Supporting Information for

High Resolution Structural Characterization of $A\beta_{42}$ Amyloid Fibrils by MAS NMR

Michael T. Colvin,‖† Robert Silvers,‖† Birgitta Frohm ‡ Yongchao Su,† Sara Linse,‡ and Robert G. Griffin*†

†Department of Chemistry and Francis Bitter Magnet Laboratory
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

‡ Department of Biochemistry and Structural Biology
Lund University
SE22100 Lund, Sweden

SUPPORTING FIGURES

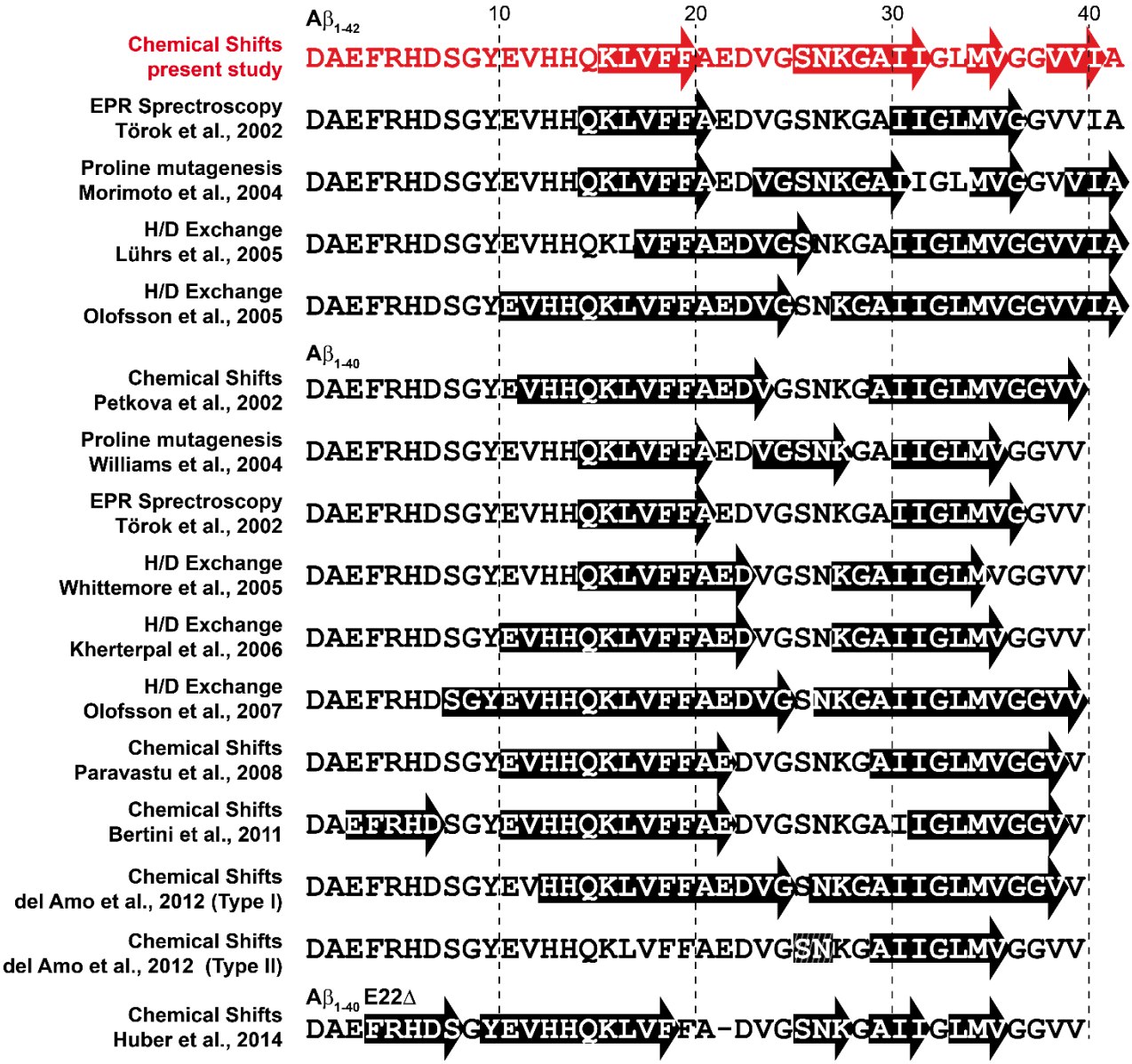

Figure S1. Comparison of the locations predicted β-strands (black arrows) and α-helix (haded square) in various Aβ fibrils.[1-14]

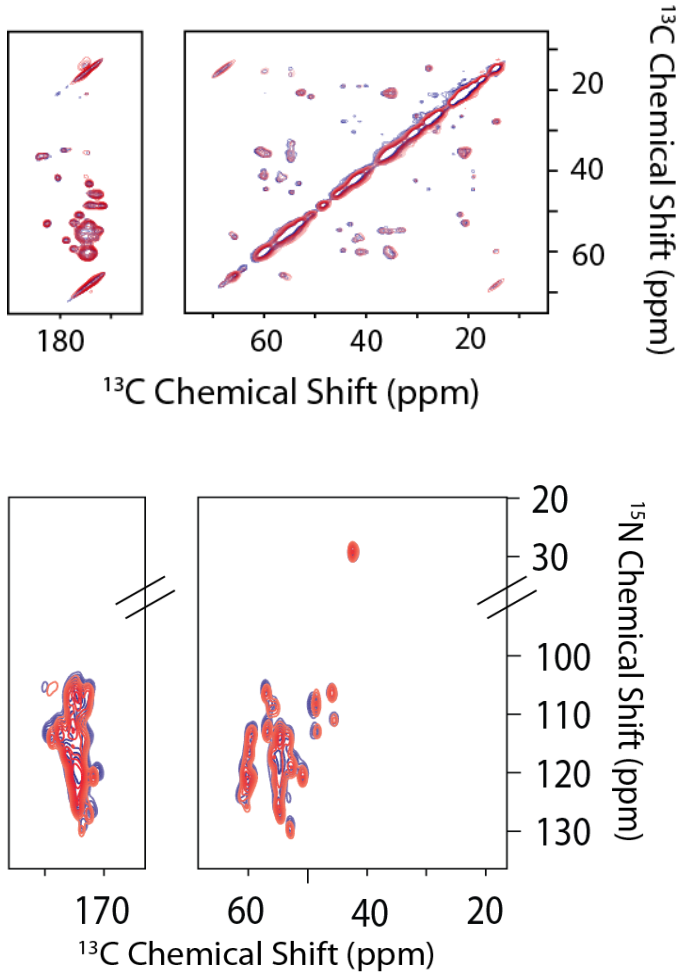

Figure S2. Overlay of samples prepared from lyophilized and rehydrated samples (blue) and samples which were always hydrated (red) demonstrating that lypholization and rehydration does not have a significant impact on the fibril structure. (top) 1.6 ms mixing RFDR spectrum recorded at 750 MHz, $\omega_r/2\pi$=20 kHz, VT gas regulated to 277 K with 83 kHz CW ^{1}H decoupling during evolution, and 83 kHz TPPM ^{1}H decoupling during acquisition. (bottom) 1.6 ms mixing ZF-TEDOR spectrum recorded at 800 MHz, $\omega_r/2\pi$=20 kHz, VT gas regulated to 277K with 83 kHz TPPM during acquisition.

SUPPORTING TABLES

Table S1. MAS NMR Assignments for $A\beta_{M_0 1-42}$ amyloid fibrils

Res Number	Res type	N	CO	CA	CB	CG	CG1	CG2	CD	CD1	CD2	CE	CZ	N
0	M			55.37	35.88	31.03						16.43		
1	D			54.28	42.26									
2	A			52.43	18.99									
3	E			56.49	29.83	35.94			183.3					
4	F			55.02	39.11	120			131.4			137.6	129.7	
5	R	121.90	176.50	54.09	33.14	27.10							159.22	
6	H													
7	D		172.16											
8	S	113.20	172.94	55.07	66.14									
9	G	110.658	172.2	48.24										
10	Y	113	176.8	55.00	41.35	135.8			132.4			117.2	156.4	
11	E	120.5	173.7	52.54	35.66	32.43			182.1					
12	V	124.6	172.1	60.25										
13	H													
14	H													
15	Q													
16	K	124.53	171.78	54.53		25.71			30.18					
17	L	132.09	174.41	54.20	44.76	28.71				22.44	25.45			
18	V	125.23	173.71	58.94	35.19	20.30								
19	F	130.35	174.38	59.89	40.29	139.61			130.5			129.67		
20	F	117.18	174.24	56.33	40.25	139.37			130.6			129.93		
21	A	123.47	176.69	52.25	20.28									
22	E	118.54	175.34	54.03	33.06	35.85			183.6					
23	D	121.95	175.36	55.42	40.98	179.95								
24	V	117.95	176.78	58.86	35.32		20.4	22.56						
25	G	117.21	173.73	47.71										
26	S	113.29	172.41	55.93	65.34									
27	N	118.53	173.76	52.81	42.70									
28	K	130.25	175.17	54.76	35.04	26.00			29.81			42.04		34.00
29	G	112.48	171.06	48.16										
30	A	125.09	175.72	50.25	21.26									
31	I	121.06	173.38	59.30	44.02		27.35	18.65		14.07				
32	I	125.74	174.12	59.67	40.95		27.32	18.64		14.11				
33	G	110.76	172.22	45.39										
34	L	110.68	178.26	56.70	41.70	27.14				20.92	25.99			
35	M	118.64	172.99	54.48	36.38	30.62						17.00		
36	V	124.60	174.68	60.15	34.52		19.49	21.22						
37	G	115.37	173.30	45.03										
38	G	110.75	174.30	48.22										
39	V	129.15	174.50	61.13	34.67		20.22	21.13						
40	V	128.18	173.77	60.83	34.56		20.70	20.32						
41	I	127.45	173.03	59.58	39.48		27.40	18.61		14.18				
42	A	134.14	182.08	52.51	20.28									

Table S2. TALOS+ predicted secondary structure

Res Number	Res Type	Prob a-helix	Prob b-strand	Prob loop	Confidence	Secondary Structure
0	M	0.333	0.333	0.333	0	L
1	D	0.333	0.333	0.333	0	L
2	A	0.022	0	0.978	0.96	L
3	E	0.028	0	0.972	0.94	L
4	F	0.028	0	0.972	0.94	L
5	R	0	0.366	0.634	0.27	L
6	H	0	0	0	0	X
7	D	0	0	0	0	X
8	S	0.018	0.07	0.912	0.84	L
9	G	0	0.064	0.936	0.87	L
10	Y	0.012	0.188	0.801	0.61	L
11	E	0	0.857	0.143	0.71	E
12	V	0	0	0	0	X
13	H	0	0	0	0	X
14	H	0	0	0	0	X
15	Q	0	0	0	0	X
16	K	0	0.892	0.108	0.78	E
17	L	0.007	0.955	0.038	0.92	E
18	V	0.002	0.998	0	1	E
19	F	0	0.945	0.055	0.89	E
20	F	0	0.462	0.538	0.08	L
21	A	0	0.168	0.832	0.66	L
22	E	0.002	0.112	0.887	0.78	L
23	D	0	0.171	0.829	0.66	L
24	V	0	0.323	0.677	0.35	L
25	G	0.003	0.207	0.79	0.58	L
26	S	0	0.34	0.66	0.32	L
27	N	0	0.83	0.17	0.66	E
28	K	0	0.821	0.179	0.64	E
29	G	0	0.634	0.366	0.27	E
30	A	0	0.852	0.148	0.7	E
31	I	0.002	0.989	0.009	0.98	E
32	I	0	0.916	0.084	0.83	E
33	G	0.02	0.293	0.687	0.39	L
34	L	1E-3	0.241	0.758	0.52	L
35	M	0	0.915	0.085	0.83	E
36	V	0	0.953	0.047	0.91	E
37	G	0	0.708	0.292	0.42	E
38	G	0	0.457	0.543	0.09	L
39	V	0	0.856	0.144	0.71	E
40	V	0.002	0.99	0.007	0.98	E
41	I	0	0.917	0.083	0.83	E
42	A	0.333	0.333	0.333	0	L

Table S3. Secondary Chemical Shifts from TALOS+

Residue	Res Type	Atom Type	Secondary Chemical Shifts	Experimental Chemical Shifts	Random Coil Chemical Shifts
0	M	CA	0.071	55.371	55.3
0	M	CB	3.28	35.88	32.6
1	D	CA	0.281	54.281	54
1	D	CB	1.46	42.26	40.8
2	A	CA	0.398	52.435	52.037
2	A	CB	-0.008	18.992	19
3	E	CA	0.089	56.489	56.4
3	E	CB	0.134	29.834	29.7
4	F	CA	-2.983	55.017	58
4	F	CB	0.107	39.107	39
5	R	CA	-2.01	54.09	56.1
5	R	CB	2.844	33.144	30.3
8	S	N	-3.666	113.209	116.875
8	S	CA	-3.131	55.069	58.2
8	S	CB	2.94	66.14	63.2
9	G	N	-0.736	110.658	111.394
9	G	CA	3.138	48.238	45.1
10	Y	N	-8.367	113	121.367
10	Y	CA	-3.1	55	58.1
10	Y	CB	2.89	41.35	38.46
11	E	CA	-3.86	52.54	56.4
11	E	CB	5.96	35.66	29.7
16	K	N	2.569	124.543	121.974
16	K	CA	-1.754	54.533	56.287
17	L	N	9.318	132.086	122.768
17	L	CA	-0.643	54.197	54.84
17	L	CB	2.697	44.756	42.059
18	V	N	3.817	125.231	121.414
18	V	CA	-3.365	58.935	62.3
18	V	CB	3.367	35.19	31.823
19	F	N	6.579	130.354	123.775
19	F	CA	1.888	59.888	58
19	F	CB	1.286	40.286	39
20	F	N	-4.025	117.176	121.201
20	F	CA	-1.669	56.331	58
20	F	CB	1.245	40.245	39
21	A	N	-0.604	123.467	124.071
21	A	CA	0.218	52.255	52.037
21	A	CB	1.283	20.283	19
22	E	N	-1.456	118.544	120
22	E	CA	-2.375	54.025	56.4
22	E	CB	3.364	33.064	29.7
23	D	N	-0.255	121.945	122.2
23	D	CA	1.418	55.418	54
23	D	CB	0.177	40.977	40.8
24	V	N	-3.136	117.953	121.089
24	V	CA	-3.443	58.857	62.3
24	V	CB	3.5	35.323	31.823
25	G	N	4.1	117.205	113.105
25	G	CA	2.61	47.71	45.1
26	S	N	-3.476	113.291	116.767
26	S	CA	-2.274	55.926	58.2
26	S	CB	2.137	65.337	63.2
27	N	N	-2.762	118.532	121.294
27	N	CA	-0.244	52.806	53.05
27	N	CB	4.216	42.703	38.487
28	K	N	8.695	130.245	121.55
28	K	CA	-1.528	54.759	56.287
28	K	CB	2.539	35.039	32.5
29	G	N	2.132	112.477	110.345
29	G	CA	3.062	48.162	45.1
30	A	N	1.6	125.087	123.487
30	A	CA	-1.784	50.253	52.037
30	A	CB	2.263	21.263	19
31	I	N	1.087	121.057	119.97
31	I	CA	-1.997	59.303	61.3
31	I	CB	6.017	44.017	38
32	I	N	1.029	125.735	124.706
32	I	CA	-1.632	59.668	61.3
32	I	CB	2.946	40.946	38
33	G	N	-2.151	110.785	112.936

33	G	CA	0.293	45.393	45.1
34	L	N	-11.609	110.681	122.29
34	L	CA	1.861	56.701	54.84
34	L	CB	-0.356	41.703	42.059
35	M	N	-2.461	118.639	121.1
35	M	CA	-0.825	54.475	55.3
35	M	CB	3.783	36.383	32.6
36	V	N	3.349	124.596	121.247
36	V	CA	-2.15	60.15	62.3
36	V	CB	2.693	34.516	31.823
37	G	N	2.741	115.366	112.625
37	G	CA	-0.073	45.027	45.1
38	G	N	0.89	110.757	109.867
38	G	CA	3.117	48.217	45.1
39	V	N	8.169	129.15	120.981
39	V	CA	-1.168	61.132	62.3
39	V	CB	2.845	34.668	31.823
40	V	N	4.837	128.176	123.339
40	V	CA	-1.469	60.831	62.3
40	V	CB	2.735	34.558	31.823
41	I	N	3.055	127.45	124.395
41	I	CA	-1.72	59.58	61.3
41	I	CB	1.479	39.479	38
42	A	N	7.183	134.139	126.956
42	A	CA	0.474	52.511	52.037
42	A	CB	1.275	20.275	19

Table S4. Acquisition parameters

	3D NCACX	3D NCOCX	3D CONCA	2D ^{13}C-^{13}C-DARR	2D ^{13}C-^{13}C-RFDR	2D ^{13}C-^{15}N-TEDOR	2D ^{13}C-^{13}C-TOBSY
^{1}H Larmor frequency (MHz)	800	750	750	800	800	800	800
Isotope labeling	U-^{13}C^{15}N	U-^{13}C^{15}N	U-^{13}C^{15}N	U-^{13}C^{15}N	U-^{13}C^{15}N	U-^{13}C^{15}N	U-^{13}C^{15}N
MAS frequency (kHz)	12.5	12.5	12.5	20	20	20	21
TRANSFER 1	HN-CP	HN-CP	HC-CP	HC-CP	HC-CP	HC-CP	HC-INEPT
^{1}H field (kHz)	62.5	62.5	62.5	62.5	62.5	62.5	-
X field (kHz)	50	50	83	62.5	62.5	83	-
Shape	Ramp (100-70%)	Ramp (100-70%)	Ramp (100-70%)	Ramp (100-70%)	Ramp (100-70%)	Ramp (70-100%)	-
Carrier (ppm)	-	-	-	95	95	95	-
Time (ms)	2	2	1.2	1.2	1.2	1.2	-
TRANSFER 2	NC-CP	NC-CP	CN-CP	DARR	RFDR	TEDOR	TOBSY (P9-1-6)
^{1}H field (kHz)	100	100	100	20	83	83	83
^{13}C field (kHz)	30	62.5	62.5	-	62.5*	50	60
^{15}N field (kHz)	42.5	50	50	-	-	50	-
Shape	Ramp (100-90%)	Ramp (100-70%)	Ramp (100-70%)	-	-	-	-
Carrier (ppm)	55	165	165	-	95	95	30
Time (ms)	4	4	4	80	1.6	3.	9.6
TRANSFER 3	DARR	DARR	NC-CP	-	-	-	-
^{1}H field (kHz)	12.5	12.5	100	-	-	-	-
X field (kHz)	-	-	-	-	-	-	-
Shape	-	-	-	-	-	-	-
Carrier (ppm)	-	-	55	-	-	-	-
Time (ms)	80	80	5	-	-	-	-
t_1 increments	128	240	160	1024	1024	512	256
Sweep width (t_1) (ppm)	29.1			199	199		79
Max. acq. time (t_1) (ms)	27.2			12.8	12.8		8
t_2 increments	160			2048	2048		2376

Table S5. Processing parameters

	3D NCACX	**3D NCOCX**	**3D CONCA**	**2D ^{13}C-^{13}C-DARR**	**2D ^{13}C-^{13}C-RFDR**	**2D ^{13}C-^{15}N-TEDOR**	**2D ^{13}C-^{13}C-TOBSY**
Size of real spectrum (t_1)	256	240	160	2048	2048	512	512
Window function (WDW) (t_1)	Gauss	Gauss	Gauss	Squared sine	Squared sine	Gauss	Gauss
WDW - LB (Hz) (t_1)	20	20	20	-	-	20	20
WDW - GB (t_1)	0.1	0.1	0.1	-	-	0.05	0.03
WDW - SSB (t_1)	-	-	-	3.5	3.5	-	-
Size of real spectrum (t_2)	512	260	240	4096	4096	1024	8192
Window function (WDW) (t_2)	Gauss	Gauss	Gauss	Squared sine	Squared sine	Gauss	Gauss
WDW - LB (Hz) (t_2)	20	20	20	-	-	20	20
WDW - GB (t_2)	0.1	0.1	0.1	-	-	0.05	0.03
WDW - SSB (t_2)	-	-	-	3.5	3.5	-	-
Size of real spectrum (t_3)	4096	1024	1024	-	-	-	-
Window function (WDW) (t_3)	Gauss	Gauss	Gauss	-	-	-	-
WDW - (Hz) (t_3)	20	20	20	-	-	-	-
WDW - GB (t_3)	0.1	0.1	0.1	-	-	-	-
WDW - SSB (t_3)	-	-	-	-	-	-	-

References

(1) Morimoto, A.; Irie, K.; Murakami, K.; Masuda, Y.; Ohigashi, H.; Nagao, M.; Fukuda, H.; Shimizu, T.; Shirasawa, T. *J Biol Chem* **2004**, *279*, 52781.

(2) Luhrs, T.; Ritter, C.; Adrian, M.; Riek-Loher, D.; Bohrmann, B.; Doeli, H.; Schubert, D.; Riek, R. *P Natl Acad Sci USA* **2005**, *102*, 17342.

(3) Bertini, I.; Gonnelli, L.; Luchinat, C.; Mao, J. F.; Nesi, A. *J Am Chem Soc* **2011**, *133*, 16013.

(4) Huber, M.; Ovchinnikova, O. Y.; Schutz, A. K.; Glockshuber, R.; Meier, B. H.; Bockmann, A. *Biomolecular NMR Assignments* **2014**.

(5) Petkova, A. T.; Ishii, Y.; Balbach, J. J.; Antzutkin, O. N.; Leapman, R. D.; Delaglio, F.; Tycko, R. *P Natl Acad Sci USA* **2002**, *99*, 16742.

(6) Paravastu, A. K.; Leapman, R. D.; Yau, W. M.; Tycko, R. *P Natl Acad Sci USA* **2008**, *105*, 18349.

(7) Olofsson, A.; Lindhagen-Persson, M.; Sauer-Eriksson, A. E.; Ohman, A. *Biochem J* **2007**, *404*, 63.

(8) Kheterpal, I.; Wetzel, R. *Accounts Chem Res* **2006**, *39*, 584.

(9) Williams, A. D.; Portelius, E.; Kheterpal, I.; Guo, J. T.; Cook, K. D.; Xu, Y.; Wetzel, R. *J Mol Biol* **2004**, *335*, 833.

(10) Olofsson, A.; Lindhagen-Persson, M.; Sauer-Eriksson, A. E.; Ohman, A. *Amyloid* **2006**, *13*, 50.

(11) Olofsson, A.; Sauer-Eriksson, A. E.; Ohman, A. *J Biol Chem* **2006**, *281*, 477.

(12) Whittemore, N. A.; Mishra, R.; Kheterpal, I.; Williams, A. D.; Wetzel, R.; Serpersu, E. H. *Biochemistry-Us* **2005**, *44*, 4434.

(13) Torok, M.; Milton, S.; Kayed, R.; Wu, P.; McIntire, T.; Glabe, C. G.; Langen, R. *J Biol Chem* **2002**, *277*, 40810.

(14) Lopez del Amo, J. M.; Schmidt, M.; Fink, U.; Dasari, M.; Fandrich, M.; Reif, B. *Angew Chem Int Edit* **2012**, *51*, 6136.