A Model for Nano-Scale Spherical Surface Coverage and Protein Corona Formation By Amyloidogenic Peptides

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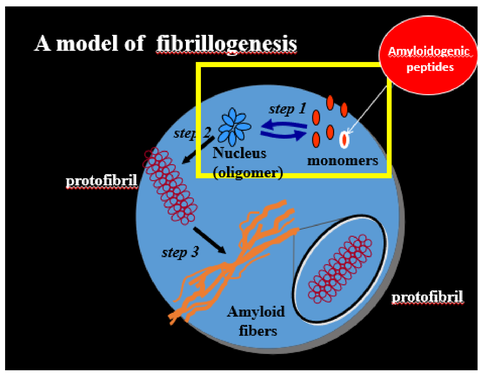
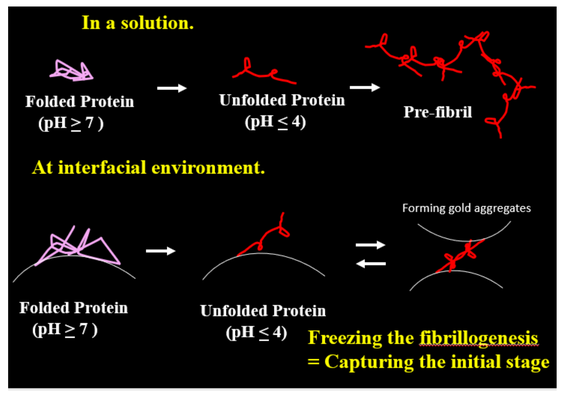
Background

Neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, are generally understood to be caused by the formation of fibers. The fibrillogenesis originates from the formation of oligomers, which in turn are formed from the association of amyloidogenic peptides such as amyloid beta 1–40 or amyloid beta 1–42 (A β_{1-40} or $A\beta_{1-42}$) or α -synuclein (α-syn). Study of these peptides is difficult because oligomer formation is transient and involves unstable intermediates. During this study, only the association of peptides was examined. This is the only step that is known to also be reversible.

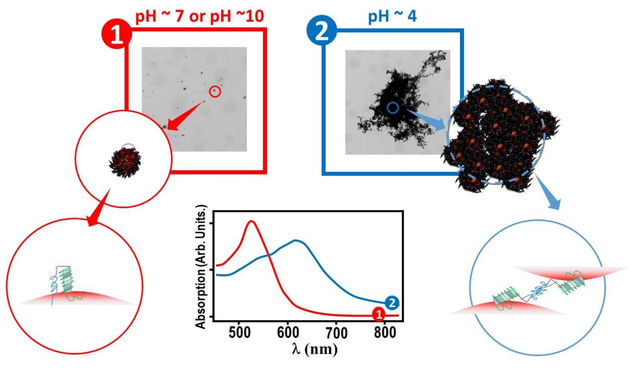
These peptides (A β_{1-40}, A β_{1-42}, α -syn) can be adsorbed onto a nano-gold surface in order to examine how they network. This networking of peptides leads to an aggregation on the gold nanoparticle surfaces. This aggregation leads to a shift in Surface Plasmon Resonance (SPR) from 530 nm to 600 nm. This allows for us to study changes in aggregation and folding based on this change in signal.



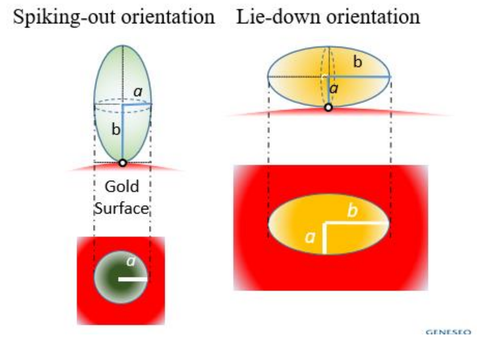
Left: A sketch showing the various steps of fibrillogenesis. Yellow box highlights only step 1, which consists of the protein corona which is the adsorption of peptides over the nano-particles.



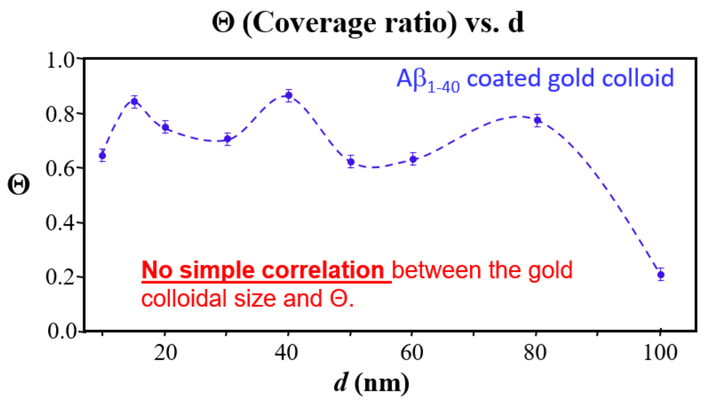
Right: A sketch showing how proteins fold and interact in solution and in interfacial environments. Our goal is to freeze and examine the final step of this process.



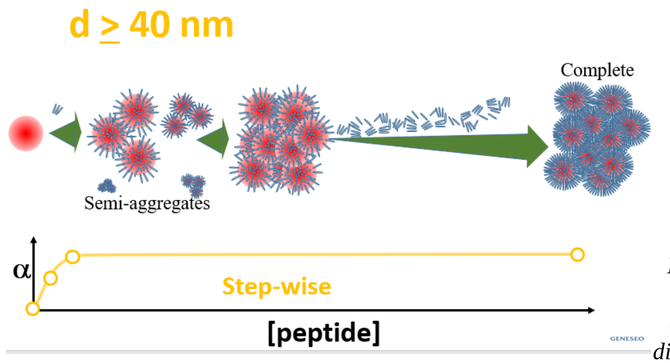
Left: A sketch showing the pH dependence of the aggregation of amyloidogenic peptides. The graph shows the corresponding shift in wavelength.

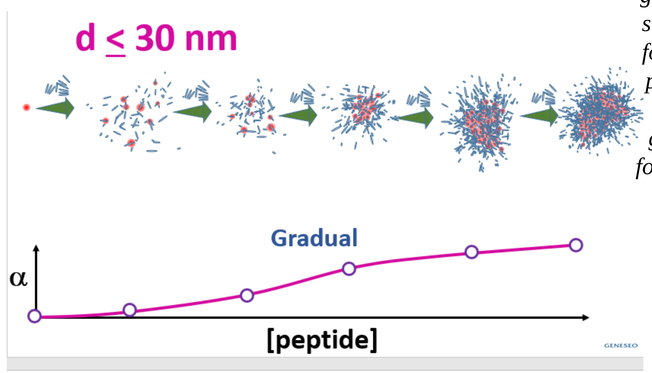


Left: A sketch showing the two possible orientations of peptides when associated with gold nano-particles. The left image is the actual observed orientation.



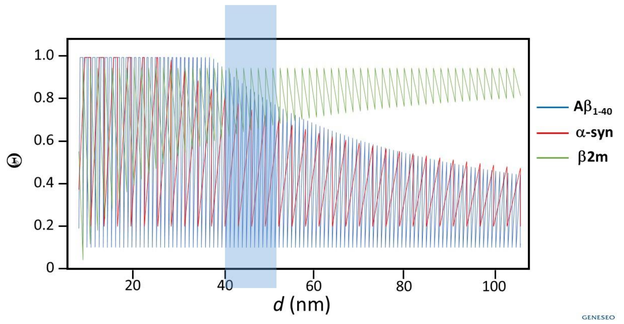
Above: A graph showing the relationship between size of a nano-particle and the tendency of peptides to cover them.

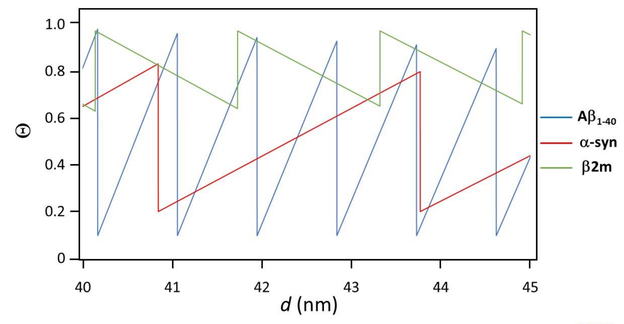




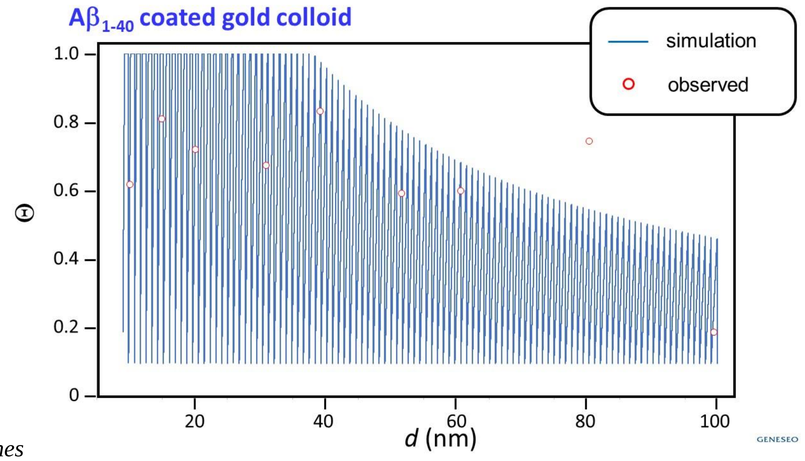
Left: Two sketches showing how aggregation rates differ based on nano-particle size. The top graph shows the rapid step-wise aggregation found on larger nano-particles. The bottom shows the slower, gradual aggregation found on smaller nano-particles.

Results





Left: A graph showing the suggested fit describing the relationship between protein coverage and nano-particle size. The bottom graph shows the section highlighted in blue in detail.



Above: The final graph showing the fit for $A\beta_{1-40}$. It notably excludes the data point representing 80nm gold particles.

Acknowledgments

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References

[1] Yokoyama, K.; Ichiki, A. A Model for Nano-Scale Spherical Surface Coverage and Protein Corona Formation By Amyloidogenic Peptides. *INT J Nanotechnol.* **2020**, 1(1), pp. 21-28.