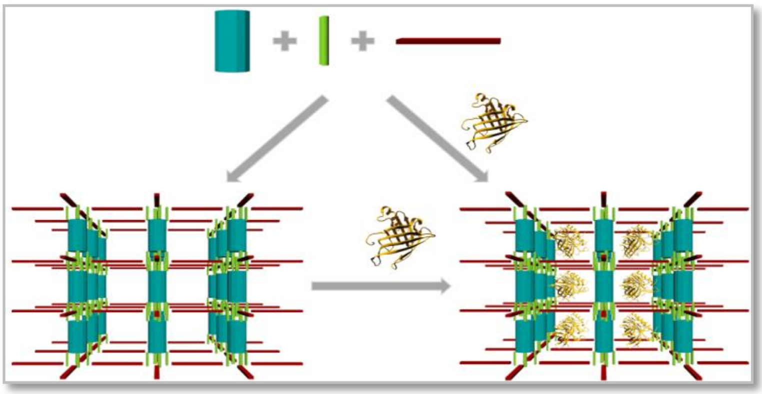
Supramolecular Peptide-Organic Frameworks (POFs)

Applications of peptides in supramolecular chemistry and, more generally, in materials chemistry have been long neglected. The inherent advantages of peptides, including biocompatibility, diversity or easy availability, were deemed insufficient to outbalance the disadvantages, connected mainly with the conformational flexibility of oligopeptides and the consequent low degree of 3D structure predictability, especially in self-assembling systems. However, the situation began to change during the last decade. With the development of analytical methods for the visualization of nanoscale objects and with the seminal papers on self-assembling amiphiphilc peptides and their medical applications, the field took off and started to grow. Most of these materials form gels and their main applications are in regenerative medicine. Considering the amazing diversity of peptides in terms of both structure and function, we believe that many more applications can be expected from peptide-based materials.

In this project, we suggest to investigate one such possibility with the aim at the construction of oligopeptide-based structured frameworks, termed Peptide-Organic Frameworks (POFs). By means of covalent synthesis, dynamic covalent chemistry (DCC) and directed self-assembly of peptidic fragments, we plan to create ordered materials, in the form of solid frameworks, gels or discrete objects. We hypothesize that owing to the inherent properties of peptidic building blocks, such materials will be highly tunable and will constitute a favorable environment for protein crystallization (see Figure). Our hypothesis is supported by the growing number of examples from the area of chemistry and biology, suggesting that ordered environments of high symmetry can greatly boost the chances of obtaining good-quality protein crystals, regardless of the presence or absence of the framework in the final crystal structure. The present research project connects the field of materials science with the field of structural biology and involves: (1) chemical synthesis of the building blocks for POFs; (2) generation of POF structures; (3) crystallization experiments with native and recombinant proteins in POF systems; (4) whenever possible, structural, spectroscopic and physicochemical characterization of the obtained systems.



The concept of the construction of supramolecular peptide-organic frameworks (POFs) and their application for protein crystallization; blue-marcrocylic blocks, green-peptide linkers, red-additional spacers.

A successful realization of the project can, in the long run, bring many benefits to several areas that exploit the structural information about biological macromolecules. For example, structure-guided drug design requires the determination of protein structures with high resolution and precision. Macromolecular crystallography is still the best method to determine protein 3D structure with atomic resolution. However, it is critically dependent on the ability to grow good-quality single crystals. Some types of proteins are notoriously recalcitrant to crystallization and new crystallization methods are needed and are constantly being developed (e.g. LCPs, surface entropy reduction, chemical cross-linking, etc.). Our supramolecular peptide-organic frameworks, being themselves a scientific novelty, have the potential to facilitate protein crystallization and/or improve the crystal quality. Since this concept is entirely new, it opens a completely new avenue towards structure discovery in molecular biology. Moreover, during the course of the project we expect to observe and study novel protein-peptide interactions, which in the future may lead to the design of supramolecular peptidic materials for different new applications.