**Abstract**

Pore forming toxins are a class of proteins secreted from a wide variety of pathogens. These toxins are implicated in several diseases such as cholera, anthrax, tuberculosis and food poisoning. The toxin proteins are secreted from the virulent source in a water soluble form. Upon binding to the plasma membrane the proteins undergo a sequence of oligomerization steps to form a functional pore that leads to cell death. Due to pore forming nature of these proteins, they are referred to as pore forming toxins (PFTs). Pore forming toxins are broadly classified into $\alpha$ and $\beta$ pore forming toxins based on the secondary protein structure that interacts with the membrane. In this thesis we are primarily interested in understanding the underlying kinetics and oligomerization pathways that govern pore formation for Cytolysin A (ClyA) which is an $\alpha$ toxin and Lysenin which belongs to a class of $\beta$ pore forming toxins. Although structural aspects of PFTs have been widely investigated the kinetics of pore formation has received little attention.

Using fluorescent dye leakage experiments we develop a model that relates the oligomerization kinetics to the dye leakage function based on a Poisson process. Excellent predictions of the temporal evolution of the leakage are obtained for reversible sequential kinetics of pore formation. Non-sequential kinetics did not capture the observed data. An essential ingredient in the model is the inclusion of leakage through intermediate oligomers or 'arcs' which are membrane inserted and capable of leakage. Inclusion of these intermediates allows us, for the first time, to capture both the short and long time components of the dye leakage function.

We obtain a forward oligomerization time constant of 5 s, whereas the backward time constant is about 200 s. Reversibility ensures a constant supply of the monomers on the membrane surface. The oligomerization time is found to be the slowest step in contrast to the conformational step reported in the literature. Our model predictions are consistent with the growing pore model for pore formation.

In the last part of the thesis we attempt to determine the structure of membrane inserted ClyA toxin molecules on supported membrane platforms using atomic force microscopy (AFM). The challenges associated with imaging these molecules and associated pore complexes will be discussed.