Investigation of Zinc Metal Ion Effect on Amyloid Beta Protein Structure

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INTRODUCTION

Amyloid Beta-Peptide (1-40) is a protein linked to the initial stages of Alzheimer's disease, with aggregation of this peptide contributing to the development of the disease. Previous research has revealed favorable attachment of Aβ(1-40) to the surface of gold nanoparticles, with the peptides forming a protein station that is able to interact with other such protein stations in solution. Such a station may be instrumental in creating a device that can attract Aβ(1-40) in humans before a serious degeneration into Alzheimer's disease occurs. Additionally, there are many unknowns in the role of metal cations, such as those of calcium, copper or zinc, in fibrillogenesis - the development of polypeptide chains associated with neurodegenerative disease - and their interaction with amyloidogenic peptides. Consequently, our research group decided to investigate whether the addition of Zn^{+2} ions into a solution of Aβ(1-40) and gold nanoparticles had any effect on the aggregation of peptides.

METHODOLOGY

We examined the shift of the Surface Plasmon Resonance (SPR) band of Aβ(1-40) coated nano-gold colloids as a function of the change of an external pH at about 25◦C by utilizing Cary 5000 Model UV–vis-NIR Spectrophotometer of Agilent (Santa Clara, CA, USA). The pH of solution was hopped between acidic at pH 4 and basic condition around pH 10 by inserting HCl and sodium hydroxide (NaOH) with pre-tested amount to maintain pH ~4 and pH~10, respectively. Some fine adjustments of pH made were made after a HCl or NaOH infusion in order to keep the pH levels as close to the intended values as possible. In both schemes each spectrum was processed with components of the band expressed by a Gaussian profile by Peak Fit function of OriginPro 2018b (Origin Lab), and the spectrum area weight average peak position of the spectrum in the region between 520 nm and 600 nm was extracted.

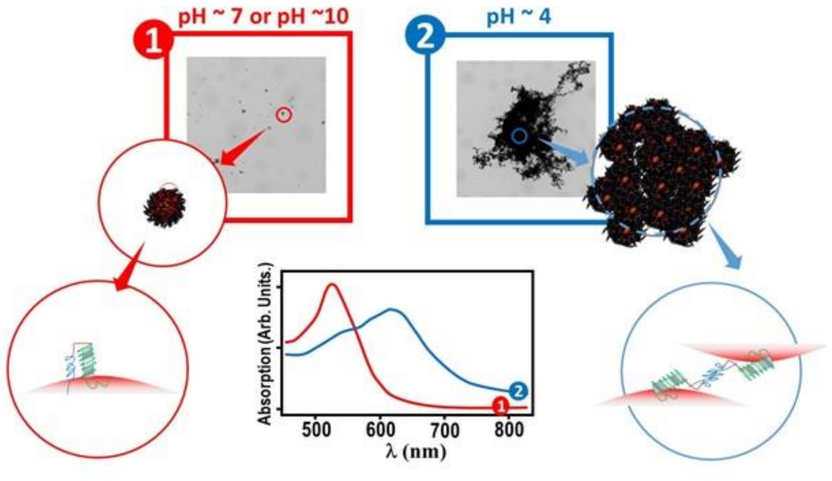

Figure 1. A diagram illustrating the physical changes in conformation that occur in Aβ(1-40) coating the gold nanoparticles during the pH hop experiment at pH = 4 and pH = 10.

RESULTS

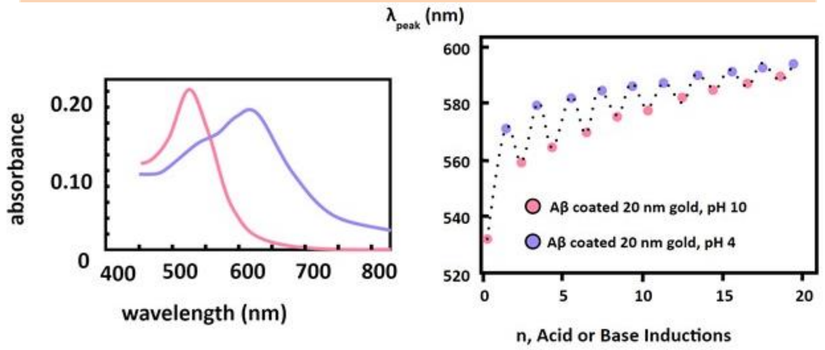

Figure 2: The pH hop experimental scheme and corresponding spectral shifts.

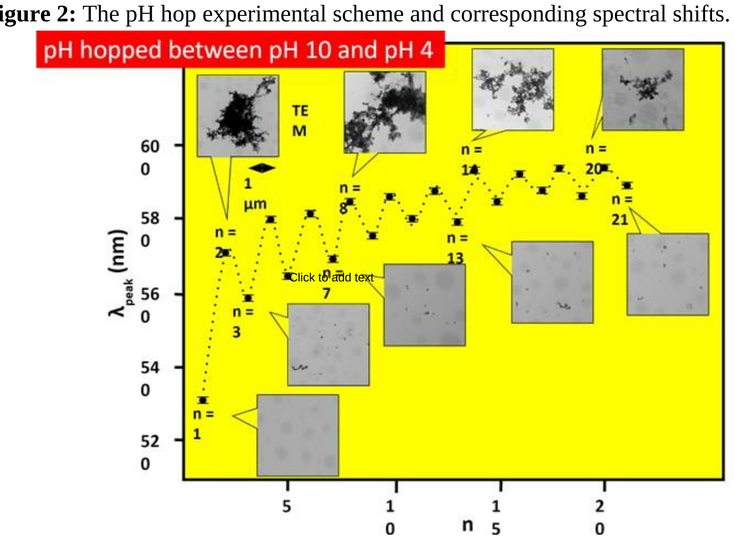

Figure 3: TEM image of Aβ(1-40)-coated Au-20 nm at different operation numbers.

The undulation feature was explained by **Eqn. (1)**

$$\lambda_{peak}(n) = A + B(n-1)^C + De^{(n-1)E}coscos\,(n\pi) \qquad (1)$$

An initial peak position at neutral pH(*i.e.*, $\overline{\boldsymbol{\lambda_{peak}}}$ (n = 1)) is given by A – D, and the parameters B and C show the average wave peak position shift as pH varies between pH ~3 and pH ~10. The parameters D represents a degree of reversibility amplitude, where $\overline{\boldsymbol{\lambda_{peak}}}$ (n = even) - $\overline{\boldsymbol{\lambda_{peak}}}$ (n = odd), and E is a damping (E < 0) or amplifying (E > 0) factor for the repetitive undulation.

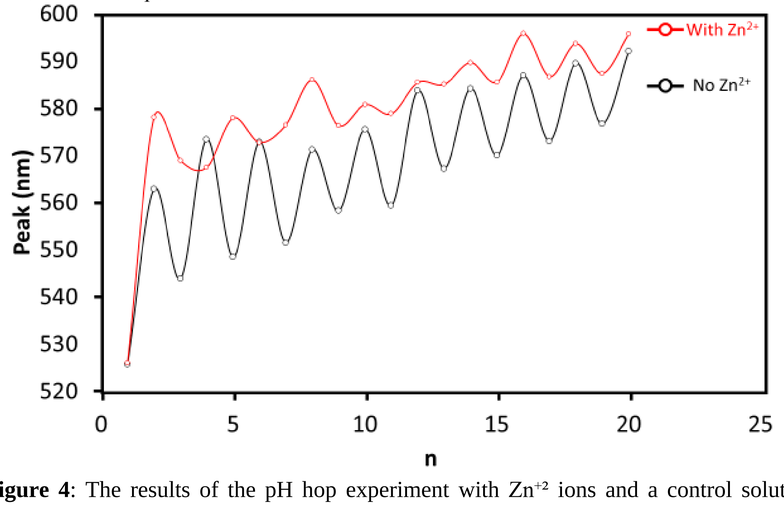

Figure 4: The results of the pH hop experiment with Zn^{+2} ions and a control solution illustrates that the Zn^{+2} solution with Aβ(1-40) and the gold nanoparticles exhibits a decreased amplitude between acid and base peaks and the inability to return to a lower peak in acidic conditions. The peaks are also out of phase with Zn^{+2} compared to no Zn^{+2}.

DISCUSSION

The results from the pH hop experiment Zn^{+2} ions and a control solution illustrates the decreased reversibility of Aβ(1-40) protein folding in the solution with the metal cations. This is demonstrated by the flattening of the peaks at a higher peak wavelength as compared to the sample without Zn^{+2} ions (Figure 4), suggesting that the Zn^{+2} ions interact with the Aβ(1-40) peptides in such a way that they are stuck in a particular conformation.

plausible interaction between Zn^{2+} and $A\beta_{1-40}$ Coated Gold

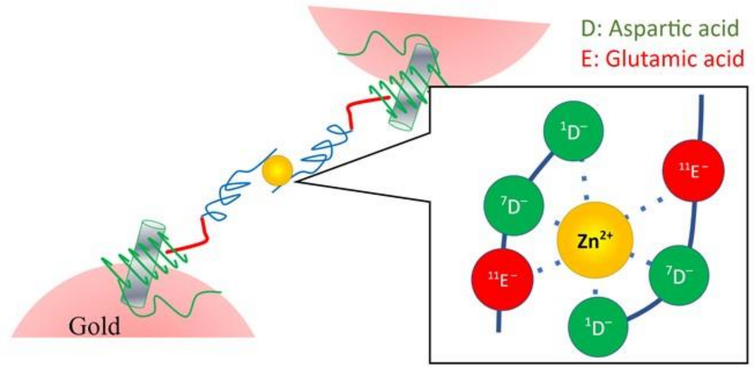

Figure 5: Zn^{+2} binding with glutamic acid and aspartic acid may prohibit disassembly of the Aβ(1-40) peptide folded complex.

CONCLUSION

The Aβ(1-40) and gold nanoparticles' wavelength peaks oscillate as the pH shifts between acidic and basic. "Zinc coordination significantly decreases the solvation energy for large Aβ(42) oligomers and thus enhances their aggregation tendency" [3]. This idea is visualized by plausible interactions between Zn^{+2} and amino acids (Figure 5). If an adhesive force exists between Aβ(1-40) and Zn^{+2}, it could promote the aggregation of amyloidogenic peptides to inhibit fibrillogenesis.

FUTURE DIRECTIONS

In order to visualize what is occurring with the Zn^{+2} ions and Aβ(1-40) particles in solution to cause the results we have obtained, we are collecting data through Raman imaging. This data will soon be submitted for publication.

We are also in the process of measuring the effects of different concentrations of Zn^{+2} ions in solution in order to better understand the effects of Zn^{+2} on Aβ(1-40) and how these peptides interact with the ion.

Further research can be done to observe the interactions between Aβ(1-40) and other metal ions like iron and copper. Continuing the research of metal ions and their effect on amyloidogenic peptides will be viable for therapeutic development for treating and preventing Alzheimer's disease.

REFERENCES

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