# PhD PROJECT PROPOSAL

## PhD PROJECT TITLE

Foldamer-mediated topological assembly of polymer-based nanoparticles

## PhD SUPERVISORY TEAM

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## PhD PROJECT DETAILS

*Project abstract*
Foldamers are synthetic oligomers that adopt topological helical structures through mimicking the folding patterns of biological systems. However, they lack essential properties required for their application in material science, such as thermal resilience or the ability to form stable self-assembled nanostructures. On the other hand, polymers are a promising class of materials with tuneable mechanical properties and the ability to self-assemble to generate nanoparticles. By combining the unique features of foldamers and polymers, we aim to obtain a class of new hybrid nanomaterials which morphology and size can be orthogonally tuned through modification of either the polymer or foldamer components.

*Application of Topology*
The interdisciplinary project proposed herein will combine the ability of foldamers to adopt a topological helical structure when in contact with a variety of solvents and the ability of polymeric materials to self-assemble into nanoparticles of controlled dimensions and morphology. The helical, and chiral, structure of foldamers is essential to achieve topological assemblies that can be used in a variety of applications, from enantiomer separation to drug delivery. As such, this project perfectly fits within the 'Topological Design in Soft Matter and Chemistry' and the 'Topological Design in Health and the Life Sciences' CDT themes.

## DETAILED PROJECT DESCRIPTION

**Background:** Inspired by sophisticated biological helices that are responsible for complex functions in living systems, chemists have been challenged to develop artificial helical structures not only to mimic biological functions but also for their potential applications in materials science, for example as nanoreactors for asymmetric catalysis, ferroelectric liquid crystals, and sensors.[1]

Foldamers are synthetic oligomers that adopt stable helical structures through mimicking the folding patterns of biological systems to generate structures of well-defined size and shape.[2] Foldamers are principally investigated with the main goal of designing large molecules with predictable structures that can be used for a variety of synthetic and analytical applications including catalysis and sensing.[3] Despite these important features, the potential application of foldamers in materials science has barely been explored, partially due to the fact that materials obtained from their supramolecular assembly often lack essential properties required for their optimal performance, such as thermal resilience or the ability to form stable self-assembled nanostructures.

Polymers have emerged as a promising class of materials as a consequence of their ease of synthesis and tuneable thermo-mechanical properties. Moreover, their ability to self-assemble into nanostructures of diverse morphologies and precise dimensions makes them particularly attractive for a wide range of applications in medicine, storage, transport, and catalysis.[4,5] Helical polymers are of great interest because of their intrinsic chirality and optical activity, which open the doors to a diverse range of applications in asymmetric catalysis and nanomedicine.[6] However, the synthesis of helical polymers is limited by a low variety of commercially available enantiomeric monomers, and their prohibitive costs has considerably affected the scalability of these materials.

**This project:** In this project, we will address the current limitations associated with the use of individual foldamers and polymers by creating a new class of hybrid foldamer-polymer materials that combine and optimize the desirable features of both individual platforms. These hybrid materials, containing both a chiral, hydrophobic part, and a hydrophilic polymer tail, will be self-assembled to form controlled nanostructures in a range of different solvents, which morphology and size can be orthogonally tuned through modification of either the polymer or foldamer components. With this work, we aim to exploit the foldamer-mediated topological control over the properties of the resultant hybrid materials and in doing so generate chiral nanoparticles without the need for expensive materials or time-consuming assembly procedures. These nanostructures will be assessed for their ability to encapsulate model small molecules, such as fluorescent dyes, and their ability to preferentially sequestrate one of the enantiomers from a racemic mixture. During the course of the project, a diverse range of libraries of foldamer-polymer structures will be created in order to permit optimization of the performance of these hybrid materials.

**Objectives: i)** To create a new generation of hybrid foldamer-polymer materials and fully characterize them using well-established analytical techniques. Systematically rationally designed libraries of compounds will be generated wherein fundamental structural features (e.g. foldamer and/or polymer length, nature of the foldamer and/or polymer side chains and terminal groups) will be varied to provide a broad scope of substrates for subsequent structure-activity relationship studies. **ii)** To determine the properties of the foldamer-polymer scaffolds and establish structure-activity relationships on the influence of key structural features (e.g. oligomer length, terminal group, polymer molecular weight and composition) on their chiral content, self-assembly, and ability to separate enantiomers from a racemic mixture. **iii)** To optimize the performance of the foldamer-polymer materials as effective chiral nanostructures through rationally designed libraries of compounds, to determine the effect of important structural features on their activity.

**References: 1.** Yashima *et al.*, *Chem. Rev.* 2009, 109, 6102-6211; **2.** S. J. Pike *et al.*, *Chem. Eur. J.* 2014, 20, 15981-15990; **3.** Goodman C. M. *et al.*, *Nat. Chem. Biol.* 2007, 3, 252-262; **4.** Arno M. C. *et al.*, *J. Am. Chem. Soc.* 2017, 139, 16980-16985; **5.** Arno M. C. *et al.*, *Nat. Commun.* 2020, 11, 1420. **6.** Leigh T. *et al.*, *Nat. Rev. Chem.* 2020, 4, 291-310.

**Training:** The CDT student will receive in-depth training and will gain extensive experience in a wide range of standard and advanced synthetic organic chemistry techniques as well as receiving training in a wide range of polymerisation techniques (ring-opening, step-growth, and free radical polymerisations) and size exclusion chromatography for polymer analysis. The student will also receive training and gain in-depth knowledge of a diverse range of analytical techniques in order to fully characterise the novel hybrid foldamer-polymer materials, including NMR and IR spectroscopy, mass spectrometry, circular dichroism spectroscopy, single crystal X-ray diffraction and powder X-ray diffraction. Moreover, training in nanoparticle self-assembly techniques as well as nanostructure characterisation using dynamic and static light scattering, small-angle X-ray scattering, and transmission electron microscopy will be provided. Finally, fluorescence spectroscopy, high-performance liquid chromatography, and mass spectrometry will be used to assess the ability of the hybrid nanoparticles to encapsulate a variety of substrates.

**The team:** This project is highly interdisciplinary in nature based on merging the fields of foldamers and polymer chemistry to create a new type of hybrid nanomaterial for applications in asymmetric catalysis. The project combines the research expertise of Dr Pike in the field of supramolecular chemistry with the design and synthesis of novel functional foldamers and Dr Arno in the field of polymer chemistry and nano-formulation.