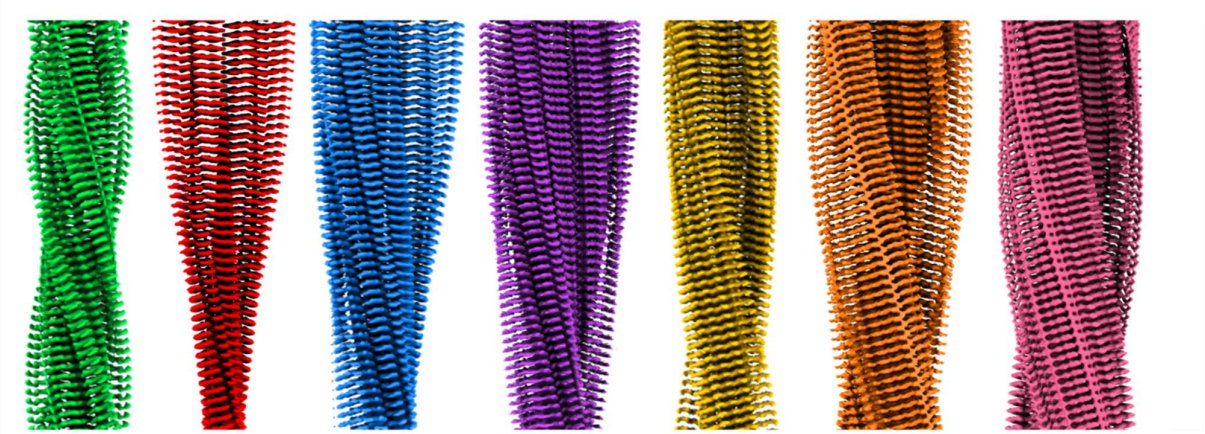
4 year PhD Studentship Available, October 2026 Start

Understanding and controlling amyloid fibril polymorphism



A 4-year PhD project funded at the standard UKRI stipend rate by the University of Leeds, is available to support a new Wellcome-funded research programme. The studentship will be jointly supervised by Prof Sheena Radford and Prof Neil Ranson in the Astbury Centre for Structural Molecular Biology.

Description

Diseases such as Alzheimer's, Parkinson's and type-2 diabetes are amongst the most pressing health issues facing society, and none are currently curable. In these diseases, normally well-behaved proteins aggregate into amyloid fibrils. Why proteins form amyloid fibrils and how this causes disease, however, remain unknown. By contrast with folding of globular proteins wherein the same structure results every time the polypeptide sequence folds, cryoEM has shown that each protein sequence can form many different amyloid structures when assembled in test tubes, yet a single 'disease-specific' structure is found in disease. Why is unknown. Solving this problem will open the door to new routes to diagnosis and patient-specific therapy in amyloid disease.

Work leading to this project, and the working environment

Combining real time measurement of amyloid assembly and cryoEM of fibril structures formed, we have made exciting new discoveries that set the scene for this PhD project. Specifically, we have: (1) discovered new fluorescent dyes that can distinguish between different amyloid structures; (2) shown that small molecule drugs can change the pathway of amyloid formation, creating new fibril folds; and (3) revealed that the amyloid fibrils formed early in aggregation are different to those formed at the end of assembly. These discoveries were made possible by the close collaborative work of our groups and the fantastic equipment for structural biology in the Astbury Centre in Leeds, including world-class cryoEM and other facilities.

This PhD project

The project will combine biochemical and biophysical assays to map the pathway(s) of protein aggregation into amyloid. You will also use cryoEM to solve structures formed throughout assembly. By combining these data you will derive new models that describe the molecular events underpinning assembly into different amyloid structures and learn how solution conditions, including cofactors such as the glycosaminoglycans and metabolites that are present in cells but are typically missing *in vitro*, determine selection of disease-specific amyloid structures. By reproducibly creating the amyloid structures from disease, we will accelerate efforts to diagnose and treat amyloid disease.

This 4-year PhD project is funded at the standard UKRI stipend rate by the University of Leeds,

supporting a new Wellcome-funded research programme. We are looking for a talented, creative and ambitious researcher with excitement to learn new techniques to join our team.

Previous publications of the supervisors can be found at
https://astbury.leeds.ac.uk/people/professor-sheena-radford/ or
https://astbury.leeds.ac.uk/people/prof-neil-ranson-director/

If you're interested in joining us please contact Sheena Radford (s.e.radford@leeds.ac.uk) or Neil Ranson (n.a.ranson@leeds.ac.uk), please send a copy of your CV too!