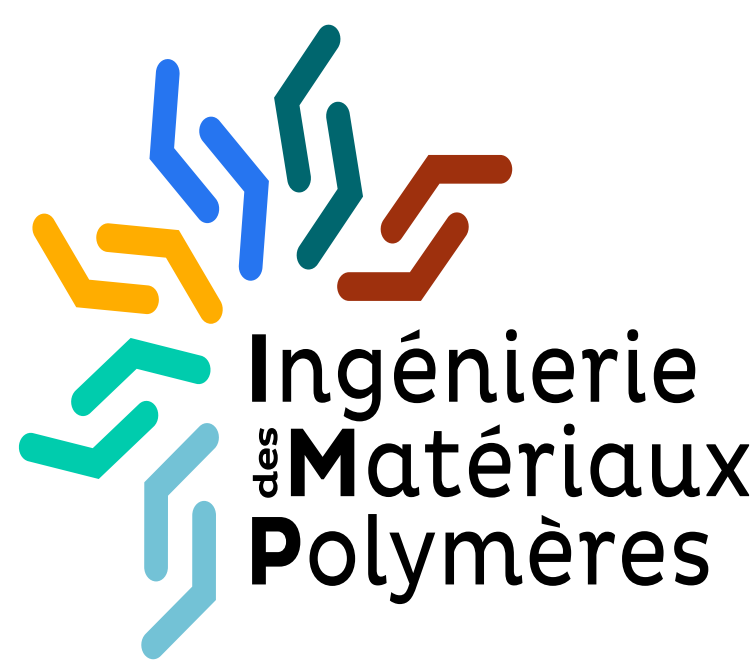


DEVELOPMENT OF PH-RESPONSIVE BIODEGRADABLE MICELLES FOR TARGETED DRUG DELIVERY



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Introduction

Context and Objective:

Current pH-responsive copolymer micelles:

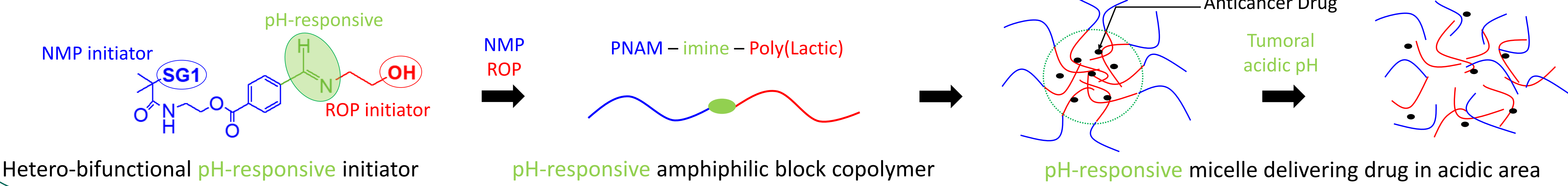
- attractive for targeted drug release (minimizing side effects)
- copolymers laborious to prepare and containing PEG (hypersensitivity issues).^[1-2]

We aim to develop easily achievable pH-responsive micelles based on alternative to PEG

Strategy:

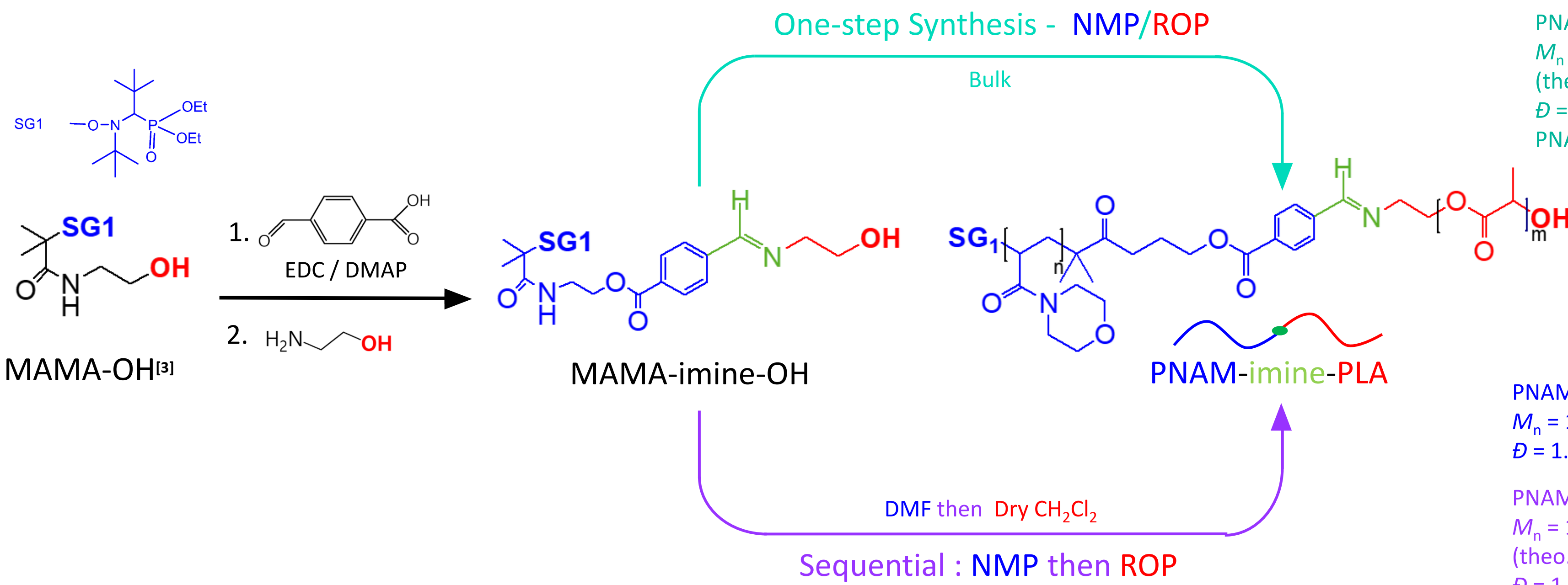
pH-responsive hetero-bifunctional initiator

- Wide range of block copolymers achievable
- One-step synthesis
- Alternative to PEG e.g. poly(4-acryloylmorpholine) (PNAM)

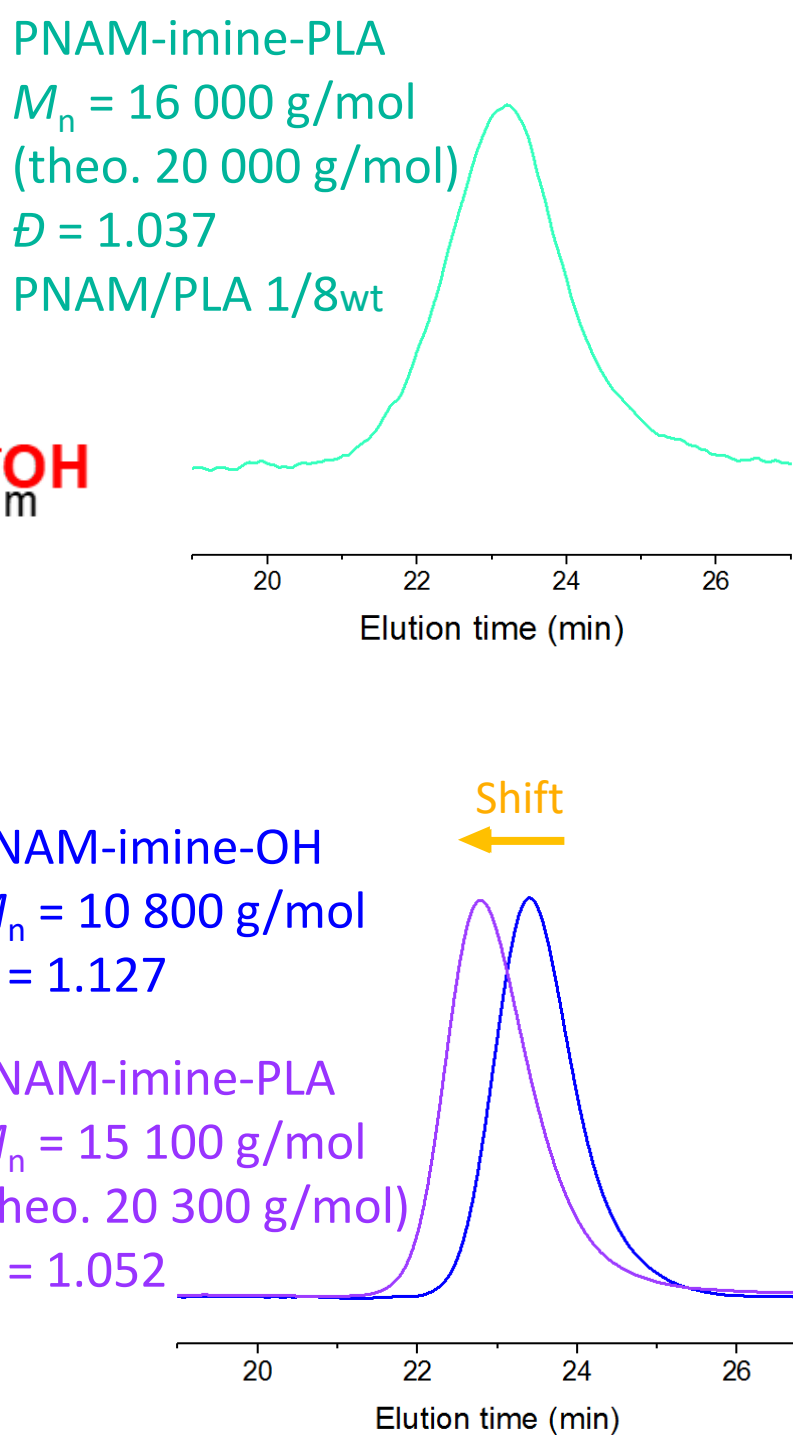


Copolymer Synthesis and Characterizations

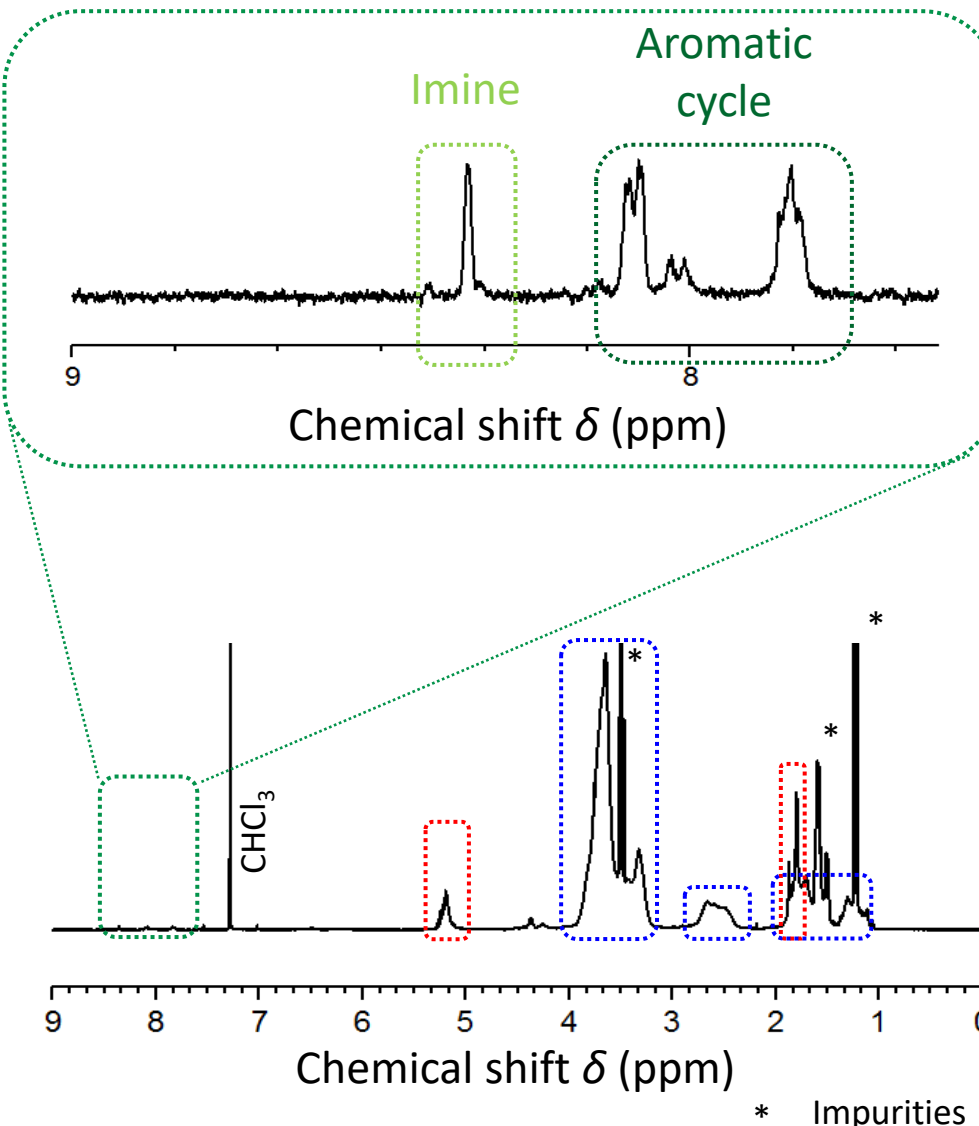
Synthesis



Size Exclusion Chromatography (SEC)



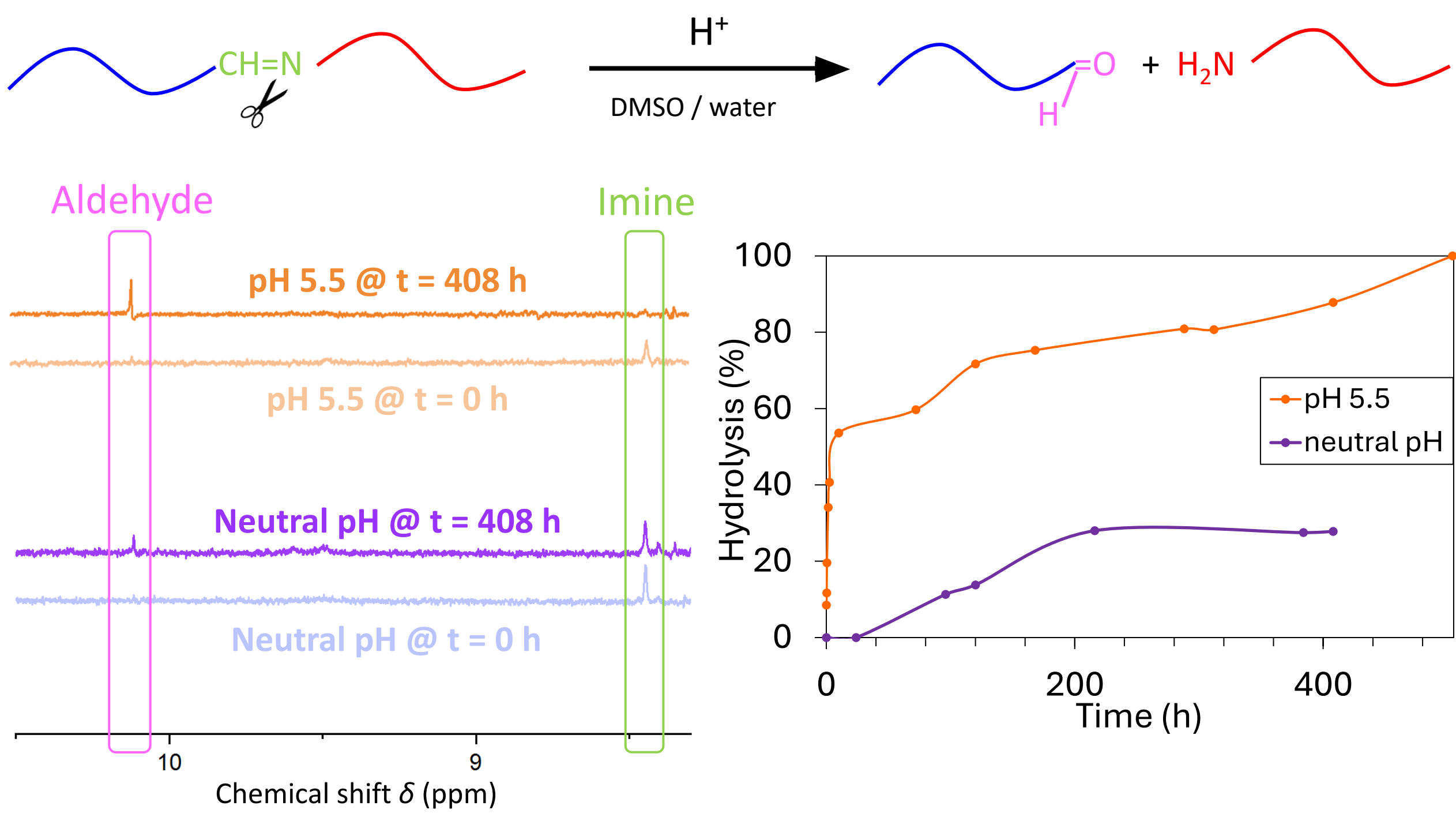
¹H NMR



✓ pH-responsive amphiphilic block copolymer synthesized (confirmed by ¹H NMR and SEC) via a one-step or sequential process.

pH-Responsiveness of copolymer

Imine hydrolysis in acidic conditions (¹H NMR):



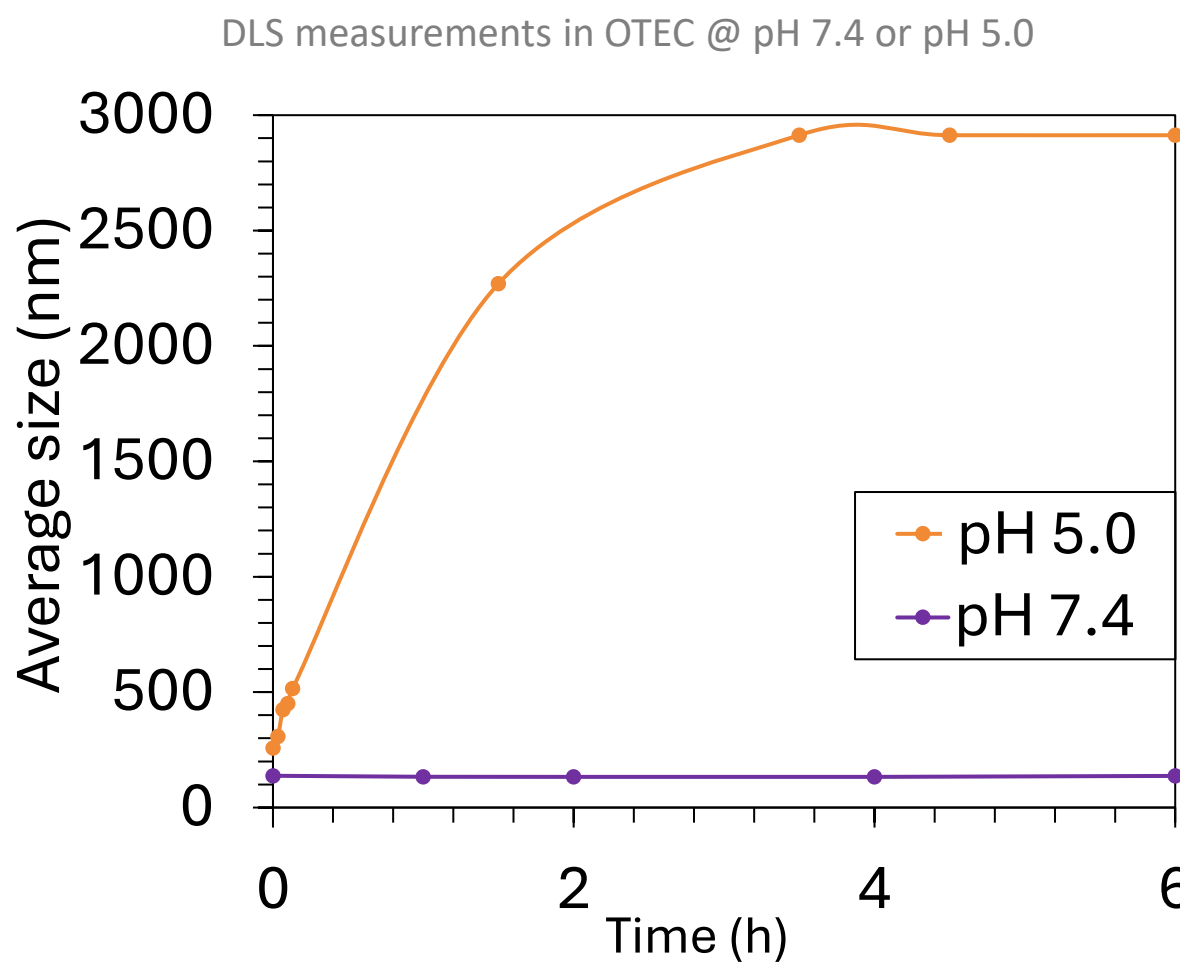
✓ PNAM-imine-PLA : triggered cleavage at acidic pH

Micelles & Drug Delivery

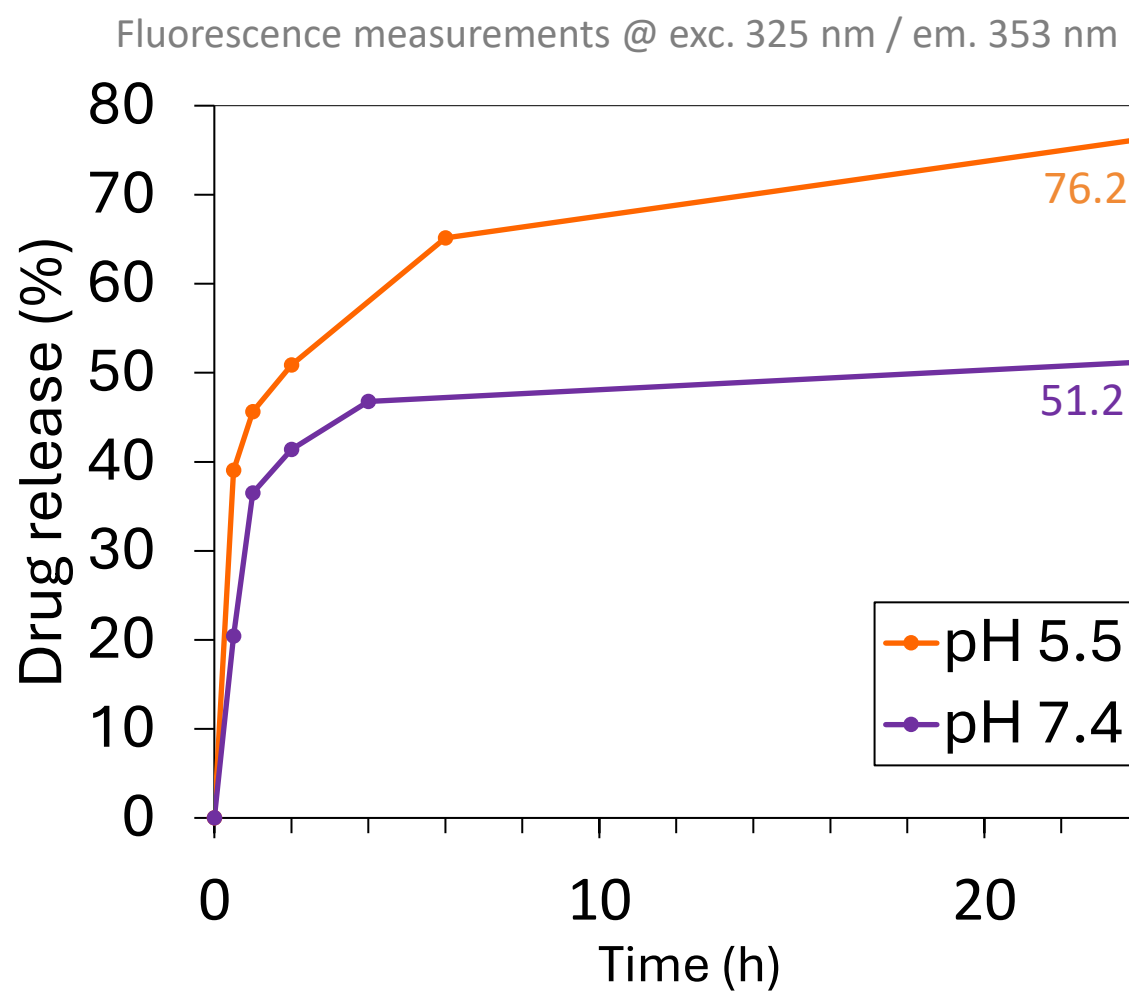
- Micelles via nanoprecipitation (From Acetone into PBS)
- Post-encapsulation of the drug (Imiquimod) and release

CMC = 80 µg/mL

pH 7.4 : 134.6 ± 2 nm, PDI 0.14
pH 5.0 : > 2 000 nm, PDI 0.64



✓ Acid-triggered destabilization of micelles



✓ Acid-triggered drug release

Conclusions & Outlooks

- pH-responsive hetero-bifunctional initiator: obtained and permitted **controlled synthesis of amphiphilic block copolymer** PNAM-imine-PLA.
- Copolymer demonstrated **pH-responsive behavior under acidic conditions**
- Micelles showed pH-responsive behavior: **confirming its potential for stimuli-responsive delivery applications**.



➤ Future work : aim to minimize release at neutral pH and enhance it under acidic conditions.

References

- [1] : Cabral, H.; Miyata, K.; Osada, K.; Kataoka, K. Block Copolymer Micelles in Nanomedicine Applications. *Chem Rev* **2018**, *118* (14), 6844–6892.
- [2] : Gignes, D.; Trimaille, T. Advances in Amphiphilic Poly(lactide)/Vinyl Polymer Based Nano-Assemblies for Drug Delivery. *Adv. Colloid Interface Sci.* **2021**, *294* (102483).
- [3] : Vinas, J.; Chagneux, N.; Gignes, D.; Trimaille, T.; Favier, A.; Bertin, D. SG1-Based Alkoxyamine Bearing a N-Succinimidyl Ester : A Versatile Tool for Advanced Polymer Synthesis. *Polymer* **2008**, *49*, 3639–3674.