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Cryo-EM of Aβ Fibrils from Mouse Models find tg-APP$_{\mathrm{ArcSwe}}$ fibrils resemble those found in sporadic Alzheimer's disease patients

SUPPLEMENTARY DATA

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Supplementary Table 1

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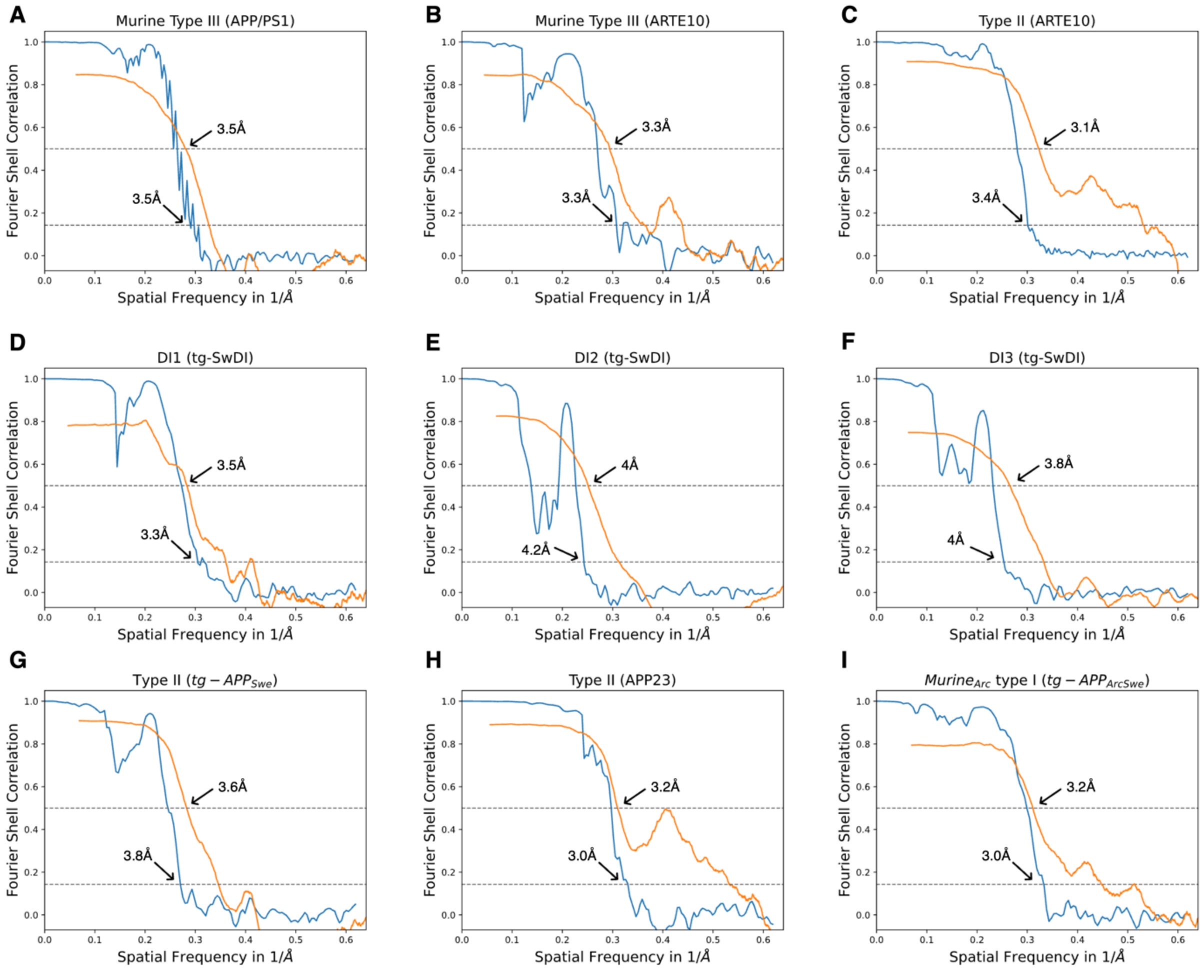


Figure S1: FSC curves for cryo-EM maps and structures of (A) APP/PS1 murine type III, (B) ARTE10 murine type III, (C) ARTE 10 type II, (D) DI1, (E) DI2, (F) DI3, (G) tg-APP$_{\text{Swe}}$ type II, (H) APP23 type II, and (I) tg-APP$_{\text{ArcSwe}}$ murine$_{\text{Arc}}$ type I fibrils. FSC curves for two independently refined half maps are shown in blue; FSC curves for the refined atomic model against the final cryo-EM map in orange.

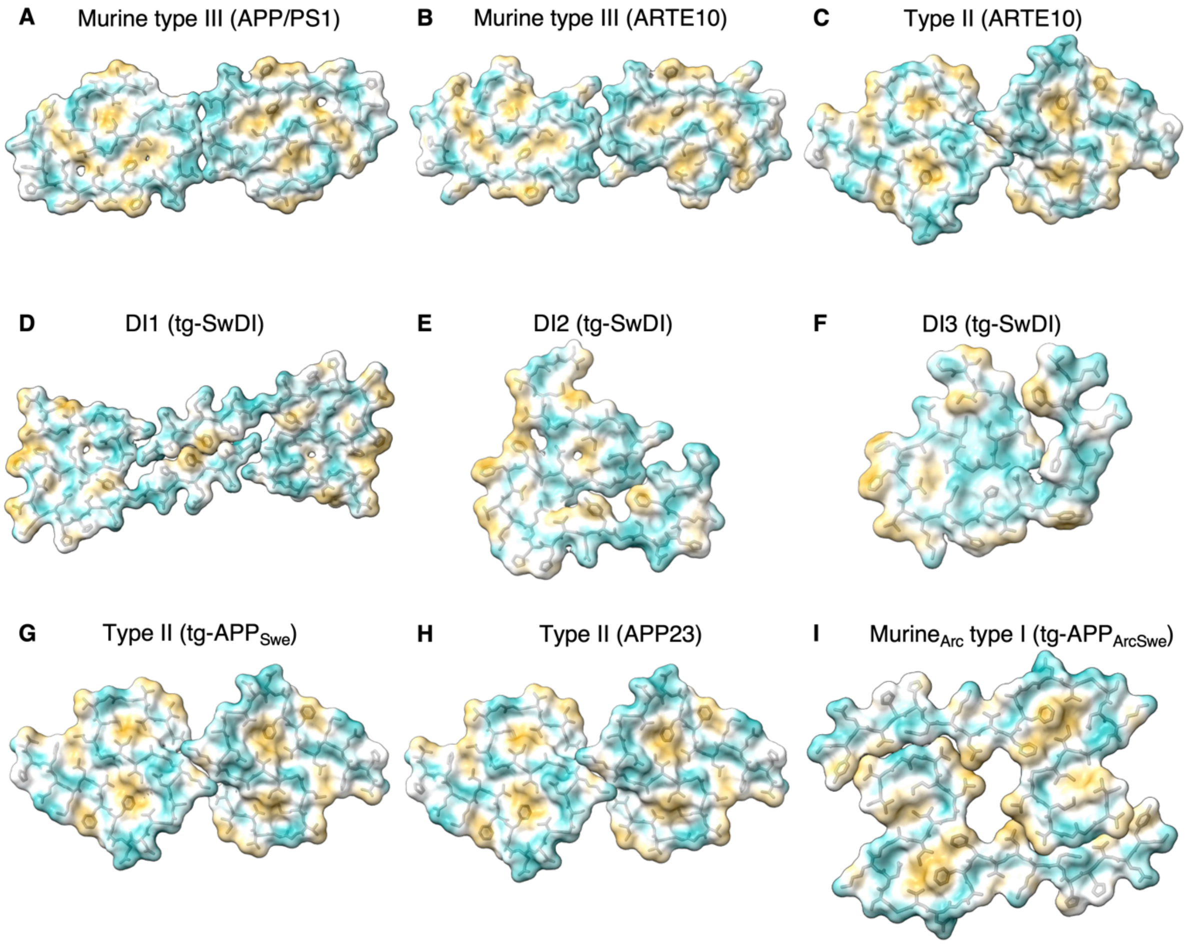


Figure S2: Molecular lipophilicity potential (MLP) maps for (A) APP/PS1 murine type III, (B) ARTE10 murine type III, (C) ARTE10 type II, (D) DI1, (E) DI2, (F) DI3, (G) tg-APP$_{\text{Swe}}$ type III, (H) APP23 type II, and (J) murine$_{\text{Arc}}$ type I. Coloring on the surface ranging from cyan (most hydrophilic) to white to yellow (most lipophilic/hydrophobic).

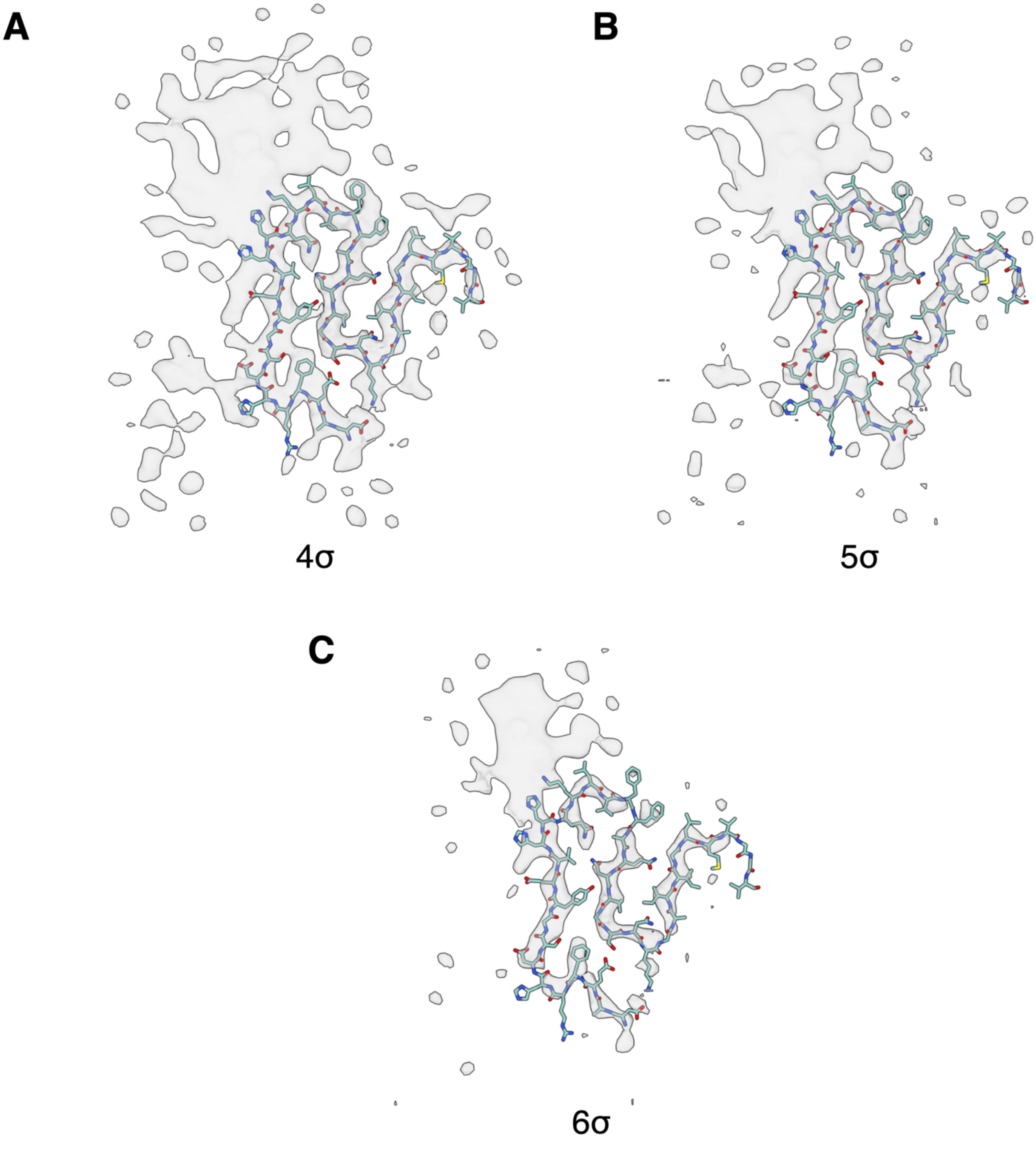
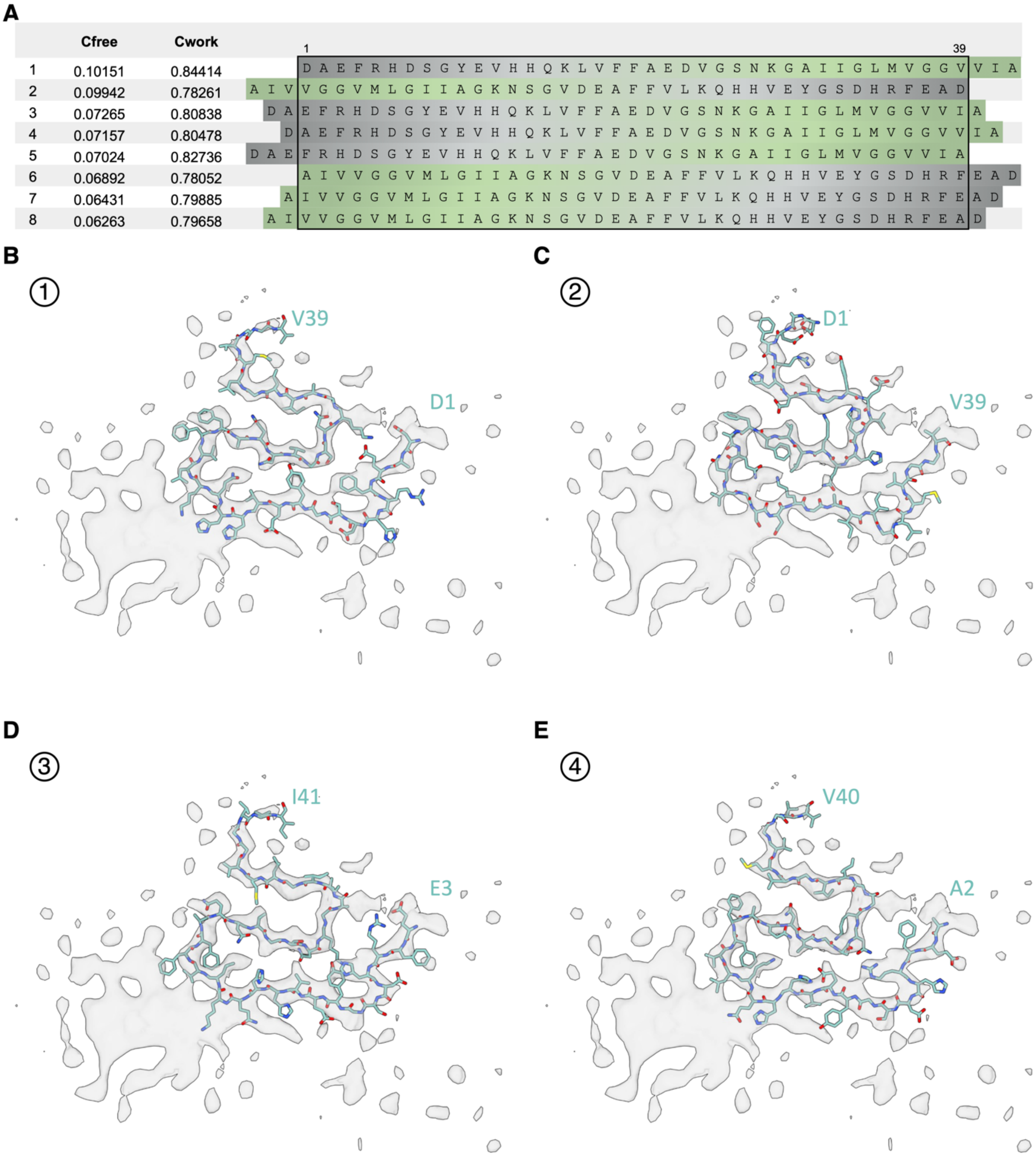


Figure S3: DI2 density map at different thresholds. At (A) 4σ, (B) 5σ, and (C) 6σ



	Cfree	Cwork		1 39	
1	0.10151	0.84414		D A E F R H D S G Y E V H H Q K L V F F A E D V G S N K G A I I G L M V G G V	V I A
2	0.09942	0.78261	A I V	V G G V M L G I I A G K N S G V D E A F F V L K Q H H V E Y G S D H R F E A D	
3	0.07265	0.80838	D A	E F R H D S G Y E V H H Q K L V F F A E D V G S N K G A I I G L M V G G V V I	A
4	0.07157	0.80478	D	A E F R H D S G Y E V H H Q K L V F F A E D V G S N K G A I I G L M V G G V V	I A
5	0.07024	0.82736	D A E	F R H D S G Y E V H H Q K L V F F A E D V G S N K G A I I G L M V G G V V I A	
6	0.06892	0.78052		A I V V G G V M L G I I A G K N S G V D E A F F V L K Q H H V E Y G S D H R F	E A D
7	0.06431	0.79885	A	I V V G G V M L G I I A G K N S G V D E A F F V L K Q H H V E Y G S D H R F E	A D
8	0.06263	0.79658	A I	V V G G V M L G I I A G K N S G V D E A F F V L K Q H H V E Y G S D H R F E A	D

Figure S4: DireX analysis of DI2. (A) The table contains the C_{work} and C_{free} values from the DireX fitting of all possible eight sequence assignments (black box) in both possible C_{α}-chain directions into the DI2 density maps**.** The C_{free} value was used to rank the results. The N-terminus of the sequence is coloured in grey, the C-terminus is coloured in green. (B) The most favourable sequence fit. (C)-(E) The 2nd to 4th most favourable sequence fit.

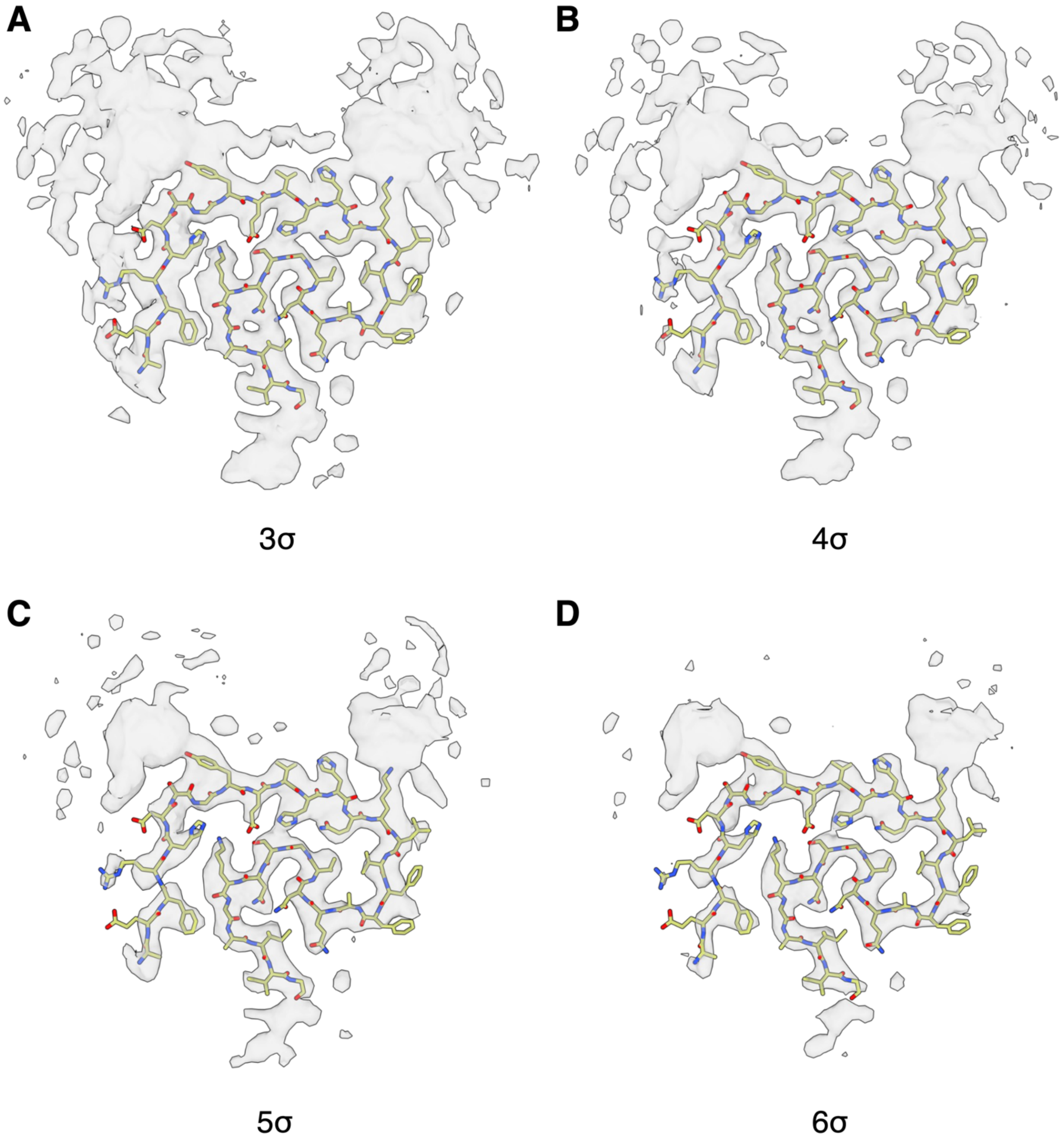
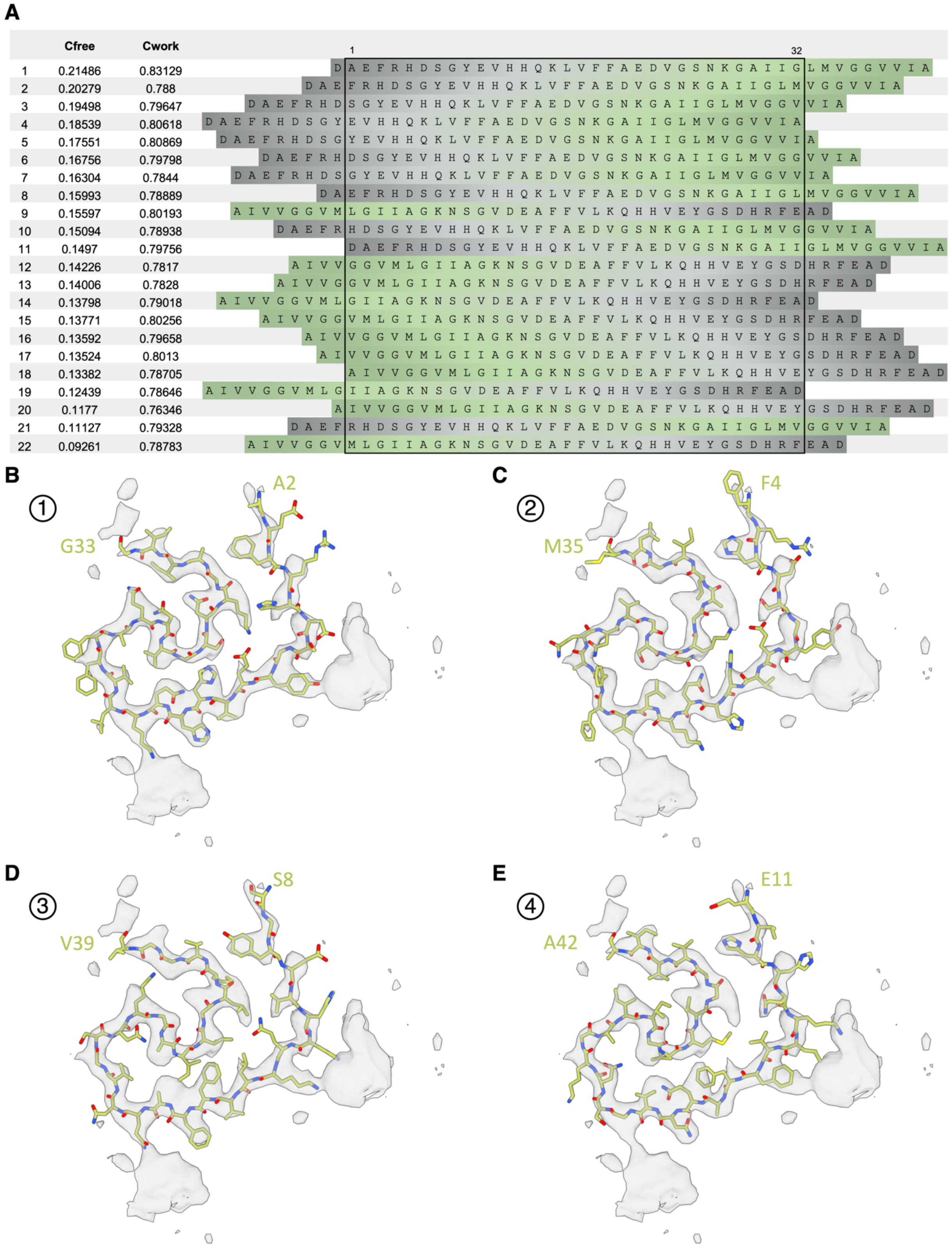


Figure S5: DI3 density map at different thresholds. At (A) 3σ, (B) 4σ, (C) 5σ, and (D) 6σ.



	Cfree	Cwork		1 32	
1	0.21486	0.83129	D	AEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIG	LMVGGVVIA
2	0.20279	0.788	DAE	FRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLM	VGGVVIA
3	0.19498	0.79647	DAEFRHD	SGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGV	VIA
4	0.18539	0.80618	DAEFRHDSGY	EVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA	
5	0.17551	0.80869	DAEFRHDSG	YEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVI	A
6	0.16756	0.79798	DAEFRH	DSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGG	VVIA
7	0.16304	0.7844	DAEFRHDS	GYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV	IA
8	0.15993	0.78889	DA	EFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGL	MVGGVVIA
9	0.15597	0.80193	AIVVGGVM	LGIIAGKNSGVDEAFFVLKQHHVEYGSDHRFE	AD
10	0.15094	0.78938	DAEFR	HDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVG	GVVIA
11	0.1497	0.79756		DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAII	GLMVGGVVIA
12	0.14226	0.7817	AIVV	GGVMLGIIAGKNSGVDEAFFVLKQHHVEYGSD	HRFEAD
13	0.14006	0.7828	AIVVG	GVMLGIIAGKNSGVDEAFFVLKQHHVEYGSDH	RFEAD
14	0.13798	0.79018	AIVVGGVML	GIIAGKNSGVDEAFFVLKQHHVEYGSDHRFEA	D
15	0.13771	0.80256	AIVVGG	VMLGIIAGKNSGVDEAFFVLKQHHVEYGSDHR	FEAD
16	0.13592	0.79658	AIV	VGGVMLGIIAGKNSGVDEAFFVLKQHHVEYGS	DHRFEAD
17	0.13524	0.8013	AI	VVGGVMLGIIAGKNSGVDEAFFVLKQHHVEYG	SDHRFEAD
18	0.13382	0.78705		AIVVGGVMLGIIAGKNSGVDEAFFVLKQHHVE	YGSDHRFEAD
19	0.12439	0.78646	AIVVGGVMLG	IIAGKNSGVDEAFFVLKQHHVEYGSDHRFEAD	
20	0.1177	0.76346	A	IVVGGVMLGIIAGKNSGVDEAFFVLKQHHVEY	GSDHRFEAD
21	0.11127	0.79328	DAEF	RHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMV	GGVVIA
22	0.09261	0.78783	AIVVGGV	MLGIIAGKNSGVDEAFFVLKQHHVEYGSDHRF	EAD

Figure S6: DireX analysis of DI3. (A) The table contains the C_{work} and C_{free} values from the DireX fitting of all possible 22 sequence assignments (black box) in both possible C_{α}-chain directions into the DI3 density maps**.** The C_{free} value was used to rank the results. The N-terminus of the sequence is coloured in grey, the C-terminus is coloured in green. (B) The most favourable sequence fit. (C)-(E) The 2nd to 4th most favourable sequence fit.

Supplementary Tables

Table S1: Distribution of polymorphs in extracted Aβ fibril samples from different mouse models. The term "unassigned" refers to particles that were originally picked by crYOLO but discarded because they were false positives or of too low quality for high-resolution reconstruction.

Mouse Model	**Distribution**
APP/PS1	murine type III: 12.2%; unassigned: 87.8%
ARTE10	type II: 13.2%; murine type III: 0.6%; unassigned: 86.2%
tg-SwDI	DI1: 3.6%; DI2: 2.6%; DI3: 0.7%; unassigned: 93.1%
tg-APP$_{\text{Swe}}$	type II: 1.7%; unassigned: 98.3%
APP23	type II: 10%; unassigned: 90%
tg-APP$_{\text{ArcSwe}}$	murine$_{\text{Arc}}$ type I: 4.4%; unassigned: 95.6%