

## Supporting Information for

### Formation of amyloid loops in brain tissues is controlled by the flexibility of protofibril chains.

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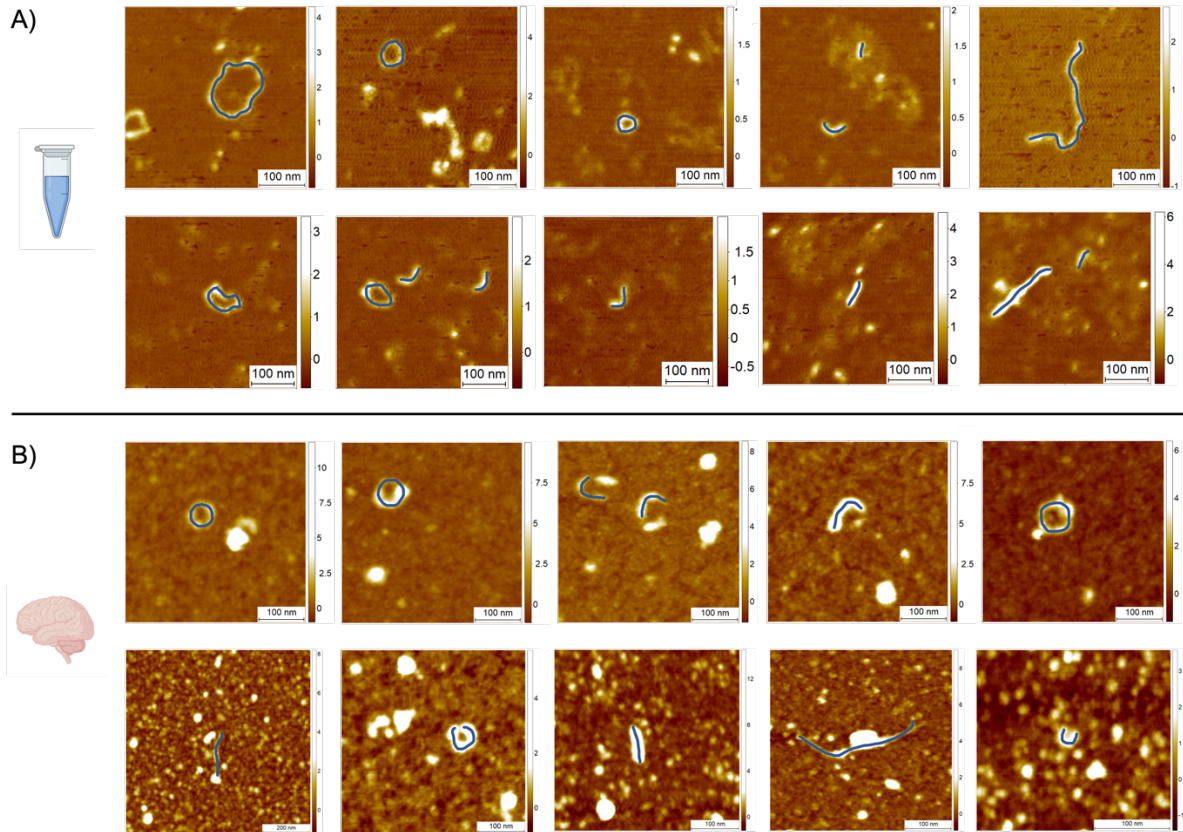
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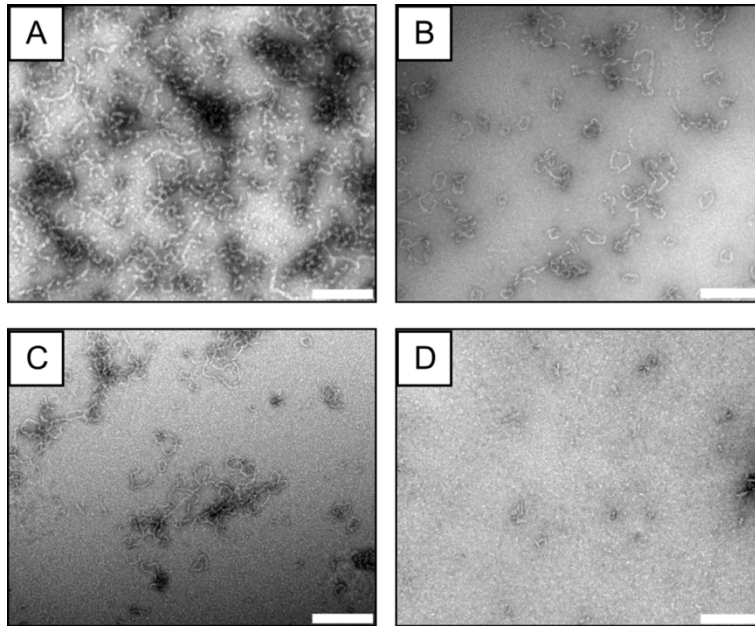
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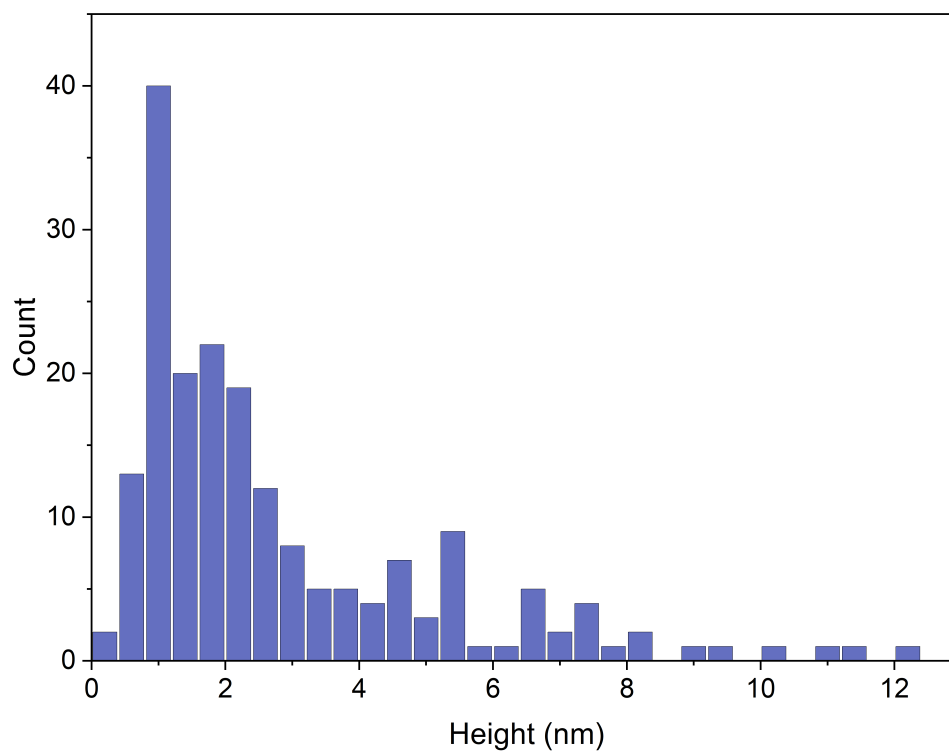
Figures S1 to S5



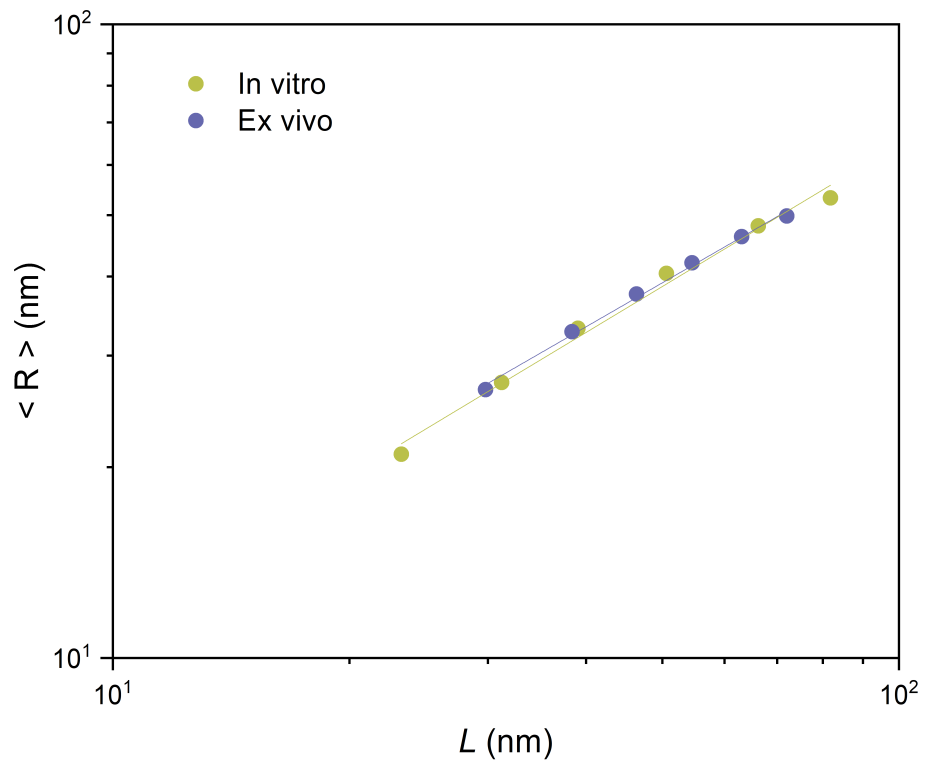
**Fig. S1.** A gallery of examples of open and closed loops of varying length for *in vitro* (A) and *ex vivo* (B) protofibrils. Loops were traced (blue lines) as a visual aid to demonstrate which particles were included in the analysis.



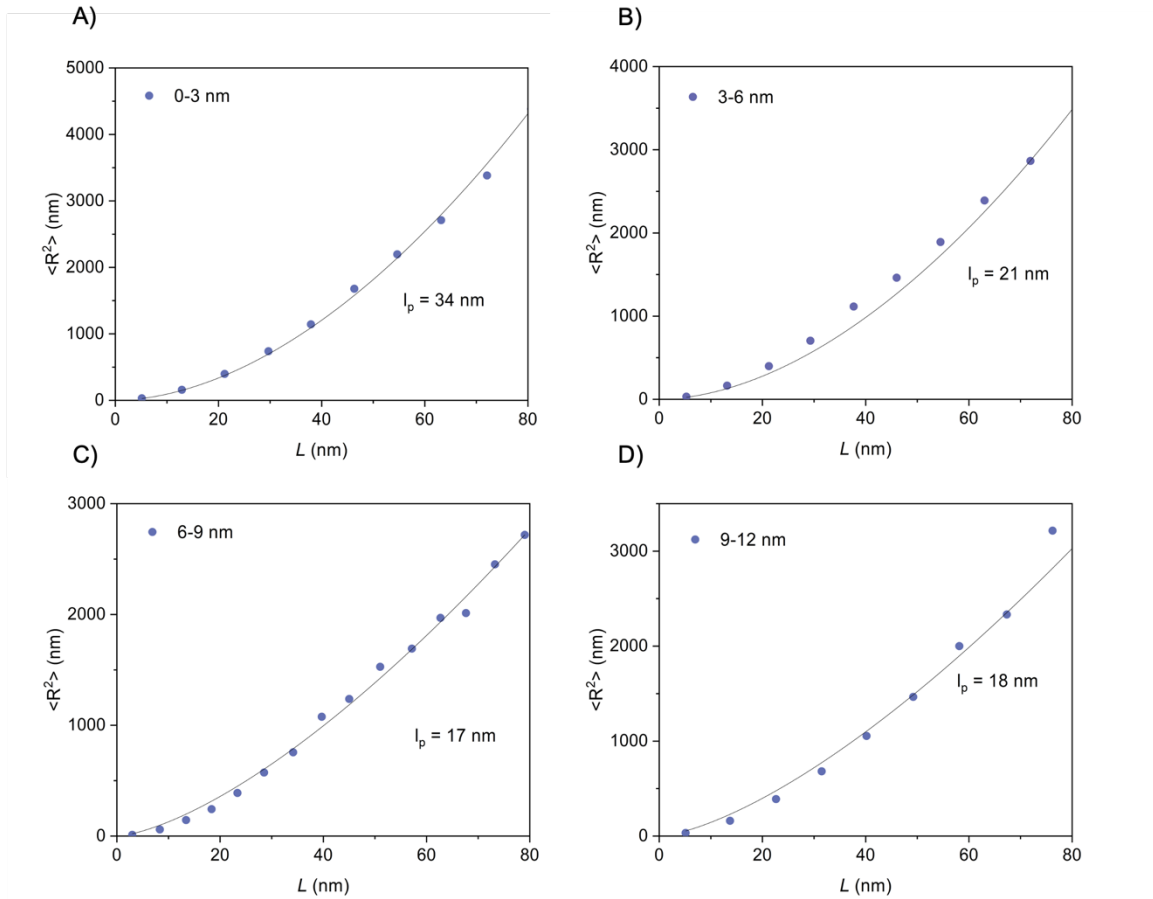
**Fig. S2.** TEM imaging of recombinant  $\alpha$ -lactalbumin aggregates}. (A-D)  $\alpha$ -lactalbumin was imaged via TEM in destabilising conditions after 2 (A), 5 (B), 14 (C), and 72 (D) hours incubation time. Protofibrillar structures are initially observed (A), followed by the observation of closed ring structures (B & C). After prolonged incubation (D), the elongated structures are no longer observed.



**Fig. S3.** The cross-sectional height distribution for *ex vivo* aggregates was measured using AFM. The mean height was  $2.8 \pm 2.3$  nm ( $n=198$ ).



**Fig. S4.** A double logarithmic plot of the end-to-end distance,  $R$ , vs the contour length,  $L$ . The scaling exponent,  $\lambda$ , provides information on the dimension of the system, with  $\lambda = 1, 0.75, 0.588$  for  $D = 1, 2,$  and  $3$  respectively.  $\lambda = 0.72$  for *ex vivo*, and  $\lambda = 0.75$  for *in vitro* protofibrils.



**Fig. S5.** Plots of contour length,  $L$  vs mean squared end-to-end distance,  $\langle R^2 \rangle$  for *ex vivo* protofibrils. Due to the heterogeneous nature of brain samples, it is likely that more than one protein species exists. Analysis was therefore performed in groups corresponding the height of (A) 1 ( $n=137$ ), (B) 2 ( $n=24$ ), (C) 3 ( $n=28$ ), and (D) 4 ( $n=9$ ) individual protofilaments.