	52.16			76.85		
10-mer	50.28			52.68		

Pomacea canaliculata

	A0A2T7NUS2		A0A2T7NUA4		A0A2T7NUV7		A0A2T7NUT7	
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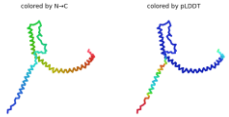
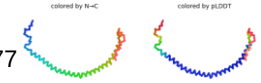
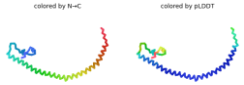
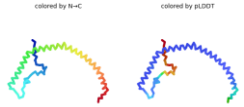
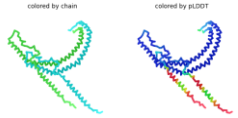
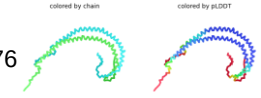
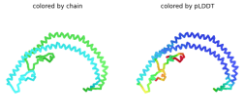
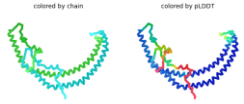
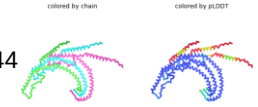
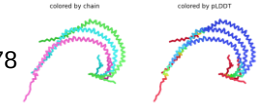
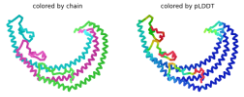
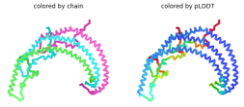
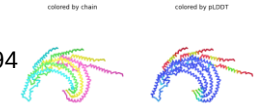
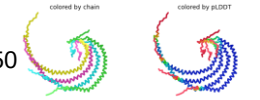
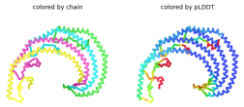
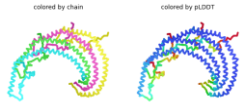
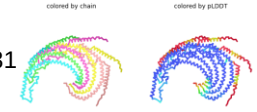
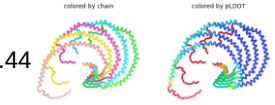
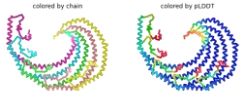
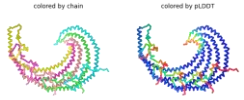
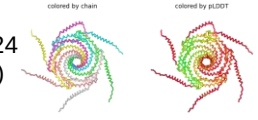
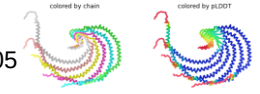
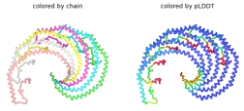
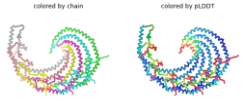
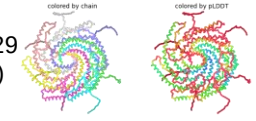
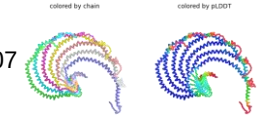
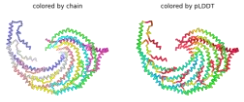
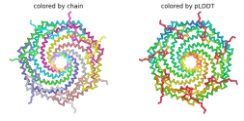
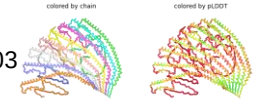
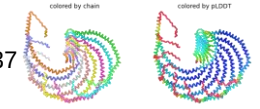
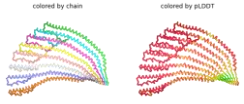
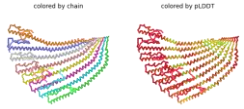
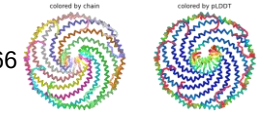
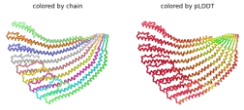
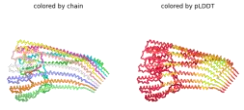
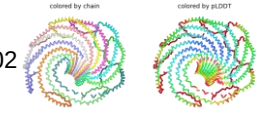
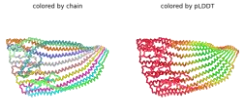
1-mer	87.54		80.77		85.86		85.17	
2-mer	82.04		76.76		82.24		80.85	
3-mer	81.44		75.78		81.75		80.06	
4-mer	80.94		75.50		78.78		80.86	
5-mer	79.31		76.44		79.97		80.61	
6-mer	55.24 (R2)		78.05		80.45		76.12	
7-mer	55.29 (R2)		78.07		62.98		66.98	
8-mer	51.03		74.37		50.80		50.94	
9-mer			71.66		50.71		48.77	
10-mer			66.02		52.01			

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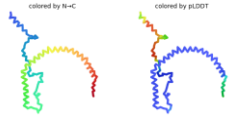
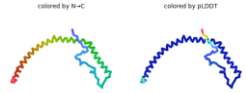
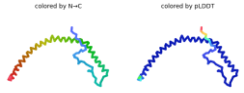
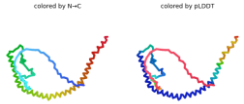
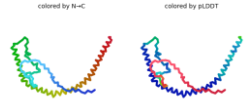
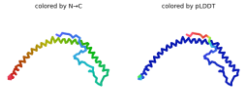
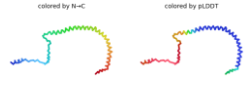
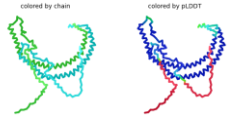
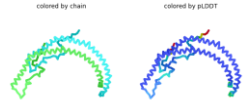
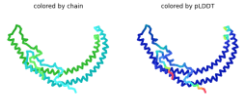
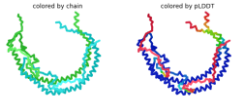
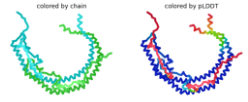
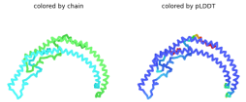
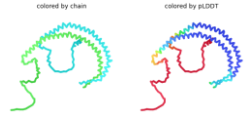
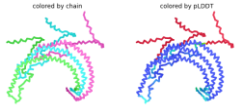
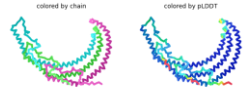
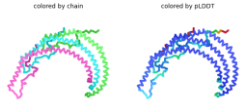
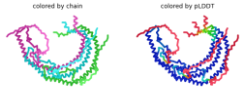
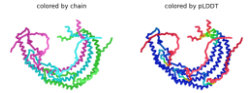
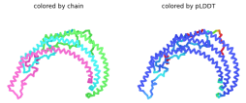
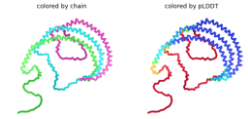
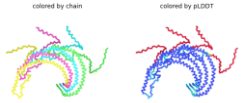
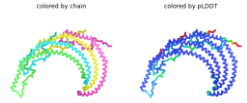
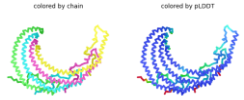
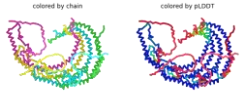
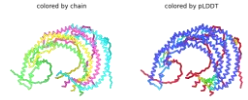
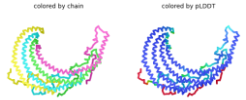
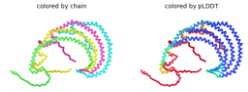
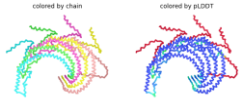
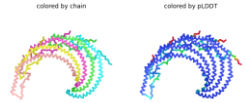
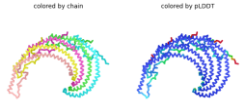
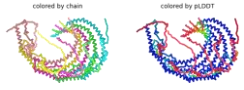
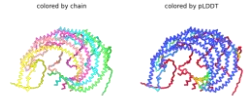
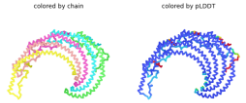
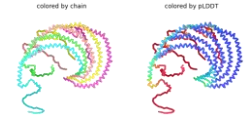
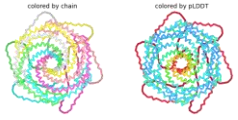
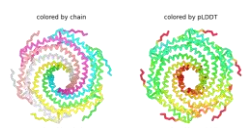
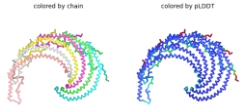
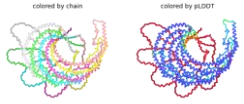
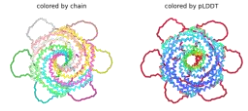
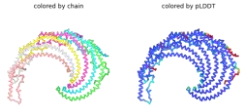
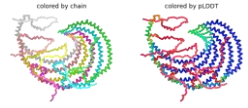
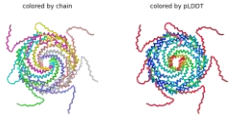
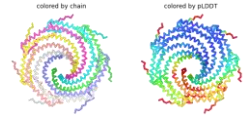
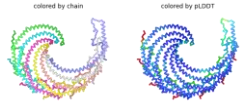
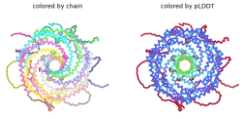
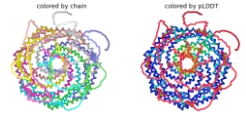
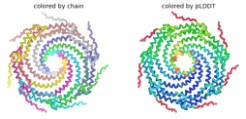
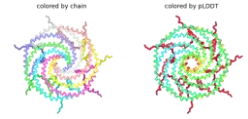
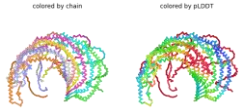
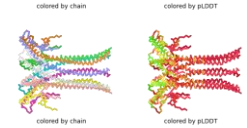
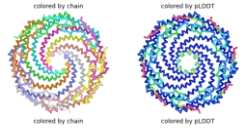
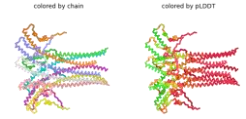
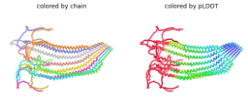
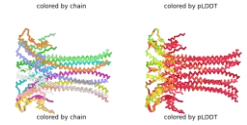
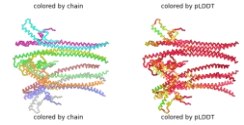
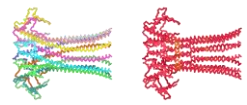
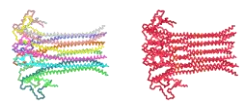
1-mer	85.99		92.28		92.89		73.34		75.90		90.71		74.41	
2-mer	81.14		88.03		89.13		74.19		74.16		86.45		71.83	
3-mer	80.93		84.64		87.16		73.84		74.00		86.38		71.06	
4-mer	80.47		87.76		86.74		73.45		73.86		85.14		71.16	
5-mer	79.51		88.36		88.19		73.08		73.15		87.03		70.41	
6-mer	65.86 (R3)		65.38 (R4)		88.29		69.13		65.29 (R2)		86.86		68.22	
7-mer	69.32 (R2)		73.82 (R2)		84.82		68.69		68.19 (R2)		75.14 (R2)		57.11	
8-mer	61.24		52.28		85.09						53.04		58.00	
9-mer			49.61		49.15									
10-mer			42.15		42.17									

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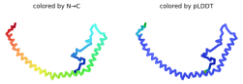
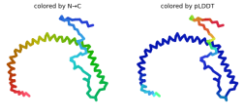
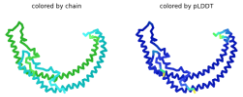
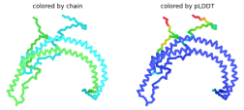
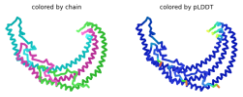
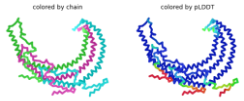
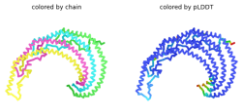
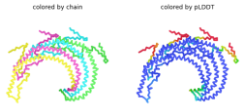
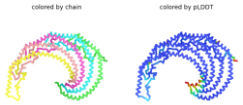
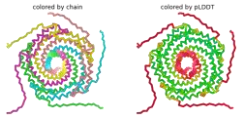
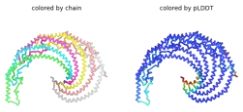
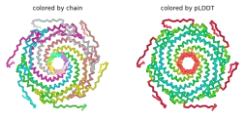
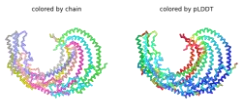
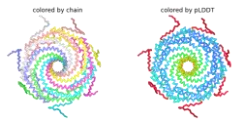
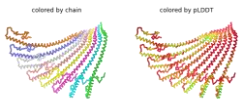
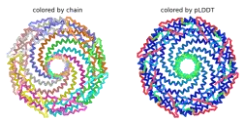
1-mer	94.45		87.16	
2-mer	92.96		89.62	
3-mer	91.70		86.85	
4-mer	89.61		85.40	
5-mer	90.29		60.84 (R5)	
6-mer	89.08		66.66 (R5)	
7-mer	75.25		72.85 (R2)	
8-mer	54.57		79.75	

Capitella teleta

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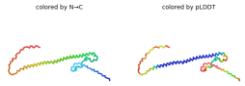
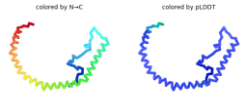
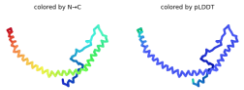
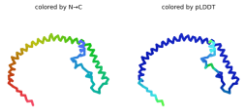
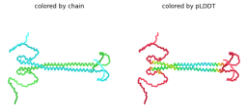
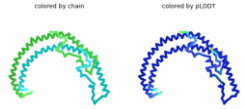
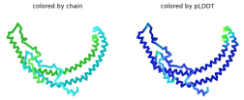
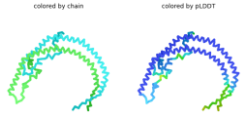
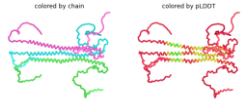
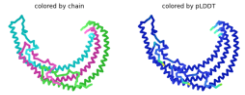
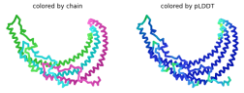
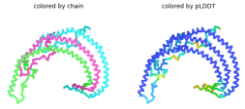
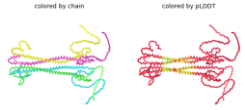
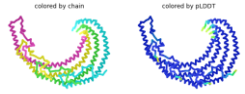
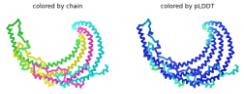
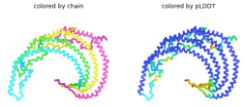
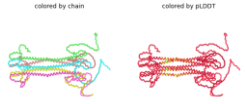
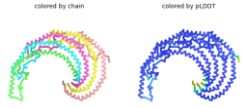
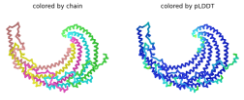
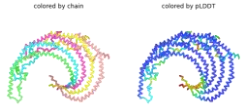
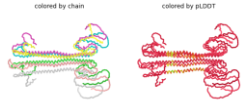
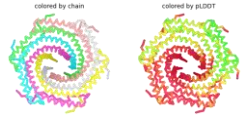
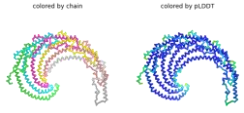
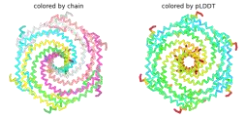
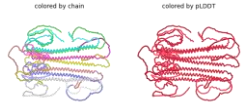
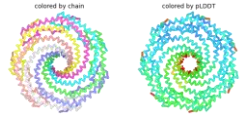
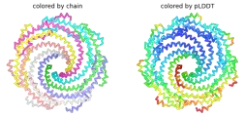
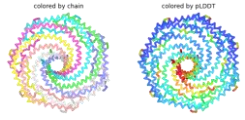
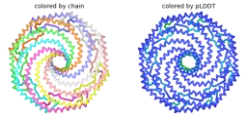
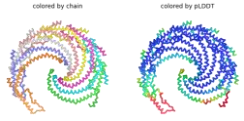
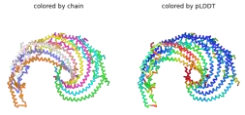
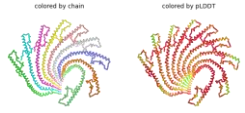
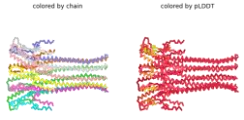
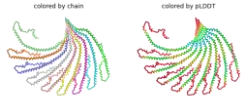
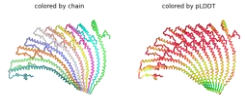
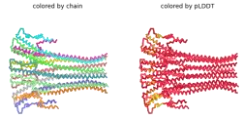
1-mer	73.81		95.01		93.47		90.74	
2-mer	52.32		92.53		89.80		87.08	
3-mer	42.62		92.93		88.78		86.82	
4-mer	36.23		92.71		89.90		85.83	
5-mer	35.00		92.03		89.31		85.64	
6-mer	35.33		56.04 (R4)		88.90		68.62 (R3)	
7-mer	33.30		76.51 (R2)		74.74 (R2)		77.14 (R2)	
8-mer			89.18		84.13		75.10	
9-mer			53.60		41.67		59.68	
10-mer			53.35		41.35