Exploring the interactions between Oligo-p-Phenylene Ethynylenes (OPEs) and Amyloid-β Aggregates

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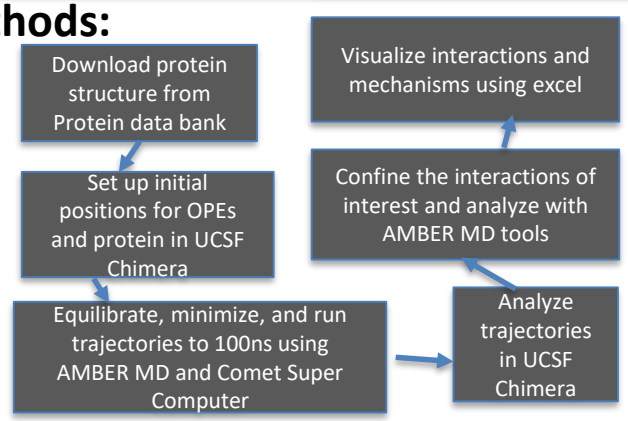
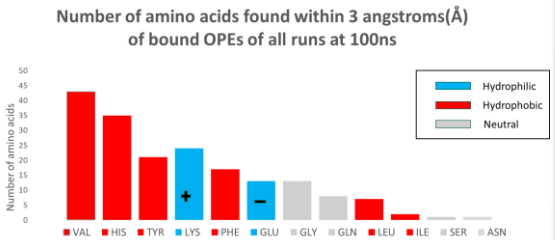
Problem: Alzheimer's Disease (AD) is the sixth leading cause of death in America. Protein misfolding and aggregation, specifically that of Amyloid-β (Aβ), in the brain causes damage to the neuronal network.

Goal: Since studies show OPEs are useful sensors for Aβ aggregates, the use of all atom molecular dynamics (MD) to explore the patterns of binding between OPEs, in particular OPE^{1-} and OPE^{2+} and Aβ, are preformed in order to gain and understanding of mechanisms that will improve detection and earlier diagnoses of AD.

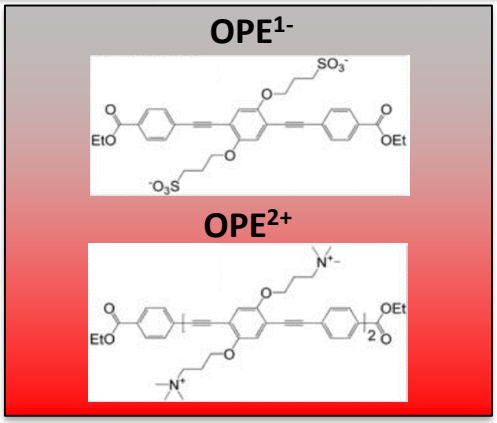
Methods:

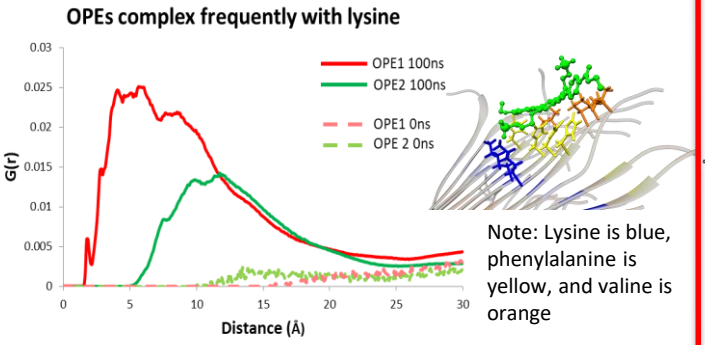


Results:

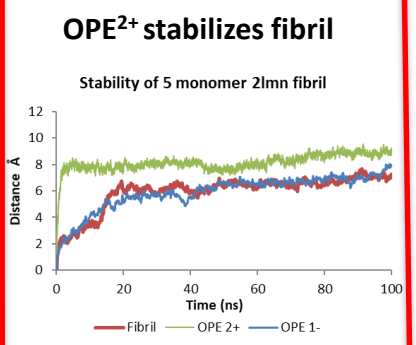


OPE^{1-} are commonly bound to hydrophobic and or positively charged regions





Note: Lysine is blue, phenylalanine is yellow, and valine is orange



Summary:

OPEs are useful sensors for Aβ aggregates. Results show promising binding patterns and mechanisms which can provide insight on earlier detection and diagnoses of AD. OPE^{1-} tends to bind to hydrophobic and positively charged or neutral amino acids. OPE^{2+} tend to bind to Valine rich areas, which are neutral and hydrophobic. Binding energies indicate strong favorable interaction between the OPEs and protofibril. In particular OPEs bound to the β-sheet result in a stronger complex than those on the tyrosine ends of the fibril.

Future Work:

1. Finish running all systems built out to 100 ns
2. Continue binding energy calculations on the systems built with a higher concentration of OPEs and smaller protofibril to further validate or change conclusions about OPE binding favorability to regions on the protofibril.
3. Carry out analysis of OPE backbone conformations (bound vs. unbound) to gain insights into OPE fluorescence sensing.