P2.315: Helical Polymers for Biological Applications

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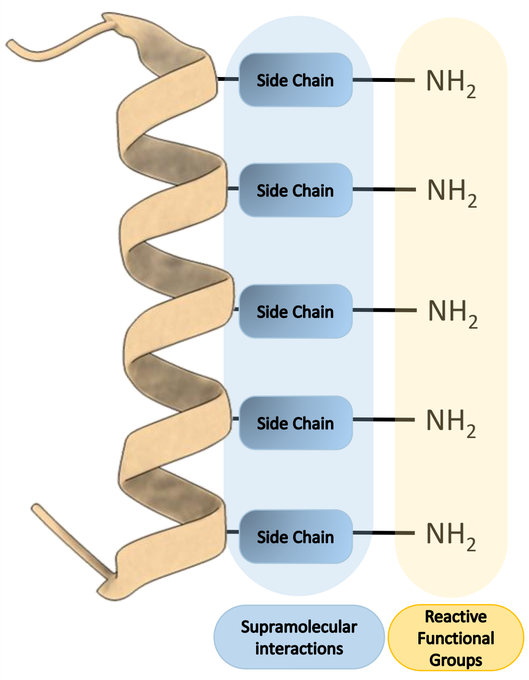
Introduction

Helical polymers have significant biomedical potential due to their simple synthesis via transition metal catalysis and polymerization. Their side chains can be functionalized using "click chemistry" (e.g., CuAAC, imine formation), enabling diverse properties. By mimicking natural helices, these polymers offer controlled size, defined conformation, and enhanced features like cell-penetration, making them ideal for drug delivery and artificial virus design. [1,2,3]

Natural viruses rely on protein-receptor interactions for cell entry, but their therapeutic use is limited by immunogenicity and pathogenic risks. Artificial viral analogues aim to replicate their efficiency while improving safety and control, leveraging helical polymers to mimic protein recognition.[4]

This project seeks to design helical polymers, understand their molecular architecture, and evaluate their biocompatibility to develop safer artificial viruses.

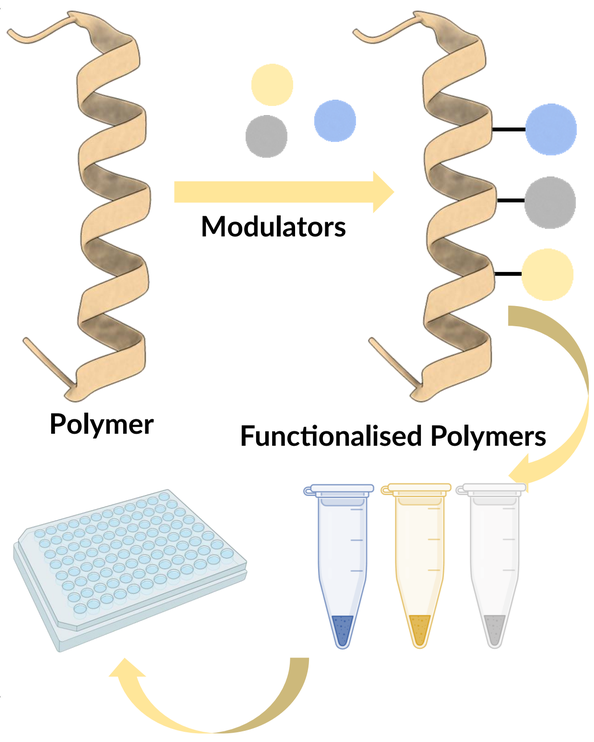
Synthetic Technique



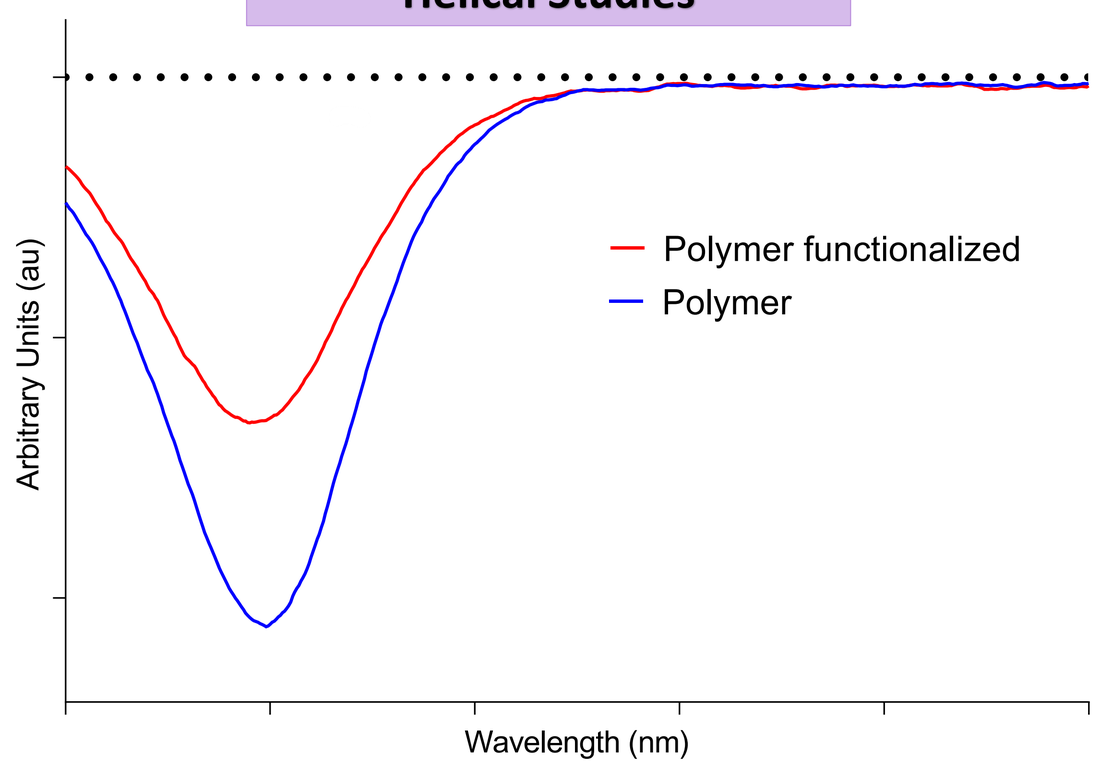
The synthetic tecnique is based in the polymerization of alkynes to form poly(acetylene)s favorizing the helical conformations in the process. This helicity is stabilized through supramolecular interactions alongside the sidechains (H-bonds, π-stacking, hydrophobic interactions, etc).

The end of the side chains contains functional groups that react through dynamic chemistries, such as imine formation, which allows to obtain a large library of polymers with an easy synthesis.

The synthesis of a large library of polymers is done using a derivative of post-polymerization modification method, *in-situ* post polymerization modification method, reported by Fernandez-Trillo and collegues[5,6]. The method is based on the synthesis of a polymer using ortogonal chemistries that do not affect the side branches to be later functionalized using dynamic chemistries. This method helps to save time and costs to determine the activity of a library of compounds.



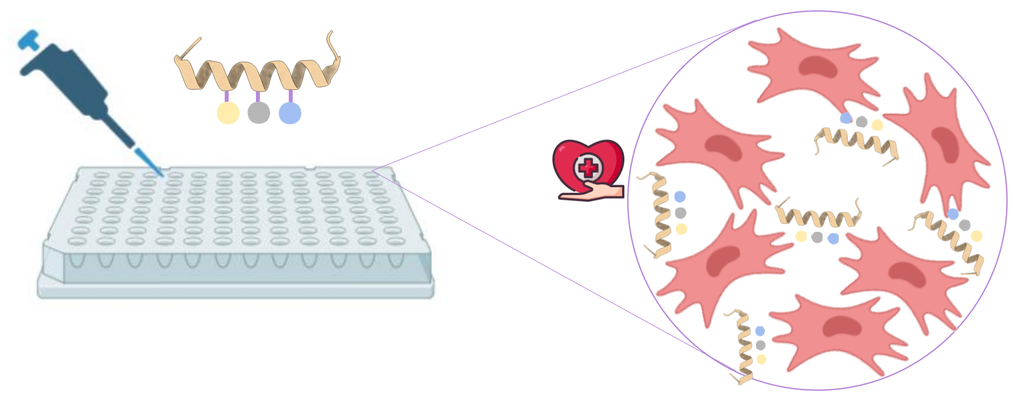
Helical Studies

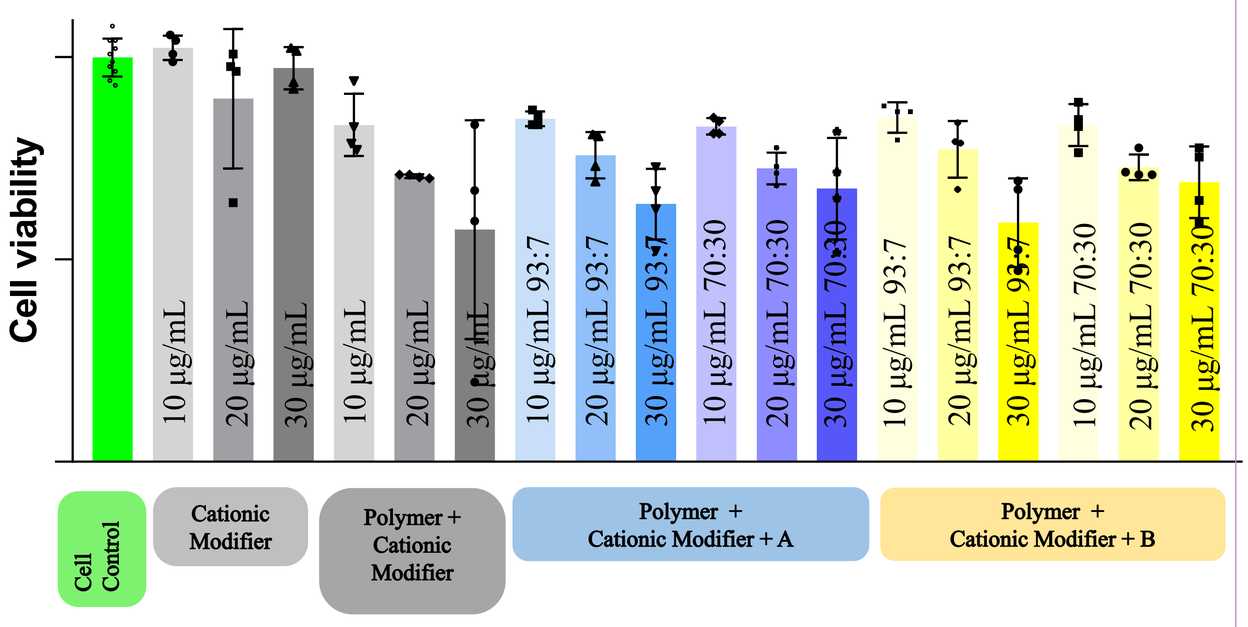


The chiral polymer was latter functionalized and a comparative of the free polymer and the funtionalized (25 % functionalized) was done.

In the graph is observed that the intensity of the free polymer is reduced. This is because the rotation of the side chain is more difficult in the functionalize polymer due to steric effect, having as a result a weaker rotation that gives a less intense band.

Biological Screening

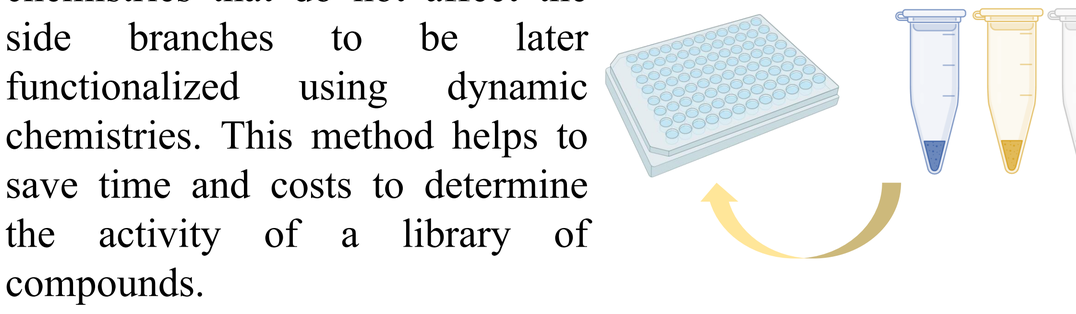


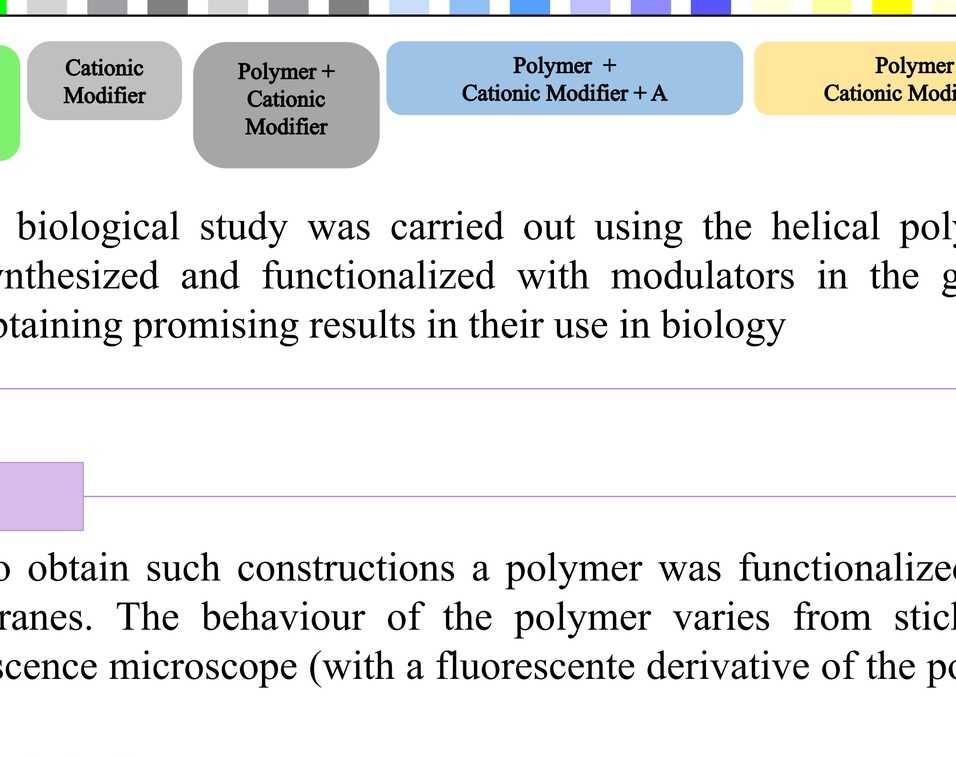


A biological study was carried out using the helical polymer synthesized and functionalized with modulators in the group obtaining promising results in their use in biology

Arficicial Viruses

Supramolecular assemblies consisted in polymer-lipid interactions were done. To obtain such constructions a polymer was functionalized with different aldehydes, modulating polymer's performance towards lipidic membranes. The behaviour of the polymer varies from sticking to membranes to penetrate the liposome. The interaction was followed using a fluorescence microscope (with a fluorescente derivative of the polymer) and a fluorimeter recording the fluorescence changes along time and additions.[6]





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