Chemical & Physical Sciences
UNIVERSITY OF TORONTO
MISSISSAUGA

**COLLOQUIUM**
**TUESDAY, 17 MARCH 2015**
**11:00 AM - 12:00 NOON**
**KN132**

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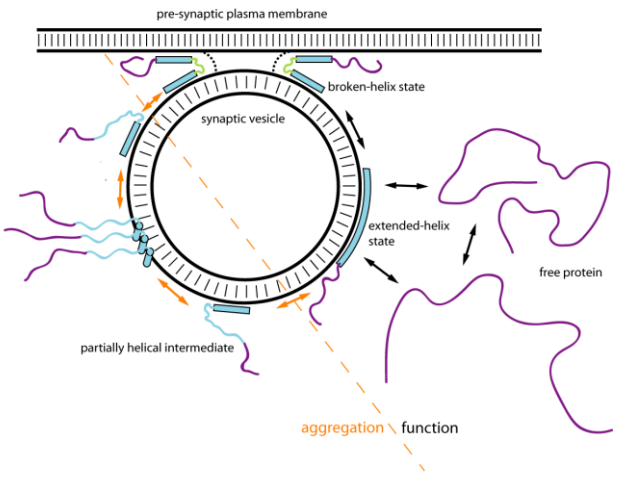
## Functional interactions of disease-linked disordered proteins: Alpha-synuclein, Tau and Complexin




The proteins alpha-synuclein and tau are linked to Parkinson's and Alzheimer's disease, respectively, yet little is known about their normal physiological functions, while complexin, a protein more loosely linked to neurological and psychiatric disorders, has several opposing functions whose mechanisms remain poorly understood. All three proteins are completely or highly disordered when free in solution. Structural characterization of different states of alpha-synuclein has lead us to propose a model in which the protein can bridge between the synaptic vesicle and plasma membranes. This model also has implications for membrane-induced synuclein aggregation. These topics will be discussed in the context of one of the most recent Parkinson's disease associated synuclein mutations. Tau is normally a microtubule binding protein, but can also bind to membrane surfaces, an interaction that may be either physiologically or pathologically relevant. Recent work in the lab has confirmed that tau-membrane interactions are mediated by short amphipathic helices, which may also play a role in mediating membrane- or microtubule-induced aggregation. Complexin contains a central helix motif that binds to assembled SNARE complexes, and this interaction is key to two opposing functions, enhancing synchronous exocytosis and inhibiting spontaneous vesicle fusion. Binding of the disordered C-terminal domain of complexin to membranes is critical for its inhibitory function. We have shown that such binding is highly dependent on membrane curvature, and that a local structural transition to a helical conformation, again necessary for function, only occurs upon binding to highly curved membranes such as synaptic vesicles. Thus complexin's function is regulated by a membrane curvature dependent structural transition.