

**MENTION « SCIENCES DU MÉDICAMENT »**  
**Parcours M2 : PHARMACOTECHNIE ET BIOPHARMACIE**

---

**Informations indispensables**

Laboratoire d'accueil : Institut Galien Paris-Saclay, UMR CNRS 8612, Université Paris-Saclay

Adresse complète du lieu du stage : Bâtiment Henri Moissan, 17, avenue des Sciences, 91400 Orsay

Nom de la personne responsable : Simona MURA

Numéro de téléphone :

Adresse e-mail : simona.mura@universite-paris-saclay.fr

Dates de stage : 20 janvier – 18 juillet 2025

---

**Titre du Sujet** : Advanced hybrid hydrogels for sustained drug delivery

---

*Présenter en 1 à 3 pages maximum (1) le contexte de la problématique du sujet, (2) les objectifs du stage et (3) un résumé du programme de travail.*

Hydrogels are water-swollen three-dimensional networks made of hydrophilic and amphiphilic natural and synthetic polymers. Due to their high-water content, porous structure and the soft, rubberlike nature, biodegradable polymer hydrogels have gained a wide interest for a broad range of biomedical applications.<sup>1,2</sup> Among them, injectable hydrogels are extremely promising as reservoirs for localized drug delivery, aiming to enhance drug bioavailability and optimize pharmacological activity while minimizing systemic toxicity.<sup>3</sup>

This approach, known as locoregional administration, has the potential to improve the therapeutic index of drugs by enabling targeted delivery and by reducing the required doses and dosing frequency compared to systemic administration. For instance, in oncology, it holds promise for the treatment of peritoneal malignancies while intraarticular administration can be beneficial for the treatment of osteoarthritis (OA).

Indeed, gel-based materials that can be injected in these cavities have the potential to effectively retain drugs and release them in a controlled manner, leading to high drug concentrations in the local area for extended periods of time. They can represent an attractive alternative to the current treatment however, insufficient benefits have been obtained so far. The main challenges associated with using hydrogels as drug delivery systems are their low stability due to insufficient mechanical strength and the rapid release of only physically encapsulated drugs. The performance of hydrogels can be improved by combining them with nanoscale drug carriers.<sup>4</sup> Nevertheless, if the nanocarriers lack strong interactions with the hydrogel matrix, they may escape and be quickly eliminated.

We are currently working to address these issues by designing advanced hybrid systems through the precise engineering of a hydrogel matrix and medicated nanocarriers.

Now we aim to rationally ascertain how the combination of the building components will enable to meet the specified requirements.

The hybrid systems need to possess injectability, appropriate mechanical strength, and achieve a desirable drug payload with controlled spatio-temporal release.

## Methodology

- **Formulation and characterization of drug loaded nanoparticles**

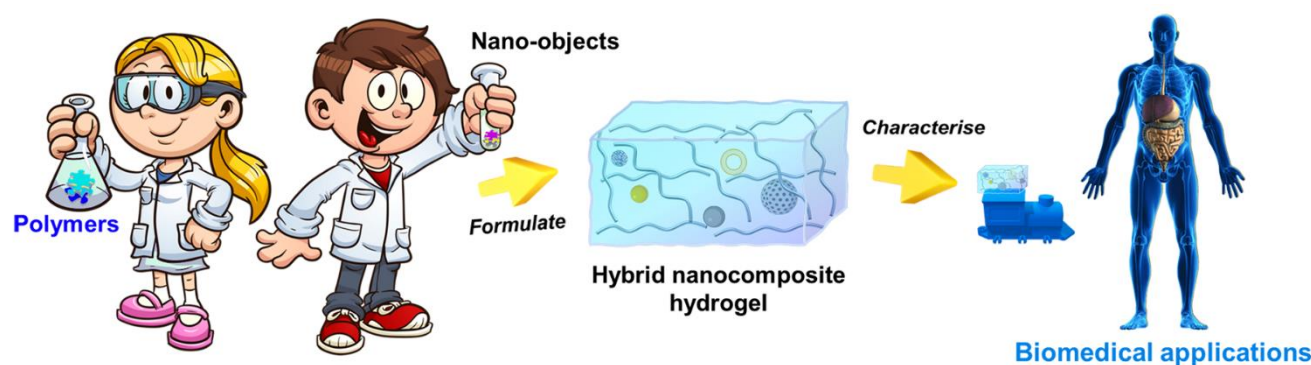
According to their hydrophilic (a small peptide) or hydrophobic (paclitaxel) nature, drug loaded nanoparticles (NPs) will be prepared by water-in-oil-in-water double emulsion solvent evaporation or nanoprecipitation method using a biodegradable polymer (e.g., polylactide, PLA)

Formulated nanocarriers will be characterized in terms of size, morphology and surface charge. Colloidal stability and drug release will be assessed in different media representative of the physio-pathological conditions (e.g., 37° C, phosphate buffer, serum-containing cell culture medium, synovial/peritoneal fluid)

- **Formulation and characterization of the hybrid hydrogel**

Hydrogels will be prepared by physically mixing an appropriate volume of nanoobjects with a solution of the hydrogel precursor prior to gelation. Hyaluronic acid (HA) a linear polysaccharide and poly(lactic-co-glycolic acid)-*b*-poly(ethylene glycol)-*b*-poly(lactic-co-glycolic acid) (PLGA-*b*-PEG-*b*-PLGA) triblock copolymer well-known for their biodegradability, biocompatibility are suitable as the main component of the injectable gel matrix.

The resulting hybrid hydrogel will be characterized in terms of macromolecular structure, drug loading, gelation time and temperature, swelling behavior, rheological and mechanical properties. The drug release kinetics will be determined in different media (PBS and human plasma).



## References

1. Y Li, J Rodrigues and H Tomás, *Chem Soc Rev* **2012**, 41, 2193-2221 [10.1039/C1CS15203C](https://doi.org/10.1039/C1CS15203C)
2. BV Slaughter, SS Khurshid *et al.*, *Adv Materials* **2009**, 21, 3307-3329 [10.1002/adma.200802106](https://doi.org/10.1002/adma.200802106)
3. SJ Buwalda, KWM Boere *et al.*, *J Control Release* **2014**, 190, 254-273 [10.1016/j.jconrel.2014.03.052](https://doi.org/10.1016/j.jconrel.2014.03.052)
4. P Thoniyot, MJ Tan *et al.*, *Adv. Sci.* **2015**, 2, 1400010 [10.1002/advs.201400010](https://doi.org/10.1002/advs.201400010)