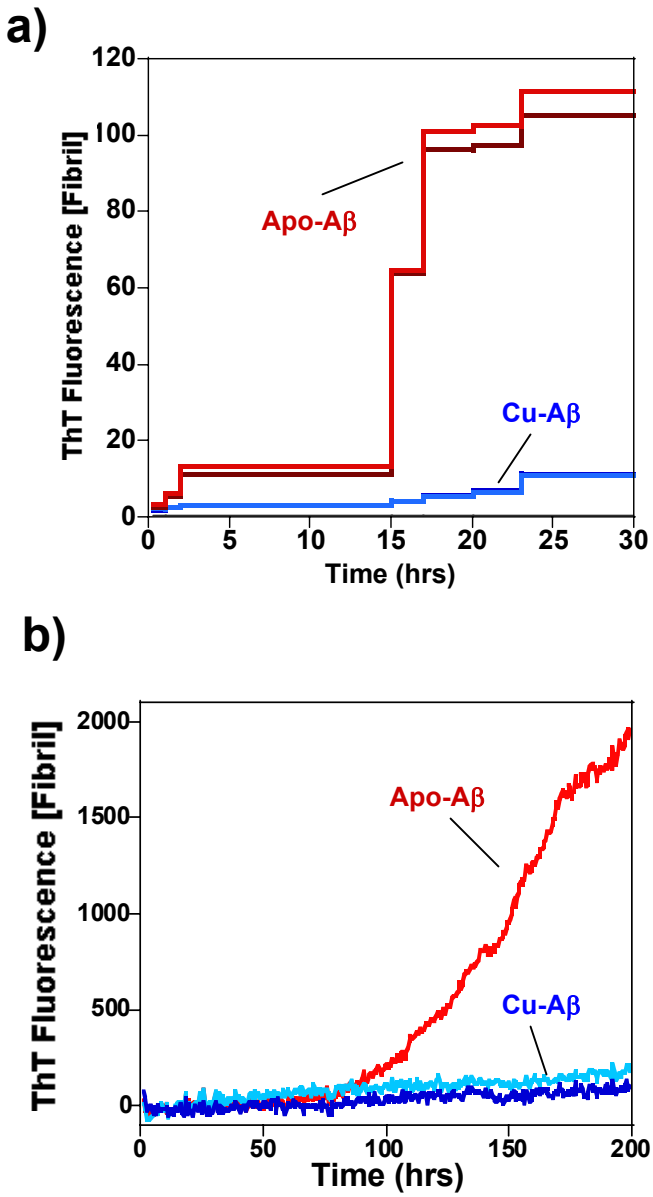
Supplemental Table S1.

		Nucleating Rate (x 10^{-3})	Elongation Rate (x10^{-3})
(a)	Apo 50% Cu^{2+}	0.037 (0.017) 0.16 (0.03)	0.117 (0.007) 0.147 (0.004)
(b)	Apo 100% Cu^{2+}	0.19 (0.07) 0.15 (0.06)	0.098 (0.008) 0.19 (0.00)
(c)	Apo 100% Cu^{2+}	0.41 (0.08) 1.1 (0.4)	0.073 (0.005) 0.14 (0.02)

Supplemental Table S1, shows the nucleating and elongation rate obtained from Equation 2 (Morris *et al* 2008) for the same data shown in Figure 1. k_1 describes the monomer converting into a nucleating species. While k_2 describes monomer addition on to the nucleating species (elongation). It should be noted that k_2 is simply an average rate of multiple additions and assumes that the rate constant is independent of fibre size.

$$[B]_t = [A]_0 - \frac{k_1/k_2 + [A]_0}{1+k_1/k_2[A]_0 \exp(k_1+k_2[A]_0)t} \qquad \text{(Eq 2)}$$

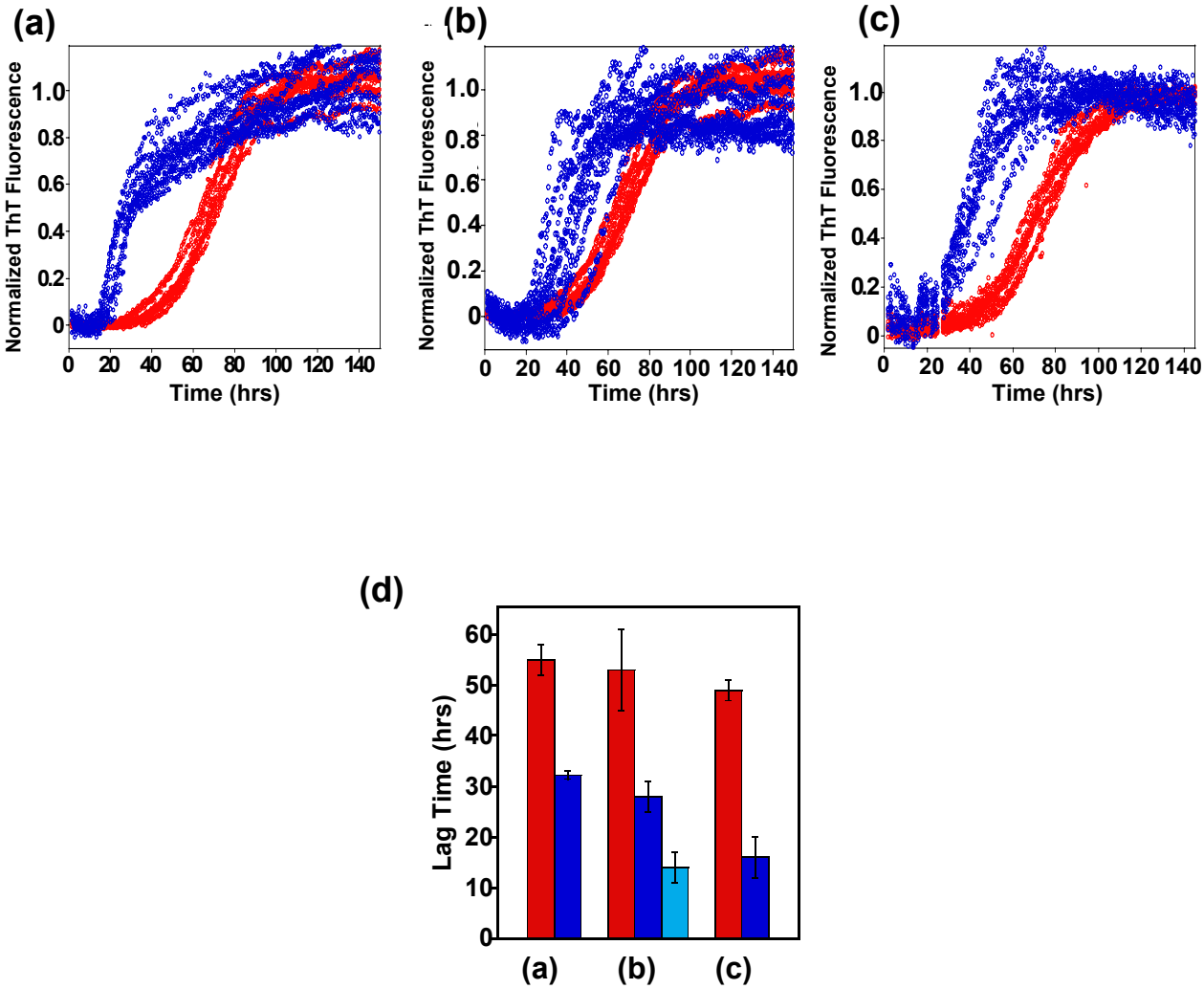
Where $[B]_t$ is the fibrillar concentration as measured by the ThT signal and $[A]_0$ is the total concentration of Aβ in monomeric and fibrillar form: $[A]_0=[B]_t+[A]_t$ (where $[A]_t$ is the amount of monomer at time t). k_1 (units of hrs^{-1}) is proportional to 1/lag time and $k_2[A]_0$ is proportional to the slope during elongation.



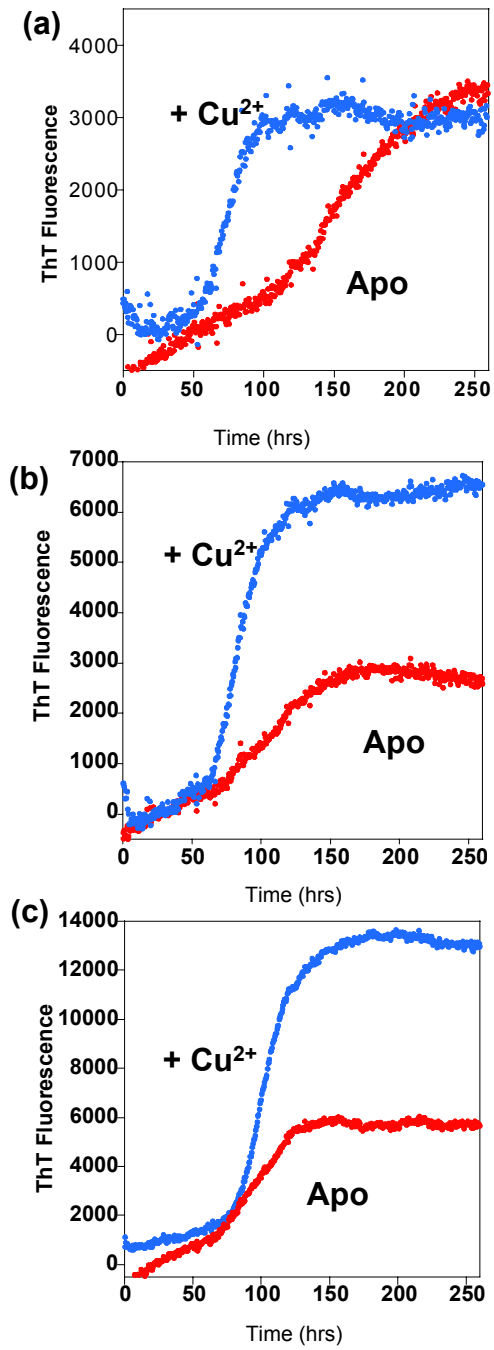
Supplemental Figure S1: Cu^{2+} only at high Aβ concentration or supra-stoichometric levels will inhibits fibre formation.

a) 50 µM Aβ(1-40). Apo Aβ (red traces). Cu^{2+} ions, 0.5 mole equivalent (blue traces).

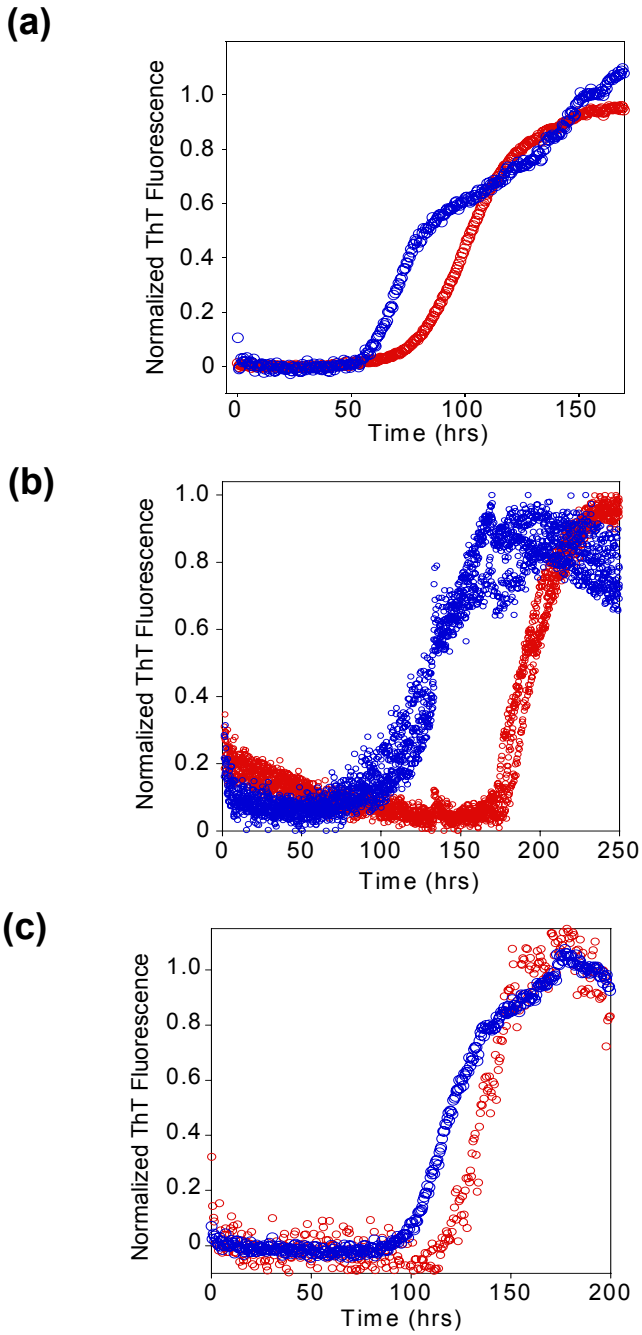
b) 5 µM Aβ(1-40). No Cu^{2+} ions (red trace); 2 mole equivalents of Cu^{2+} (light blue) and 4 mole equiv Cu^{2+} (dark blue). Average of n=6, 50 mM HEPES buffer and 160 mM NaCl, pH 7.4 at 30 ºC, 30 seconds agitation every 30 minutes.



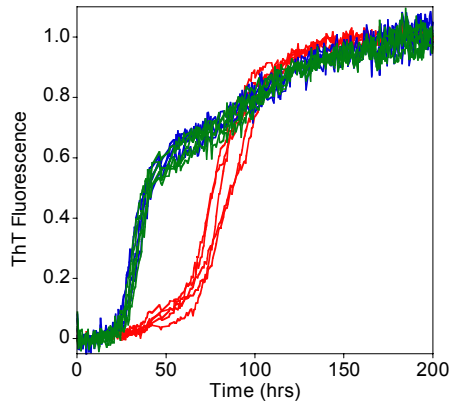
Supplemental Figure S2: Cu^{2+} accelerates Aβ fibril growth. Comparison of Cu^{2+} loaded (blue traces) and Cu^{2+}-free (red traces). Aβ(1-40) at 5 μM, pH 7.4 in the presence of a) 2.5 μM Cu^{2+}, or 5 μM Cu^{2+} in b) and c). All carried out in 50 mM HEPES, 160mM NaCl, 30º C, with agitation for 30 seconds every 30 minutes. Figures b) and c) are from two separate experiments. The ThT fluorescence intensities have been normalized. Averages of the nine traces are shown in Fig. 1(b). (d) Bar-graph of t_{lag} with apo-Aβ shown as red bars, and Aβ with 1 mole equivalent Cu^{2+} (dark blue bars) and 0.5 mole equivalent Cu^{2+} (light blue bar).



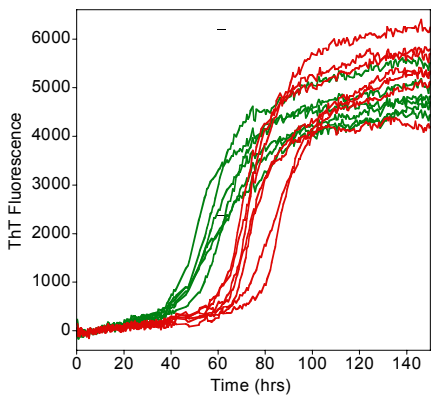
Supplemental Figure S3: Cu^{2+} accelerates Aβ(1–42) fibril growth. Aβ(1-42) at 1 μM (a), 3 μM (b) and 5 μM (c) with and without 0.5 mole equivalents Cu^{2+} ions. Growth curves are a sum of 6 traces. Absolute ThT fluorescence intensity. All carried out in 50 mM HEPES, 160mM NaCl, 30º C, with agitation for 30 seconds every 30 minutes.



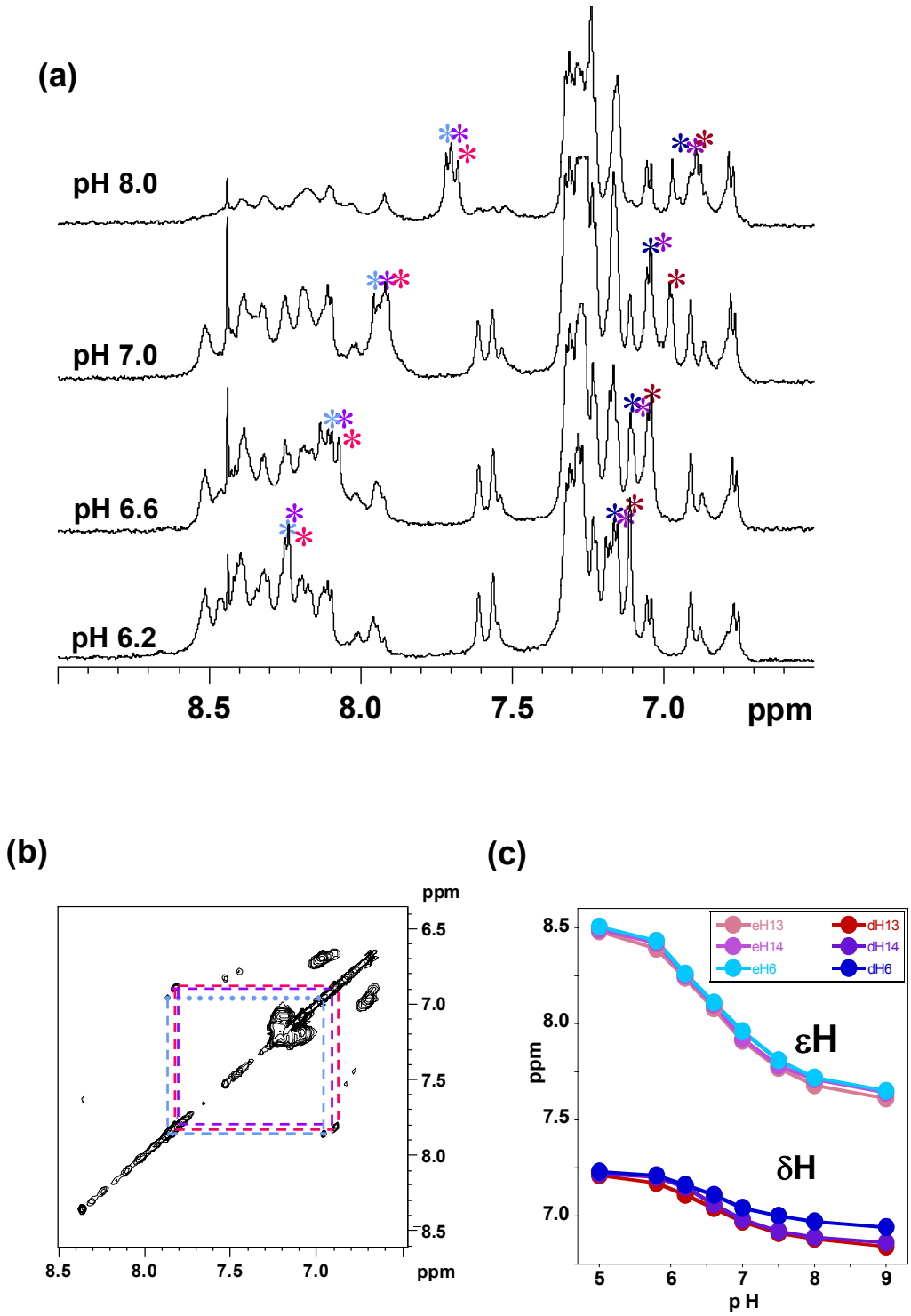
Supplemental Figure S4: Cu^{2+} accelerates Aβ fibril growth over a range of pH's. (a) pH 8 (b) pH 8.5 and (c) pH 9. Blue traces are for Aβ(1-40) with 1 mole equivalent Cu^{2+}, red traces are for apo Aβ(1-40). (a) and (c) are means of the fluorescence from six growth curves. Aβ(1-40) at 5 μM in 50 mM HEPES, 160 mM NaCl.



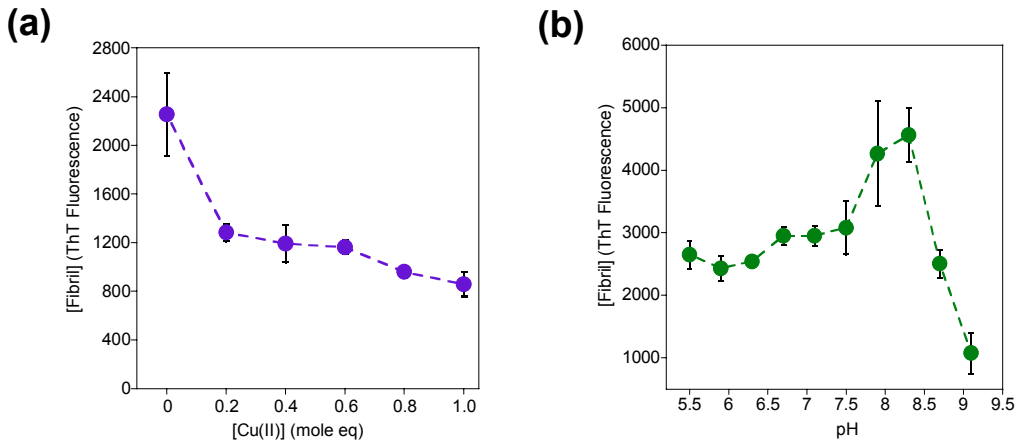
Supplemental Figure S5: Fibril growth with Cu^{2+} as a $Cu(Gly)_2$ chelate. Comparison of 5 µM Aβ(1-40) with no Cu^{2+} (red spectra), 2.5 µM Cu^{2+} (blue spectra) and 2.5 µM $Cu^{2+}(glycine)_2$ chelate (green spectra). The ThT fluorescence intensities of the data have been normalized, however the addition of glycine made no difference to either the rate or intensity of the fibril growth curve compared to adding Cu^{2+} alone and the sets of traces (2 x 5 traces) overlap. 5 µM Aβ(1-40) in 50 mM HEPES, 160 mM NaCl, pH 7.4, 30º C, with agitation for 30 seconds every 30 minutes.



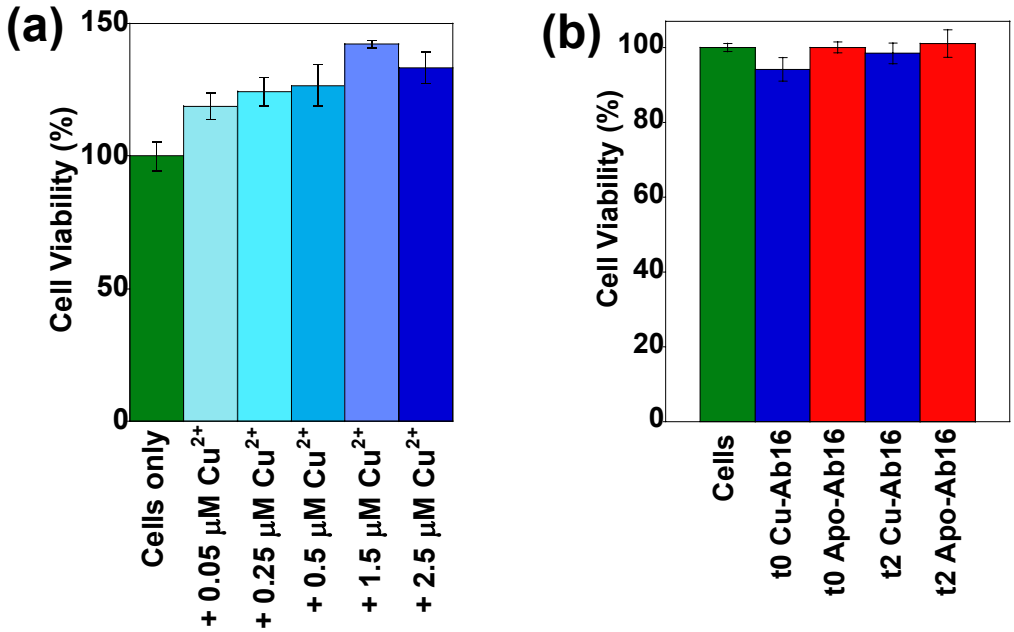
Supplemental Figure S6: Cu^{2+} induced fibrils will seed fibril formation. Comparison of 5.5 µM apo Aβ(1-40) (red traces) and 5 µM apo-Aβ with 10 % preformed (Cu^{2+} promoted) Aβ-fibrils (green traces). All carried out in 50 mM HEPES, 160mM NaCl, pH 7.4, 30º C, with agitation for 30 seconds every 30 minutes. The fluorescence intensities are absolute values.



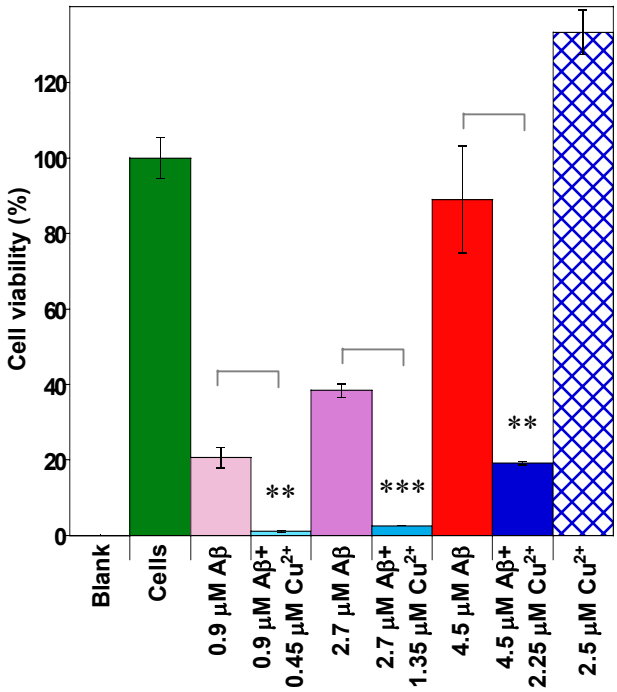
Supplemental Fig. S7: pKa measurements of Aβ histidine residues. a) A selection of 1D ^{1}H NMR spectra from a pH titration, 100 µM Aβ(1-28) in 20 mM phosphate buffer at 25 ºC. CδH and CεH singlets are highlighted. b) 2D TOCSY spectrum of histidine region of Aβ(1-28) , pH 7, 60 ms spin-lock mixing time. c) pH dependence of CδH and CεH ^{1}H chemical shift. pKa are: 6.67, 6.67 and 6.64 at 25 °C in 90% H_2O 10% D_2O. Note that the amide protons become more intense at pH 7 and below.



Supplemental Fig. S8: Effect of Cu^{2+} concentration and pH on total fibril levels. a) Effect of Cu^{2+} on the maximal ThT fluorescence signal. At 2 and 4 mole equivalent Cu^{2+} the fibril growth is inhibited. b) The effect of pH on the maximum fluorescence. 5 µM Aβ in 50 mM HEPES, 160 mM NaCl, at pH 7.4, 30 °C, with intermittent agitation.



Supplemental Figure S9: Free Cu^{2+} ions and Cu^{2+} ions bound to soluble Aβ(1-16) are not cyto-toxic. (a) Cu^{2+} ions were added as $CuCl_2$ and incubated with PC12 cells for 24 hrs, Alamar blue was then added and cell viability compared. Data is shown after 70 hours total incubation. At 6 days Alamar Blue was added again and additional readings taken (data not shown), cell viability in the presence of Cu^{2+} was again comparable to the viability of cells without Cu^{2+} ions. The cell concentration was 5.9 x 10^4 cells/ml. (b) Cu^{2+}-Aβ(1-16) was added to cells (t0) or incubated for 200 hours (t2) under fibril forming conditions to confirm fibrils did not form and to mimic the conditions of experiments with full-length Aβ. The preparations were then incubated with PC12 cells. Cell concentration was 5.9 x 10^4 cells/ml. Alamar Blue was added after 24 hrs incubation. For both (a) and (b) error bars are standard error.



Supplemental Figure S10. Cu^{2+}-Aβ(1-42) is more cyto-toxic than Aβ(1-42). Cu^{2+}-Aβ(1-42) 1, 3 and 5 µM Aβ(1-42) fibrils were formed with and without 0.5 mol eq Cu^{2+} ions. After fibril formation (monitored by ThT) the fibrils were added to 10% (v/v) PC12 cells. Cell concentration was 5.9 x 10^4 cells/ml. 2.5 µM Cu^{2+} was added to the cells alone to test Cu^{2+} toxicity. Blank is buffer only. All preparations were incubated with the cells for 24 hrs then 10% (v/v) Alamar Blue was added. The data shown here is after total incubation for 70 hrs. Error bars are standard error (s.e.m). P= 0.001 indicated by *** and P=0.01 ** .