Effect of the air-water interface on the self-assembly of human α-Synuclein

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The aggregation of soluble proteins and peptides into amyloid fibrils is the pathological hallmark of more than 50 human disorders.[1] Moreover, self-assembled amyloids are nowadays considered as appealing materials for nanotechnology applications.[2, 3] Understanding their formation would enable us developing control strategies to inhibit or enhance the self-assembly process, depending on the specific purpose.
We tested the effect of the air-water interface (AWI) on the self-assembly *in vitro* of human α-Synuclein (α-Syn), the major component of the inclusions found in the brains of patients of Parkinson's disease. Albeit artificial, the AWI is a valuable model interface and it is present in most aggregation studies performed *in vitro*. Removal of the AWI inhibits the assembly of α-Syn (Figure 1), even at protein concentration of 0.9 mM.[4] Atomic force microscopy imaging and peak force quantitative nanomechanical mapping were used to investigate the morphology of α-Syn fibrils at the AWI and their stiffness. Multiple populations of aggregates are present over time at the AWI, differing in height, length and Young's moduli. Interestingly, domains of fibrils laterally aligned with each other are frequently found in the early stages of α-Syn aggregation, suggesting a mechanism of surface-catalyzed growth.
Overall, our study provides a first description the influence of the AWI on the self-assembly of α-Syn. As surfaces and interfaces are ubiquitously present, both *in vitro* and *in vivo*, studying their effect will allow achieving a better understanding of protein aggregation.

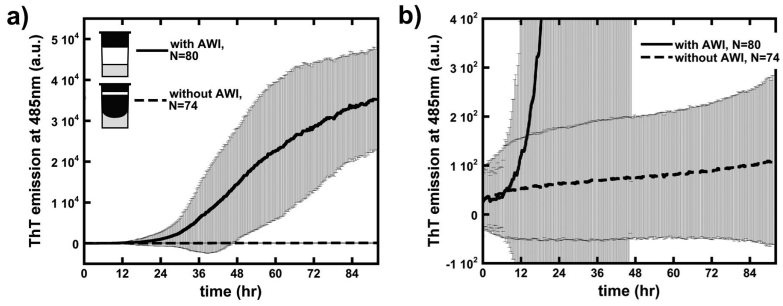

Figure 1 The inhibition of α-Syn aggregation at 0.3 mM when removing the AWI is here measured as lack of increased Thioflavin T (ThT) emission over time, where ThT is an amyloid-binding dye. Panel a) shows a scheme of the manufactured caps used to preserve/remove the AWI. Panel b) is a zoom-in of a).

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