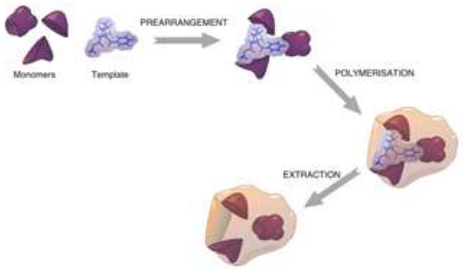
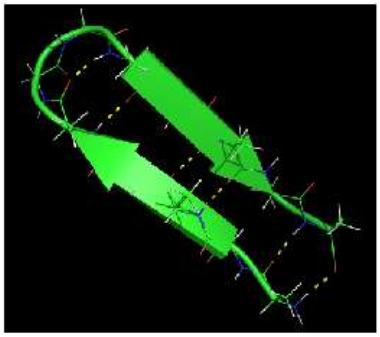
Project title: Development of molecular imprints for protein isoform detection and manipulation
Project code: OU10
Host institution: The Open University
Theme: Health and Wellbeing – healthcare technologies, chemical biology and bio-medicinal chemistry
Key words: molecular imprinting, protein, protein folding, biosensors
Supervisory team: Dr Nick Turner - Lecturer in Chemistry, School of Life, Health and Chemical Sciences, The Open University Dr Nick Chatterton - Lecturer in Chemistry, School of Life, Health and Chemical Sciences, The Open University Professor Sergey Piletsky – Professor in Bio-organic Chemistry, Dept. of Chemistry, University of Leicester





Project highlights:

- Create polymeric artificial recognition materials that will recognise between different isoforms of the same protein.
- Attempt to guide the folding of proteins to create artificial chaperones.
- Gain expertise in organic synthesis, synthesis and analytical chemical techniques.

Overview:

Traditionally, molecular imprinting (MIP) studies have targeted small molecules (bioactives, toxins, etc.), however in the past decade the field of protein imprinting has expanded rapidly. Protein imprinting has a number of unique challenges including mass transfer, maintaining stability of the polymer when the template is removed, heterogeneity in the surface of the protein, locating a suitable target for molecular recognition and the effects of the polymerisation mixture/reaction on the protein and protein-monomer complex.

Alongside biosensor opportunities, molecular imprinting has the potential for labelling, stabilising, or even modifying protein structure. However a far more exciting prospect is the synthesis of polymers for not only specific recognition of proteins, but to actually influence protein structure and performance. The potential for novel theranostics exist using this type of material.

Dr Turner has led work that has developed recognition systems for protein isoforms and helped create materials that offer stabilisation and increased performance of enzymes (with Prof. Piletsky).

In this project we will look at two model systems that have experimentally defined folding parameters, a model β-hairpin and a small prion-like protein as targets. Molecular imprints of these will be created using structured polymeric nanomaterials (fibres and particles), imparting high affinity and specificity into the materials.

Once the materials have been generated and their specificity demonstrated towards a particular folding conformation we will employ them to analyse their potential to alter the targets protein structure and functionality (i.e. can an imprint of a certain shape be used to guide a misfold or random state protein back into the defined shape) and therefore demonstrating the hypothesis.

Using a combination of synthetic methods, novel polymer chemistry and analytical approaches, this project seeks to develop methodology for development of these materials as a proof-of-concept towards future studies.

Methodology:

The successful candidate will use a combination of organic synthesis (to produce novel monomeric components); and polymer chemistry to synthesise the molecularly imprinted materials. Nanoscale chemistry (the formation of nanoparticles and nanowires) will be used to obtain high affinity polymers.
A varied range of analytical methods will be used to study the protein-polymer interactions. These will include sensing platforms such as surface plasmon resonance and quartz crystal microgravimetry to study the affinity and specificity of the imprints.
Spectroscopic methods, such as fluorescence and circular dichroism will be employed to study the folding of the peptide structures.

Training and skills:

As this is an interdisciplinary project, the student will acquire a wide range of skills in synthesis and analytical sciences, supported by excellent centrally managed laboratories at the OU. The Turner group works within the UK imprinting community and the successful candidate will be given the opportunity to interact throughout their program of study. The student will have the opportunity to carry out part of their research work at the University of Leicester laboratories working with state-of-the-art instrumentation for MIP synthesis.

Possible timeline:

Year 1: Literature review, Synthesis of novel monomers, initial target evaluation, synthesis of initial test polymers.
Year 2: Studies into polymer-protein affinity and specificity. Development of spectroscopic methodologies for protein analysis.
Year 3: Directed folding of protein structures using molecularly imprinted materials.

Further reading:

Peng, *et al* (**2014**) Trifluorosilane induced structural transtitions in beta-lactoglobulin in sol and gel. *Colloids and Surfaces B: Biointerfaces,* 119, 6-13

Guerreiro, *et al* (**2014**) Influence of Surface-Imprinted Nanoparticles on Trypsin Activity, *Advanced Healthcare Materials,* 3,(9), 1426 – 1429

Turner N., *et al* (**2007**). Recognition of Conformational Changes in β-Lactoglobulin via Molecularly Imprinted Thin Films. *Biomacromolecules,* 8 (9), 2781 -2787

Turner, N., *et al* (**2006**). From 3D to 2D: A Review of the Molecular Imprinting of Proteins. *Biotechnology Progress,* 22 (6), 1474 – 1489

About the supervisory team

Dr Nick Turner (Lecturer in Analytical Science, The Open University) is interested the development and use of artificial recognition elements, the creation of hybrid biological/polymer materials and trace compound analysis via biosensors.
Dr Nick Chatterton (Lecturer in Chemistry, The Open University) has interests in the generation of nanomaterials for drug delivery, created through electrospinning and electrospray methods.
Professor Sergey Piletsky (University of Leicester) lead one of the largest molecular imprinting groups in the UK and has considerable experience with generation of nanoparticle synthesis.

Please contact: **nicholas.turner@open.ac.uk** for further information.

Applicants will have:

Good undergraduate degree in chemistry, or a related discipline, with an interest in protein chemistry, polymer chemistry or analytical sciences. As this project has a strong interdisciplinary focus, you must be enthusiastic, have good communication skills and are flexible in your approach to working.

Applications should include:

- a cover letter outlining why the project is of interest and how your skills match those required
- an academic CV
- contact details of two academic references
- an Open University application form

Applications should be sent to Science-PhD-Recruitment@open.ac.uk by the closing date.