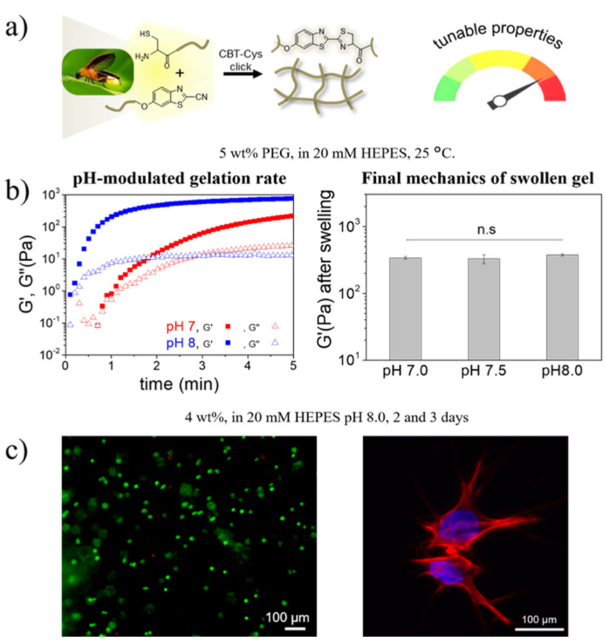
Development of firefly-inspired bioinks with tunable stress-relaxing, self-healing and viscoelastic properties

Reversible hydrogels that show adaptable, stress-relaxing and self-healing properties are envisioned as powerful biomaterials that can closely mimic the dynamic character of native cell microenvironments. In particular, dynamic hydrogels that are compatible with biofabrication technologies (for example, extrusion-based 3D bioprinting) are expected to enable artificial tissue models with tunable viscoelasticity.

Inspired by the biochemistry of fireflies, we have recently applied the biosynthesis of luciferins towards polyethylene glycol (PEG) hydrogels with tunable properties for cell encapsulation [1-2]. Building up on this hydrogel system, in a follow up project, we want to endow these materials with self-healing, stress-relaxing and printable properties. In this project, novel firefly-inspired hydrogel bioinks based on dynamic covalent crosslinks will be developed and their potential use to fabricate 3D bioprinted tissues will be tested. We will focus on understanding the system at the molecular/materials/cells levels.

This project involves the synthesis of functional polymers and derived hydrogels, their biomaterials characterization (rheological, physical chemical, biological) and their formulation as adaptable matrices for 3D cell culture. Special attention will be paid to the tunability of the system at the molecular level (by controlling the crosslinking chemistry) because this will determine the self-healing and viscoelastic properties of derived materials. Moreover, the influence of crosslinks reversibility on the behavior of encapsulated cells (morphology, survival at long culture times, gene and protein expression) will be studied. Finally, this platform will be adapted as bioink for extrusion-based bioprinting. Printability of these materials will be tested and cell survival will be quantified.



Keywords: firefly-luciferin-inspired crosslinking, reversible and adaptable hydrogels, bioink, printed artificial tissues, mechanical properties, viscoelasticity.

Figure 1 a) Hydrogel formation through the luciferin-inspired reaction. b) pH-regulation of gelation rate does not affect the final mechanical strength. c) High viability of encapsulated hMSCs and study of their F-actin organization in luciferin-inspired hydrogels with cell-adhesive and cell-degradable cues.

References:
[1] M. Jin, G. Kocer, J. I. Paez*, *ACS Appl. Mater. Interfaces* **2022**, 14, 5017.
[2] M. Jin, A. Gläser, J. I. Paez*, *Polym. Chem.* **2022**, 13, 5116.