Supporting Information

Experimental

Chemicals

POMs were synthesized as previously described in the literature.^[1] A stock solution of 20 mM was prepared in ultrapure water. It was aliquoted and stored at -20°C until used. Diluted stock solutions were prepared freshly before used. A stock solution of Cu(II) at 20 mM was prepared by dissolving CuSO₄·5H₂O (Sigma Aldrich) in ultrapure water. HEPES buffer was bought from Sigma Aldrich and dissolved in ultrapure water to a final concentration of 0.5 M, and pH was adjusted to 6.9 by addition of NaOH. A stock solution of sodium ascorbate (Sigma Aldrich) at 10 mM was daily prepared in ultrapure water. A stock solution of Thioflavin T (Acros Organics) at ca. 5 mM was prepared by dissolving the powder in ultrapure water, with further titration by UV-vis spectroscopy (ϵ_{412} - ϵ_{500} = 36 000 M⁻¹cm⁻¹).^[2] From this stock solution, 250 μ M aliquots were prepared and kept at -20 °C until use. All the peptides were bought from GeneCust (Dudelange, Luxembourg) with a purity grade > 98 %. Stock solutions of human $A\beta_{16}$ (sequence DAEFRHDSGYEVHHQK-COOH) were prepared at ca. 5 mM by dissolving the powder in ultrapure water, and their concentration was determined by UV-vis absorption of Tyr10 considered as free tyrosine (ϵ_{276} - ϵ_{296} = 1410 M⁻¹cm⁻¹). The human A β_{40} peptide (sequence DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV-COOH) was purified to obtain only a monomeric fraction prior its aggregation according to a previously reported protocol.^[3] The peptide concentration was measured by UV-vis absorption of Tyr10 at basic pH (ϵ_{293} - ϵ_{360} = 2400 $M^{-1}cm^{-1}$).

UV-vis spectroscopy

UV-vis spectra were recorded on an Agilent 8453 spectrometer, equipped with a Peltier temperature controller unit that maintained the solution temperature at 25 °C.

Ascorbate consumption

The spectra of consumption of ascorbate, which mirror the production of ROS,^[4] were obtained as a function of time by measuring the absorbance of ascorbate at 265 nm (ϵ = 14 500 M⁻¹cm⁻¹) with a correction for baseline drift at 800 nm.

Thioflavin T assay

Kinetics of aggregation by the Thioflavin T (ThT) assay were recorded using a FLUOstar OPTIMA (BMG Labtech) plate reader. The experiments were prepared in 384-wells non-binding plates

(Greiner BioOne) by dissolving the appropriate quantities of each reactant, in presence of ThT at 10 μ M. 0.1 μ M of EDTA was added (i.e.: 0.5% of [A β_{40}]) to sequestrate trace metal ions. We have controlled that EDTA has no effect on the aggregation of the A β_{40} peptide (except those related to the removal of trace metal ion). ThT was excited at 440 nm and the emission was set at 490 nm. Four independent experiments were mathematically analyzed with at least four replicates for each condition.

Transmission Electron Microscopy (TEM)

Samples were taken after aggregation for 6 days in the 384-well plates and collected by same conditions criteria. They were prepared for electron microscopy by using the conventional negative staining procedure. An aliquot (20μ L) of solution was absorbed on Formvar-carbon-coated grids for 2 min, blotted, and negatively stained with uranyl acetate (1%) for 1 to 2 min. Grids were examined with a TEM (Jeol JEM-1400, JEOL Inc, Pea- body, MA, USA) at 80 kV. Images were acquired by using a digital camera (Gatan Orius, Gatan Inc, Pleasanton, CA, USA) at magnifications between 3000 and 25000.

Fitting of the aggregation curves

The aggregation curves were fitted using the Kaleidagraph software and using the following equation:

 $F(t) = F_0 + \frac{\Delta F}{(1+e^{-k(t-t_{1/2})})} + at$ where F₀ is starting ThT fluorescence value, ΔF the

difference between the final ThT fluorescence and F_0 , k the growth rate and $t_{1/2}$ the time where the ThT fluorescence is half of ΔF value, a has been introduced to take into account a time-dependent drift of the baseline.

In the equation, the F_0 parameters are constrained while the other ones were left to be optimized.

Table S1. Kinetic parameters describing the assembly of the $A\beta_{1-40}$ and $Cu(A\beta_{1-40})$ in presence of 1 equiv. K_e^{8-} or 1 equiv. K^{4-} . Average values on at least 4 replicates, unless specified, and standard deviations (σ).

Sample		Αβ ₁₋₄₀	Αβ ₁₋₄₀ + 1 equiv. Ke ⁸⁻	Αβ ₁₋₄₀ + 1 equiv. K⁴⁻	Cu(Aβ ₁₋₄₀) + 1 equiv. Kε ⁸⁻	Cu(Aβ ₁₋₄₀) + 1 equiv. K⁴⁻
Exp. N°						
1 ^[a]	ΔF (a. u.)	2.0 ± 0.1	4.8 ± 1.5	7.4 ± 3.4	6.6 ± 1.6	4.9 ± 0.2
	t _{1/2} (h)	11 ± 1	13 ± 1	14 ± 2	15 ± 2	14 ± 2
2	ΔF (a. u.)	3.9 ± 0.3	16 ± 12	9 ^[b]	14 ± 3	14 ± 4
	t _{1/2} (h)	15 ± 1	17.5 ± 7	17.5 ^[b]	20 ± 2	15 ± 2
3	ΔF (a. u.)	3.4 ± 0.5	19 ± 4	16 ± 3	15 ± 2	9 ± 1
	t _{1/2} (h)	17 ± 3	18 ± 1	20 ± 2	24 ± 3	35 ± 4

^[a] Corresponds to the data shown. ^[b] Only one curve fitted.

Supplementary Figures.



Figure S1. The stability of K^{4-} and K_e^{8-} was observed by UV absorption spectroscopy in the absence (A and B) or presence (C and D) of Cu(II) for a period of 2.5 h. UV reading were recorded every 30 minutes, with mild agitation. Conditions: [POMs] = 20 μ M, [Cu(II)] = 18 μ M, [HEPES] = 50 mM pH 6.9, T = 25 °C. Colour code: green lines, K^{4-} ; red lines, K_e^{8-} ; blue lines, K_{cu}^{6-} ; grey lines, intermediate molecules.

 K_e^{8-} shows a single band at 226 nm and a shoulder at 253 nm (panel B). Upon solution at pH 6.9 K⁴⁻ degrades to form K_e^{8-} (Eq. S1, based on ref. ^[5]) observed by the loss of the band at 262 nm and the increase of the band at 226 nm (panel A).

$$[SiW_{12}O_{40}]^{4-} (\mathbf{K}^{4-}) + 6 \text{ OH}^{-} \rightarrow [SiW_{11}O_{39}]^{8-} (\mathbf{K}_{e}^{8-}) + WO_{4}^{2-} + 3 \text{ H}_{2}O$$
(Eq. S1)

Degradation of K^{4-} to form the lacunary form K_{ℓ}^{8-} also occurs in the presence of Cu(II) in solution (panel C) in line with the loss of one WO₄ unit by K^{4-} and the subsequent formation of the Cu(II)-POM complex K_{cu}^{6-} (blue line in panel C) while K_{ℓ}^{8-} can readily bind Cu(II) to form K_{cu}^{6-} (blue line in panel D).



Figure S2. Experimental (black dots) and calculated (red lines) kinetic of the self-assembly process of A β and Cu(A β) + 1 equivalent of Ke⁸⁻ and K⁴⁻. Conditions: [A β 40] = [Ke⁸⁻ or K⁴⁻] = 20 μ M, [Cu(II)] = 18 μ M, [HEPES] = 100 mM pH 6.9, 37 °C.



Figure S3. TEM pictures (additional). A and B: fibrils of A β 40 peptide. A: with low magnification and B with higher magnification. C: aggregates of Cu(A β 40). D and E: fibrils of A β 40 peptide made in presence of K_{ℓ}^{8-} and K^{4-} . F and G: fibrils made form Cu(A β 40) in presence of K_{ℓ}^{8-} and K^{4-} .

References.

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