SUPPLEMENTARY MATERIALS

AMINO ACID POSITION-SPECIFIC CONTRIBUTIONS TO AMYLOID β-PROTEIN OLIGOMERIZATION†

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Running title: Control of Aβ oligomerization

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Table S1. Electrophoretic migration of Aβ oligomers[a]

Band[b]	[Y^{1}]Aβ40	Aβ40	[Y^{20}]Aβ40	[Y^{30}]Aβ40	[Y^{40}]Aβ40	[Y^{1}]Aβ42	Aβ42	[Y^{20}]Aβ42	[Y^{30}]Aβ42	[Y^{42}]Aβ42
1	0.874	0.845	0.847	0.848	0.852	0.851	0.841	0.850	0.854	0.835
2	0.746	0.703	0.678	0.688	0.701	0.719	0.680	0.654	0.654	0.667
3	0.609	0.578	0.517	0.556	0.563	0.538	0.545	0.540	0.539	0.530
4	0.563	0.460	0.395	0.483	0.486	0.509	0.458	0.43	0.426	0.424
5	0.444	0.367	0.305	0.395	0.451	0.413	0.364	0.322	0.316	0.317
6	0.344	0.318	0.249	0.308	0.390	0.355	0.280	0.224	0.209	0.217
7	0.294	–	–	0.230	0.304	0.216	0.216	0.149	0.126	0.123
8	–	–	–	–	0.223	0.164	–	–	–	–
9	–	–	–	–	0.159	0.123	–	–	–	–

[a]R_f values for the bands shown in Fig. 5 are listed. [b]Band numbers are referenced to the monomer band, which is #1, and increase in magnitude with decreasing R_f values.

FIGURE LEGENDS

Fig. S1. Kinetic analysis of CD data. To obtain quantitative insight into the kinetics of the RC→α/β→β conformational conversions monitored by CD, we plot the time-dependence of θ_{222}. For systems that display significant population of α-helix states, θ_{222} is a useful estimator of α-helix content. For systems that display rapid α-helix→β-sheet conversions, θ_{222} can be used as an estimator of overall conversion rate, but not α-helix *per se*, because θ_{222} is correlated with $\theta_{215–218}$, a measure of β-sheet content. (A) Aβ40. The half-time for the development of α-helix structure is defined as the time at which θ_{222} has a value equal to half the difference between its maximum and minimum values. The time at which maximal α-helix structure occurs is defined by the point of inflection at the θ_{222} minimum. (B) Aβ42. Conversions in this system occur at a rate approximately twice that of Aβ40. The kinetic analysis thus provides information on the sum of the rates of conversion from RC→α and α→β. No minimum is observed in the Aβ42 system. This is because CD is especially sensitive to α-helix, which produces a greater absolute value of θ than is seen with β-sheet. For the Aβ40 peptides, the α-helix intermediates we have reported before (see Kirkitadze *et al.* (2001) *J. Mol. Biol.* 312:1103–1119) can accumulate because of the rate differences between its formation (causing θ_{222} of greater magnitude) and its conversion to fibrils (causing θ_{218} of greater magnitude, but less than that of θ_{222}). In contrast, for Aβ42, the maximum α-helix content is low (versus Aβ40) and the α/β→β transition occurs rapidly, so that the increasing magnitude of the θ_{218} compensates for the loss of the θ_{222} signal and a minimum is not observed. θ just keeps going down (more negative).

Fig. S2. Frequency distributions of particles examined by EM. Oligomer dimensions were determined by inspection of EM images with lens and graticule. A representative sample was obtained with particle number *n=40*. Distributions are shown for: (A), diameters of globular forms of un-cross-linked Aβ40; (B), diameters of globular forms of cross-linked Aβ40; (C), lengths of protofibrillar forms of Aβ40; (D), diameters of protofibrillar forms of Aβ40; (E), diameters of globular forms of [Tyr^{40}]Aβ40; (F), lengths of protofibrillar forms of [Tyr^{40}]Aβ40; and (G), diameters of globular forms of cross-linked [Tyr^{40}]Aβ40.

Fig. S1A

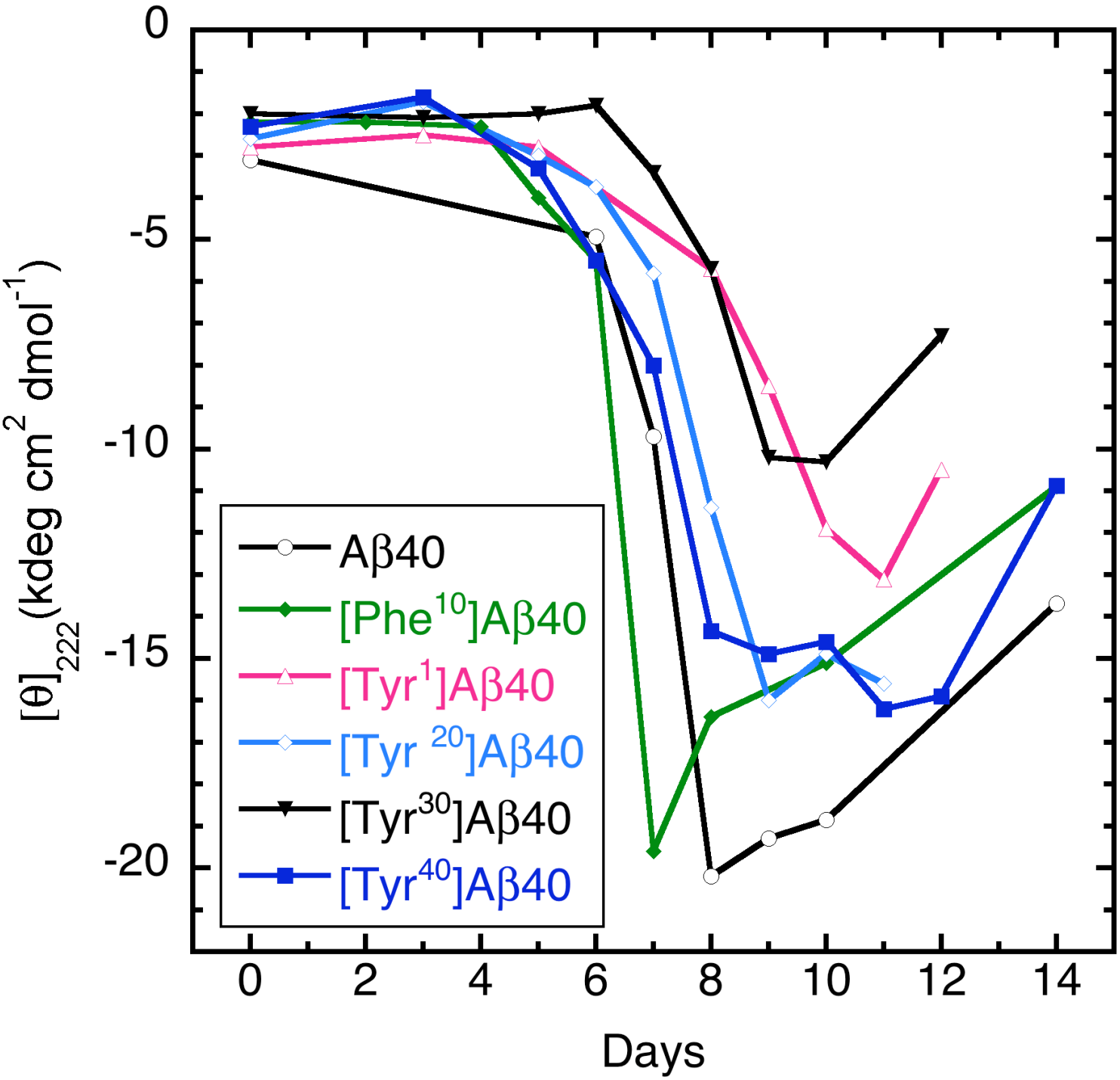

0
-5
-10
-15
-20
$[\theta]_{222}$(kdeg cm^2 dmol^{-1})
0
2
4
6
8
10
12
14
Days
Aβ40
[Phe^{10}]Aβ40
[Tyr^1]Aβ40
[Tyr ^{20}]Aβ40
[Tyr^{30}]Aβ40
[Tyr^{40}]Aβ40

Fig. S1B

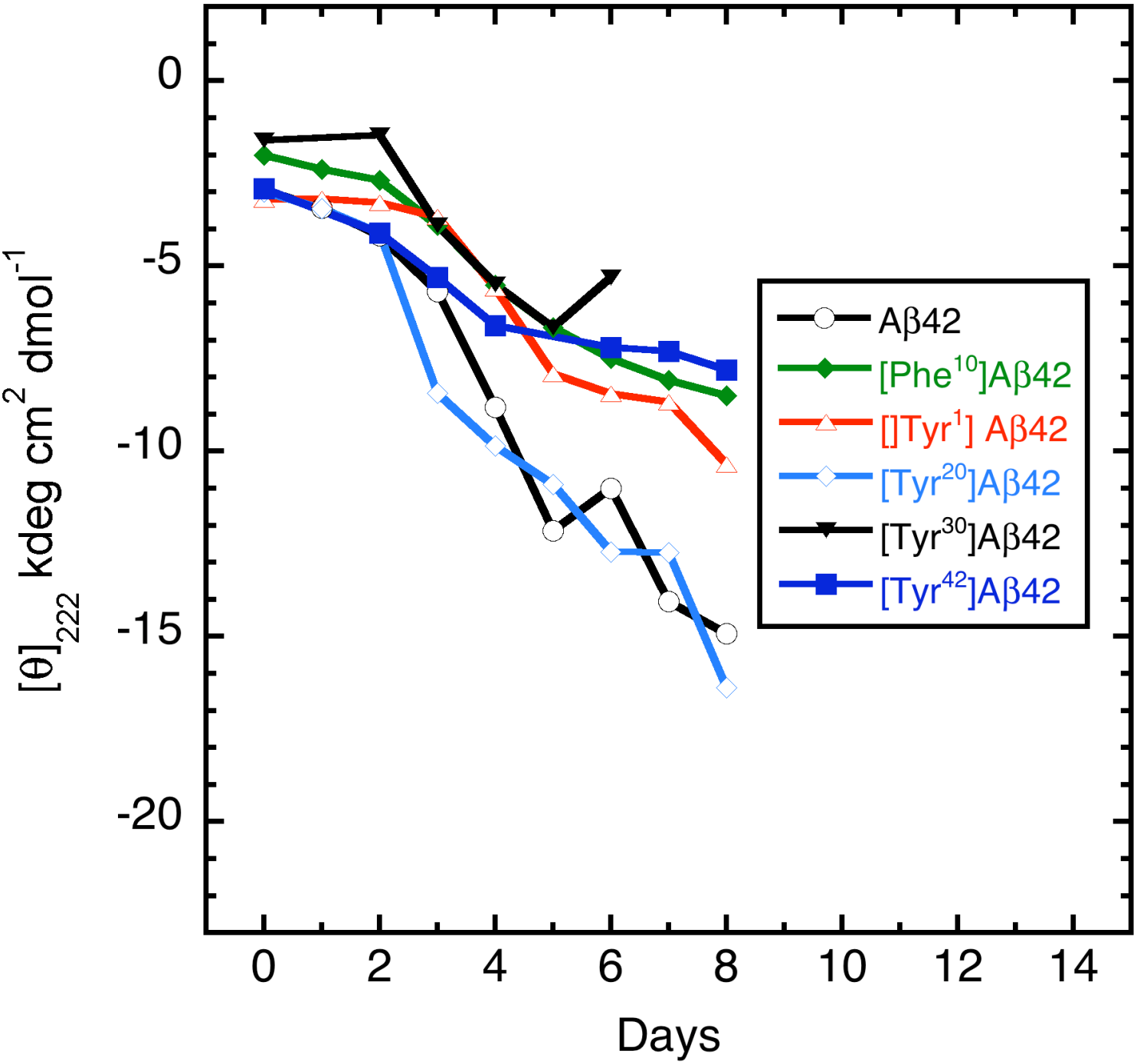
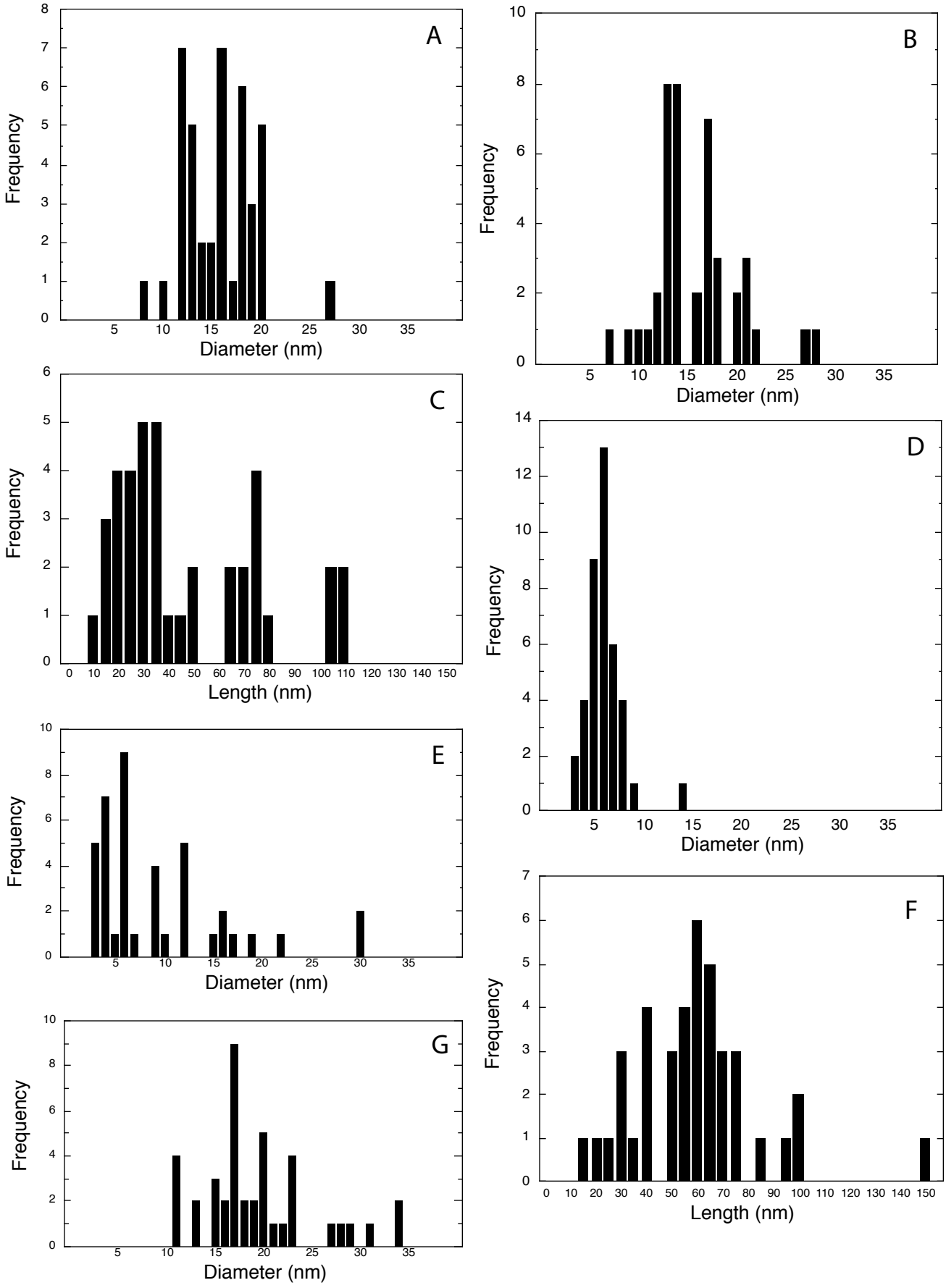

0
-5
-10
-15
-20
0
2
4
6
8
10
12
14
Days
$[\theta]_{222}$ kdeg cm^2 dmol^{-1}
Aβ42
[Phe^{10}]Aβ42
[]Tyr^1] Aβ42
[Tyr^{20}]Aβ42
[Tyr^{30}]Aβ42
[Tyr^{42}]Aβ42

Fig. S2


A
Frequency
Diameter (nm)
B
Frequency
Diameter (nm)
C
Frequency
Length (nm)
D
Frequency
Diameter (nm)
E
Frequency
Diameter (nm)
F
Frequency
Length (nm)
G
Frequency
Diameter (nm)