Numerous recent experimental studies suggest that oligomers of amyloid beta protein (Aβ) are the principal neurotoxic agents in Alzheimer’s disease. In fact, these oligomers interact with receptors, metal-ions, cell membrane and synapses causing neuronal dysfunction or even death. They also have the ability to form pores disrupting neurons homeostasis. Details of these mechanisms remain largely unknown at the molecular level and clearly structural information on these oligomers would provide crucial breakthrough in the understanding of their neurotoxicity. Yet, it is difficult to isolate specific Aβ oligomers and characterize their morphologies experimentally since they are prone to aggregation and they exist in equilibrium with monomers, fibrils and other orders of oligomers. Thus, to complement experimental results, numerical simulations are used to get insights on the molecular mechanisms of Aβ aggregation. We present our results on the amyloid beta monomer and dimer using an efficient simulation protocol that is introduced in details. We study specifically three alloforms of Aβ: Aβ1-40, which is less prone to aggregation; Aβ1-42, which is more toxic; and Aβ1-40(D23N), which is a single point mutation causing early onset Alzheimer’s disease. Our results, which are in good agreement with experiment and help understand a number of observations, show that small variation in the sequence results in important morphological changes related to the different oligomerization pathways of these allosforms.

### Protein Stability at a Carbon Nanotube Interface

**Subramanian Vaitheeswaran**, **Subramanian Vaitheeswaran.**

The interactions of proteins with solid surfaces occur in a variety of situations. Motivated by the many nanoelectronic applications of protein-carbon nanotube hybrids, we investigate the conformational transitions of hen egg white lysozyme adsorbed on a carbon nanotube. Using a C-alpha structure based model and replica exchange molecular dynamics, we show how the folding/unfolding equilibrium of the adsorbed protein varies with the strength of its coupling to the surface. The stability of the native state depends on the balance between the favorable entropy and unfavorable enthalpy change on adsorption. In the case of a weakly attractive surface when the former dominates, the protein is stabilized. In this regime, the protein can fold and unfold while bound to the surface. With increasing surface attraction, the unfavorable enthalpic effect dominates, and the native state is destabilized; the protein folds only when it is unbound. At the highest surface coupling, the entropic penalty of folding vanishes, and a folding intermediate is strongly stabilized. The beta-domain of lysozyme remains fully structured in this intermediate. This work has been supported by the National Science Foundation (Grants MCB-0543769 and DMR-0117792).

### Virus Structure & Assembly

**Contrast Variation SANS Study of DNA Packaging in Bacteriophage λ**

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Presurized DNA storage and pressure-driven DNA ejection in bacteriophage lambda provide an attractive model system for investigating DNA packaging in tight spaces. Moreover, lambda phage holds therapeutic promise as an alternative to antibiotics and vehicle for gene delivery. A wide variety of experimental and theoretical tools have been employed to interrogate DNA mechanics in lambda phage. Normally triggered ejection leads to loss of all DNA from the phage head; partial DNA ejection can be achieved by either counteracting the DNA pressure with external osmotic pressure or reducing the DNA-DNA repulsion with multivalent cations. Our objective in this study was to systematically map the lengths of DNA left inside partially ejected lambda phage. We determined the expected length of DNA inside the phage by monitoring the amount of ejected DNA with UV spectroscopy and assayed the actual length left directly with field-inversion gel electrophoresis. Previously used experimental methods, such as UV spectroscopy, were examined and used to assess the results from our modified protocols. Surprisingly, we found that lengths of retained DNA were concentrated around multiple specific lengths rather than the single equilibrium length that would fit thermodynamic models of DNA packaging in lambda phage. These DNA lengths occurred at regular intervals and highlighted unexpected conformational variants, sequence specific interactions, or discontinuities in DNA packaging. Structurally relevant patterns were observed when cobalt hexamine, magnesium chloride, spermine, and bis(ethyl) spermine were used as counterners. Taken together, our results show that thermodynamic models of DNA packaging in lambda phage need to be reevaluated to account for the size specific ejection that has been observed in our study.