PhD Proposal 2017

School: Ecole Centrale de Marseille (ECM, Centrale Marseille)	
Laboratory: Institut des Sciences Moléculaires de Marseille (*iSm2*)	**Web site: http://ism2.univ-amu.fr/equipes/Chirosciences_1.htm**
Team: *Chirosciences*	**Head of the team: Prof. Alexandre MARTINEZ**
Supervisor: Prof. Teodor Silviu BALABAN	**Email: ts.balaban@univ-amu.fr**
Collaboration with other partner during this PhD: **In France: Dr. Olga IRANZO *iSm2*, Team *Biosciences***	**In China:**

Title: Self-assembling Peptides Decorated with Functional Chromophores
Scientific field: Supramolecular Chemistry, Nanochemistry
Key words: Self-assembly, chromophores, fluorophores, electronic circular dichroism, structural elucidation, artificial antenna systems

Background, Context:

Self-assembling peptides are fascinating species with implications in Alzheimer's and prion diseases. Currently more than 50 pathologies are due protein misfolding diseases.[1,2] By elucidating the mechanism of misfolding in simpler structural models, inhibitors could be devised, both for an early diagnostic, and for therapies. A special aggregation motif includes phenylalanine-phenylalanine (FF).[3] We intend to synthesize and study FF-containing peptides decorated with functional chromophores. These chromophores can be used as structural probes using electronic circular dichroism spectroscopy because of the chiral peptide backbone. In Marseille we are equipped with state-of-the-art ECD facilities.[4]

FF-Fibers have also been extensively studied for generating nanomaterials[5] being amongst the strongest of all-organic materials while their decoration with functional chromophores displaying high photostability could have applications for photovoltaics. After self-assembly, a large collection of chromophores can thus harvest efficiently sunlight functioning as a biomimetic antenna system.[6] Previously we could mimic with self-assembling chromophores the light-harvesting system of some photosynthetic bacteria.[7]

In Marseille the Balaban group has extensive experience in the syntheses of **Building blocks (Bb**'s) compatible with the automated syntheses of peptides containing ***n* Amino acids** (**Aa**'s).[8] These peptides will be screened for their potential to self-assemble. Targeted are thus **photoactive** constructs. Figure 1 shows the general formula of the desired constructs.

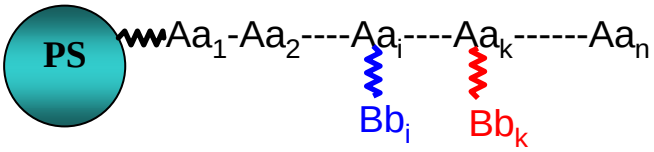


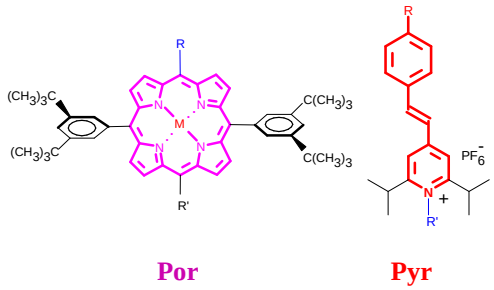
Figure 1. A peptide formed by n coupling steps of amino acids **Aa**. One or several building blocks **Bb** can be inserted at will, at any desired position within the peptide anchored on the solid support **PS.**

The building blocks **Bb**'s are either:

Chromophores capable of light absorption which can be followed by electron ejection. One speaks of photoinduced electron transfer (PeT) and the rate this process needs to be determined and optimized.

Fluorophores capable of light emission. A brilliant fluorophore must have a large extinction coefficient (ε), thus a high absorption combined with a large quantum yield (ϕ). The wavelength of the emitted light (λ_{em}) is more or less redshifted in comparison to the absorbed light (λ_{abs}). By judiciously choosing the nature of the fluorophores one can engineer an efficient excitation energy transfer (EET) between a donor Bb and an acceptor Bb. The directionality and rate of EET can thus be fine tuned by the nature of the peptides, and again these can be accurately determined and optimized.

The choice of chromophores and fluorophores is based on the synthetic expertise accumulated by our group with Porphyrinoids (**Por**)[9] and Pyridinium Salts (**Pyr**)[10] shown in Figure 2. The latter can be obtained in rather large amounts from cheap starting materials and we have shown previously that such styrylpyridinium salts are extremely bright fluorophores being suitable even for single molecule imaging by fluorescence.



Por **Pyr**

Figure 2. General formulae for **Por-Bb**'s and **Pyr-Bb**'s. The substituents R and R' can be varied practically at will. The chromophoric system responsible for the photophysical properties is shown with coloured bold bonds. M can be either 2H or various metals such as Zn, Cu, Ni, Mg, Cd, etc. The blue substituents serve to incorporate the **Bb**'s into the peptide chain.

Research subject, work plan:

While the syntheses of **Bb**'s will be performed in the Balaban group of Team *Chirosciences*, the automated solid phase syntheses will be performed in the Team *Biosciences* under the supervision of Dr. Olga Iranzo who has previous extensive experience with functional peptides and ECD spectroscopy.[11] Usually PhD Theses within the Marseille Doctoral School ED250[12] are successfully completed within three years of study and a wealth of extra-laboratory didactical activities such as accelerated English and French language courses are proposed to foreign students.

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