SEMS: RESEARCH PROJECT DESCRIPTION

1. Project Background and Description

Precise Macrormolecules – A New Molecular Frontier

Nature fabricates precisely defined, monodisperse polymers, including oligonucleotides (oligos), peptides, and oligosaccharides, iteratively, using step by step monomer addition. These (bio)polymers are of high interest in healthcare and nanotechnology; and their industrial fabrication apes Nature using iterative, step by step assembly, such as in solid phase peptide and oligo synthesis. In contrast, synthetic polymers, including many used in healthcare such as poly(ethylene glycols) (PEGs), are produced industrially by statistical approaches, such as living/controlled polymerisation, inevitably resulting in polydisperse synthetic materials.

An exciting concept is to manufacture molecules which combine the extraordinary advantages imparted by precise structural and functional definition, with the broad chemical variability of synthetic polymers. This is the challenge this project will address, by creating a radical new technology for the **manufacture of precise, controlled- sequence polymers** for use in healthcare. These will be created through sequential (iterative) addition of monomer building blocks in the liquid phase, and, crucially, purification at each stage will continue in the liquid phase by **o**rganic **s**olvent **n**anofiltration (OSN). The ambition is a transformative goal, to make iterative synthesis viable for synthetic polymers. The chemistry required for iterative synthesis of PEG has been established, and this now needs to be integrated with OSN technology to achieve the breakthrough in viability that is required for the desired transformation.

The polymers produced will be used for two applications. In the first, linear exact PEGs will be used for the PEGylation of therapeutic proteins at specific sites, in order to improve the circulatory lifetime of the biopharmaceutical, In the second, PEGs comprising at least two monomers with orthogonally functional side chains will be developed as multifunctional linkers, including to antibodies as antibody drug conjugate (ADC) linkers.

2. Project Scope

1.Advance protecting group and end group chemistries for polyethylene glycol.

2. Combine iterative PEG chemistry with Organic Solvent Nanofiltration to develop processes for producing PEGs with exactly defined monomer sequences.

3. Investigate applications of exact PEGs to uses in protein PEGylation and as ADCs.

3. Desired Skills from the Student

Key skills needed for the PhD project

The student will develop chemical synthesis skills, process automation and control skills in operating the new synthesisers the project will develop, and will also use numerical techniques for analysing the system performances. They will be expected to think creatively about how new precision macromolecules could be employed to revolutionise medical and other applications, and in particular how they can be used for PEGylation of pharmaceuticals and as antibody-drug conjugate (ADC) linkers,

Students will be expected to publish the work in leading journals and present it at specialist conferences, as well as more general chemical engineering and chemistry conferences.

4. Supervisory Team

Add supervisory team details

Primary: Professor Andrew Livingston

Secondary: Dr Stellios Arseniyades (Chemistry)

Additional: (Name (inc title)/ department or company if outside SEMS).