Project proposal template
Graduate School studentships
March 2015

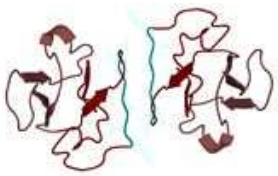
Project title	Structural bioinformatics-based modelling of protein aggregation: application to human lens crystallins
First Supervisor	Dr — Jean-Christophe Nebel
Second Supervisor	Prof. Barbara Pierscionek
School	Computing and Information Systems
Other member of supervisory team (no more than three KU supervisors in total)	
Specific requirements beyond 2:1 degree	Degree in Computing Science or Bioinformatics

Project summary

(max 4,000 characters)

The eye lens is a transparent oblate structure that refracts light and is able to adjust its refractive power in order to produce optimal image quality on the retina. The lens is made up of proteins and water. In the human lens over 95% of the proteins are crystallins, a unique family of proteins that are responsible for the refractive properties of the lens*. With age and disease, proteins undergo modifications that can lead to a loss of organisation that is needed for transparency. This leads to opacification and cataract which prevents light from traversing the lens. One of the major effects of opacification is that light is scattered. This is caused by protein aggregates that alter the tertiary structure of certain protein classes, changing the interaction between the protein classes and leads to amyloid-type aggregation. Amyloid plaques are a feature of Alzheimer's disease that has been linked to cataract.

The aim of this project is to conduct bioinformatics research (software based) to develop a protein aggregation model dedicated to crystallins so that insight could be gained about human cataract. Following exhaustive analysis of known interactions involving protein chains mediated by beta-sheet formations, models will be designed to discriminate between interactions leading to functional complexes and those responsible of amyloid-type aggregations. The latter model will be then further refined and customised to suggest a process explaining the formation of crystallin aggregates.



Model of crystallin aggregate

**: Primary sequence contribution to optical function of the eye lens, K. Mahendiran, C. Elie, J.-C. Nebel, A. Ryan and B.K. Pierscionek, Scientific Reports, 4, 5195, 2014*