Institut de science des matériaux
ALLIANCE SORBONNE UNIVERSITÉ

AAP 2025 iMAT

Time-Controlled Self-Assembled Materials

A. Scientific context of the project

Supramolecular materials are composed of self-assembled molecular building blocks held together by non-covalent interactions.[1] However, most artificial systems lack the complexity of their natural counterparts because their assembly occurs at thermodynamic equilibrium. In contrast, most supramolecular biological materials exist only through the constant dissipation of energy, enabling features such as self-healing and homeostasis. There is thus a growing interest for artificial metastable systems that assemble dynamically and in a kinetically controlled manner for applications in time-sensitive information storage, controlled release or catalysis in transient nanoractors.[2] Most reported systems rely on a precursor that can be chemically transformed into a metastable product able to self-assemble.[3] However, using a conformational change to control the assembly like in the ATP-induced assembly of actin filaments[4] remains little explored. Limited examples have been published so far, such as photoswitches by Feringa[5] and Sleiman,[6] or light-powered motors used recently by Giuseppone to disrupt supramolecular hydrogels to trigger an out-of-equilibrium gel-to-sol transition.[7] These results demonstrate that switching precisely key interactions at the molecular level is a very relevant strategy to control the overall behavior of such a materials, especially to develop metastable systems.

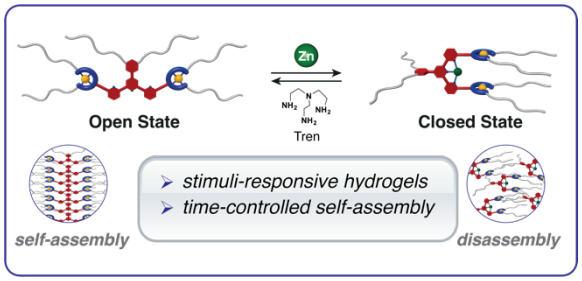

Figure 1. *Principle of self-assembly controlled by the mechanical switching of molecular tweezers*

In this doctoral project, we aim to exploit the controlled motion of switchable molecular tweezers[8] to develop time-controlled self-assembled systems in aqueous media (Figure 1). Our hypothesis is that the large conformational change between open and closed forms should influence the intermolecular interactions between the tweezers and result in the control of their self-assembly. Operating in aqueous media is a central challenge; it offers valuable opportunities to investigate hydrogen bonding and hydrophobic effects at the fundamental level. It will be instrumental for future interfacing with biological systems, ultimately enabling potential biomedical applications.

As preliminary results, Partner 1 and Partner 2 have recently exploited metal-responsive molecular tweezers to achieve a reversible gelation of toluene (Figure 2).[9] SEM, cryo-TEM and Small Angle X-ray Scattering (SAXS) experiments confirmed the formation of a fibrillar network by the open form that presents different structuring depending on the length of the side-chains. The organogel was then dissociated upon addition of Zn(II) that induced closure and lead to a solution. This project will go well beyond this initial proof of concept by leveraging the expertise of new Partner 3, toward operation in aqueous media combined with dynamic control.

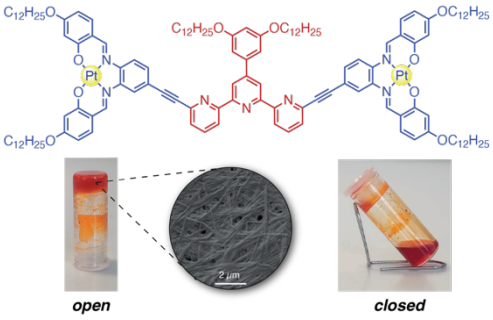

Figure 2. *Switchable organogel based on C_{12}-terpy-Pt-salen tweezers.*

Scientific approach

Task 1. Tweezers for self-assembly in aqueous environment. The first part of the work will focus on the design of tweezers able to self-assemble in aqueous environment and on the formulation of the hydrogels.

Two main complementary strategies will be explored in parallel. The first one will be to develop tweezers able to form directly hydrogels. Since LMW hydrogelators usually display amphiphilic structures,[10] the tweezers will be substituted by charged groups, oligoethylene glycol or small peptide chains (Figure 3). By combining the hydrophobic terpyridine core with more hydrophilic side chains, we expect to form self-assembled structures in polar media. In a complementary approach, we will implement tweezers with hydrophilic side chains into hydrogel formulations composed of hydrophilic polymers (e.g. crosslinked

polyethylene glycol). Based on Partner 3 previous experience in bulk polymer networks,[11] we expect that incorporating even a small amount of the tweezer will strongly impact the viscoelasticity of the materials. Indeed, the assembly of the open tweezers is expected to mechanically reinforce the gel compared to the disassembled closed form.

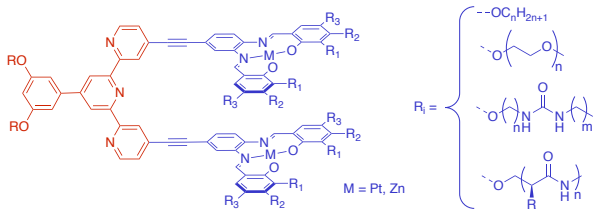

Figure 3. *Schematic representation of switchable tweezers*

In order to rationalize the structure-property relationships, an important part of this task will be devoted to the characterization of the network responsible for the gelation in water. They will be studied by complementary physico-chemical techniques by Partner 2 (electron microscopy, light scattering, small angle scattering – SANS, SAXS, on large instruments or at FCMat) and Partner 3 (rheology, optical microscopy).

Task 2. Stimuli responsive control of gelation. After identifying the first candidates for hydrogelators, we will exploit the stimuli-responsive properties of the tweezers to obtain activable hydrogels with temporal control.

First, the switching of the tweezers will be studied by sequential addition of stimuli (e.g., Zn(II) and tren) and the effect on the self-assembly will be monitored *in situ* with temporal resolution (by UV-Vis, NMR, SAXS), to investigate the expected transitions from solution to gel for both pure assemblies and doped systems.

Our ultimate objective is to exploit the conformational change of the tweezers in response to a chemical fuel, such as a decomposable carboxylic acid,[12] to achieve transient processes as already observed in toluene.[9] Here, we will explore the addition of a fuel on closed by default tweezers to trigger a conformation change to the open form enabling their self-assembly, which will disassemble once all the fuel is depleted. The study of aqueous systems will open new and rich perspectives regarding the variety of interactions at stake, leading to innovative dissipative self-assembled systems (Figure 4).

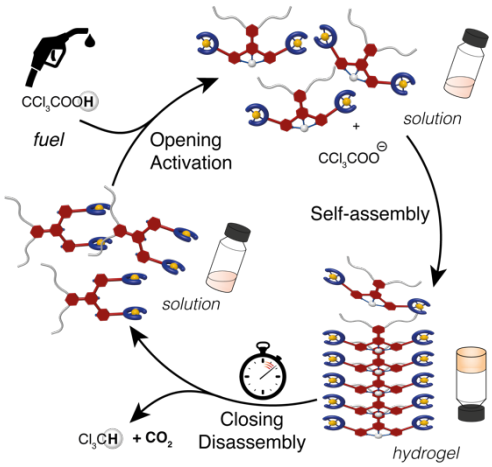

Figure 4. *Principle of time-controlled self-assembly with a decomposable acid as chemical fuel.*

The dynamics of assembly-disassembly of the hydrogels will be studied by a combination of time-resolved physico-chemical techniques, such as optical and fluorescence microscopy and scattering techniques.

Risks and mitigation

This proposal is ambitious, but the key risk—the potential inability of the switchable molecular tweezers to control self-assembly in water—is mitigated by our preliminary results in organic solvents.[9] While adaptation to an aqueous environment necessitates significant modifications, we have found that Pt-salphen functionalized with an oligoethylene glycol chains is capable of forming hydrogels, which is promising for the tweezers. The two independent approaches of direct and co-assembly also maximize the chances of success. Achieving temporal control over self-assembly remains a major challenge, yet the large variety of chemical fuels available and versatility of the tweezer's activation reduces this risk. Risks are further reduced by the expertise and complementarity of the partnership (the various techniques and instruments mentioned here, including SAXS, are all available on-site for at least one partner).

Adequacy to the call

This project aligns closely with the objectives of iMAT, as it addresses a fundamental challenge in material sciences: the implementation of stimuli-responsive, self-assembled materials in aqueous media with temporal control. Our approach exploiting the mechanical motion of molecular machines to achieve dynamic materials that can be activated by a chemical fuel akin is innovative as it mimics some biological materials. This multidisciplinary project will greatly benefit from the synergy between the three collaborating partners. While P1 and P2 have already initiated a collaboration with the co-supervision of P. Msellem's thesis (2021-2024) whose results provide ground for this proposal, this PhD project will open new venues enabled by the collaboration with P3. This partnership will extend the project scope toward a

deeper variety and understanding of these systems and move to aqueous environments, allowing a fundamental comprehension of the systems that will ultimately open perspectives for potential applications of the materials in biological contexts, such as controlled drug release.

Skills and coherence of the team

This multidisciplinary project will be tackled through the complementary skills of the three partners in supramolecular chemistry, synthesis (Partner 1), physico-chemical characterization of self-assembled systems (Partner 2) and viscoelasticity of new formulations (Partner 3).

Partner 1 (**G. Vives**, IPCM, SU) will provide the necessary expertise in synthesis and supramolecular chemistry. Since his appointment as associate professor in 2010, G. Vives has been working in supramolecular chemistry and molecular machines on the development of cyclodextrin rotaxanes and switchable molecular tweezers. He has experience in project management as well as student supervision (10 PhD, 15 M2).

Partner 2 (**C. Guibert**, LRS, SU) will bring his skills in the implementation and characterization of self-assembled systems. Associate professor at SU since 2017, has worked on several studies of supramolecular assemblies, such as gels, and has also developed an expertise in time-resolved characterization of materials at the nanoscale with scattering techniques.

Partner 3 (**Nathan J. Van Zee**, C3M, ESPCI Paris-PSL) will provide his expertise on the formulation of the gels and on the study of their rheological properties. He is CR CNRS and the leader of the Macromolecular Chemistry and Design team. He has broad experience on studying the structure and viscoelasticity of supramolecular materials. He has strong interest in the co-assembly of water molecules with supramolecular polymers and the interplay between supramolecular polymers and covalent adaptable networks.

B. Research plan with provisional calendar

The study will be divided into two related tasks that can be conducted, after having synthesized the first candidates for hydrogelators, almost in parallel. The PhD student will be co-supervised by the three partners and will work in the GOBS team of the IPCM (P1) for the synthesis and supramolecular studies, in the LRS laboratory (P2) for the materials physico-chemical characterization, and in the C3M laboratory (P3) for the formulation and rheological characterization of the polymer/tweezer systems.

	Year 1				Year 2				Year 3			
Tasks 1. Tweezers for self-assembly in aqueous environment												
Synthesis of new LMW hydrogelator tweezers												
Formulation and characterization of the hydrogels												
Tasks 2. Stimuli responsive control of gelation												
Time-controlled self-assembly studies in aqueous environment												
In-situ characterization and studies of switchable hydrogels												

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