

Company Overview

- **HTL Biotechnology** is a global leader in the development and responsible bioproduction of pharmaceutical-grade biopolymers (Hyaluronic Acid, Recombinant Collagen, Polynucleotides).
- **These biopolymers** are used by healthcare companies for the development of treatments in various cutting-edge therapeutic areas such as ophthalmology, dermatology, medical aesthetics and rheumatology.



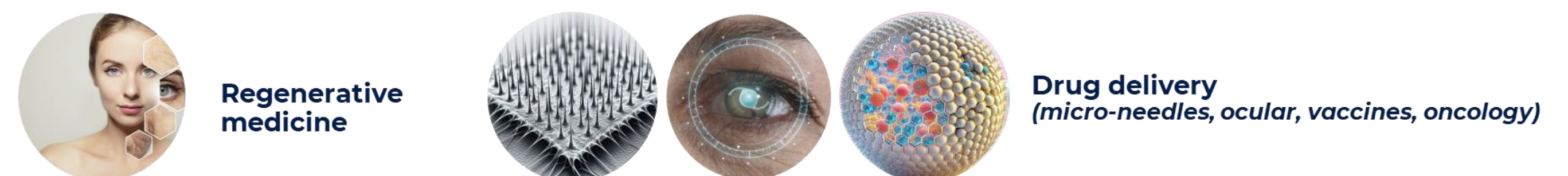
HTL's HA in the unique form of fiber

- **Our mission** is to unlock the potential of biopolymers to enhance patient's health and well-being worldwide.
- **By 2030**, our biopolymers aim to benefit over 500 million patients affected by age-related diseases and conditions, supporting the advancement of regenerative medicine.

Current applications



New applications

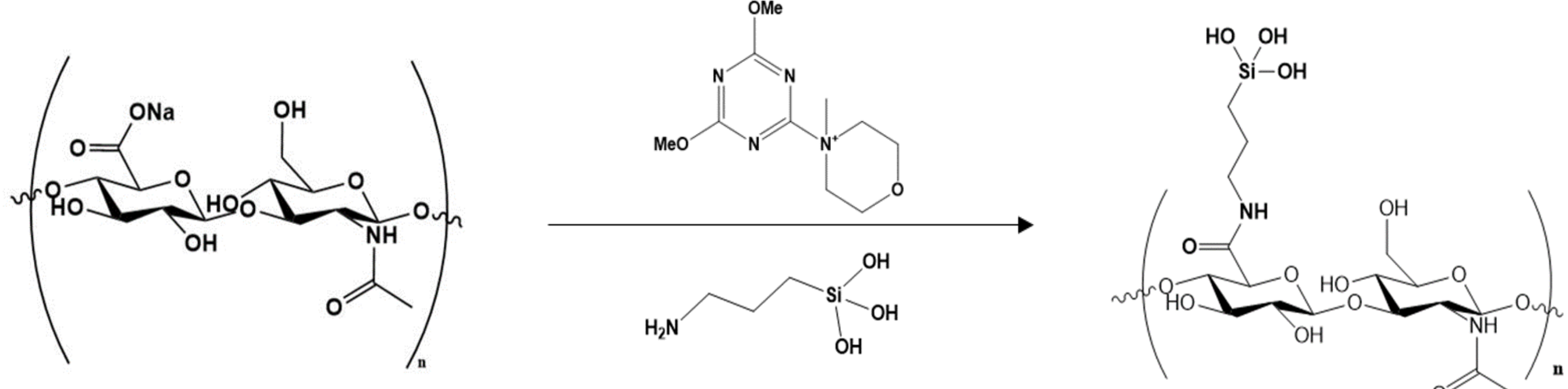


Innovative biopolymers at HTL addressing today's and tomorrow's unmet medical needs

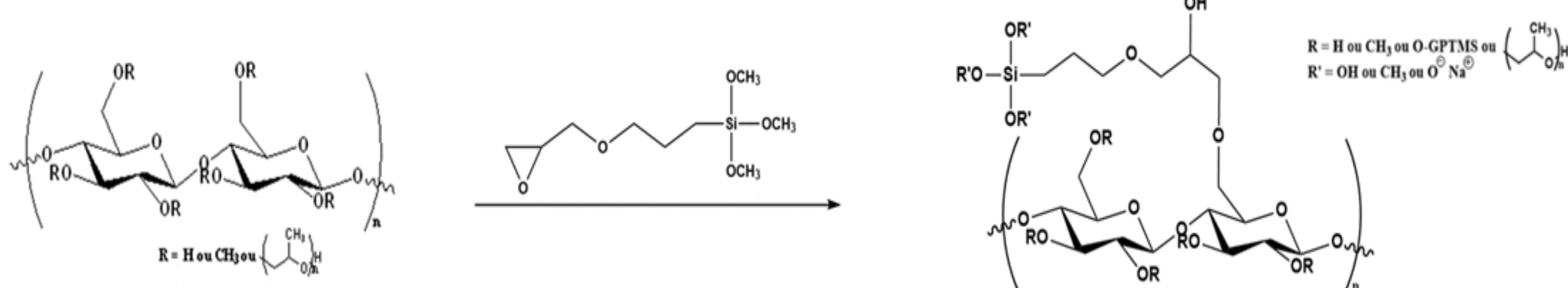
Introduction: based on **hyaluronic acid (HA)**, a glycosaminoglycan component of the extracellular matrix, we have developed a new generation of hydrogels with fully tunable rheological and mechanical properties. Through chemical modification, HA can be crosslinked using novel strategies, enabling the mimicry of a wide range of tissue environments. **Silanized HA (HA-Si)**, a hybrid organic-inorganic material, exemplifies the potential of these innovative scaffolds.

Modification of HA

- Synthesis of **HA-Si** in 2 steps:
 - 1) Activation of HA (with DMTMM)
 - 2) Amidation to graft the alkoxy-silane (APTES)

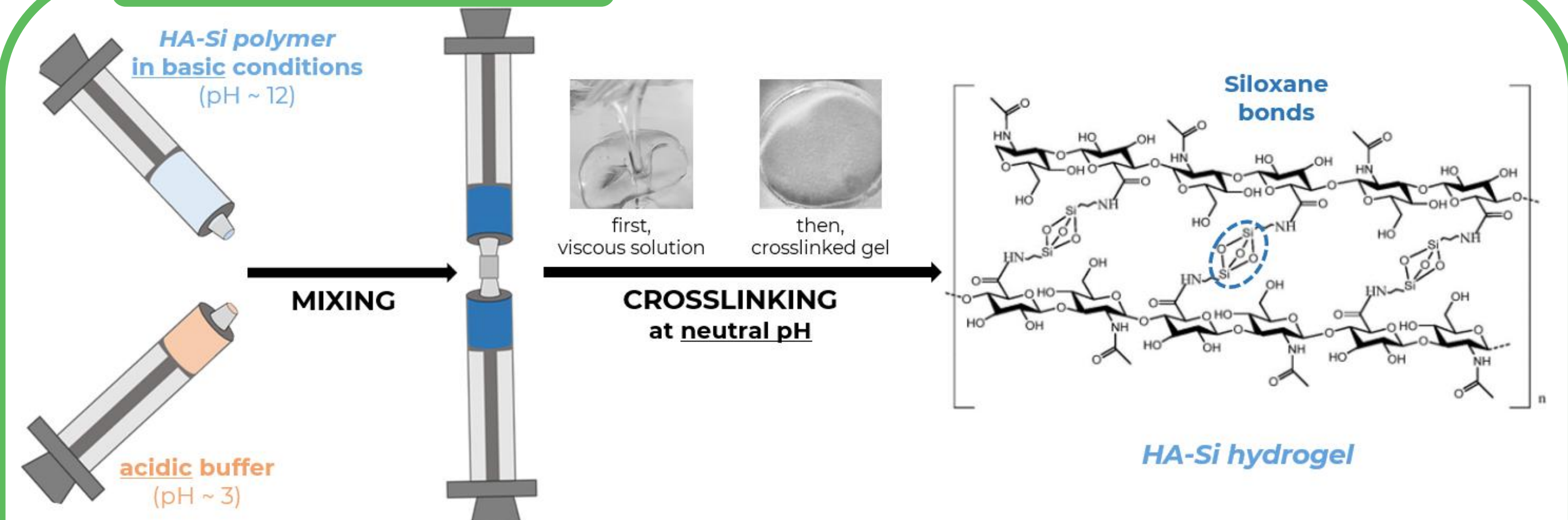


- To **tune the biodegradability and the viscoelastic properties** of HA-Si hydrogels, a silanized and non degradable polysaccharide can be added, **HPMC-Si** (silanized hydroxypropylmethylcellulose).

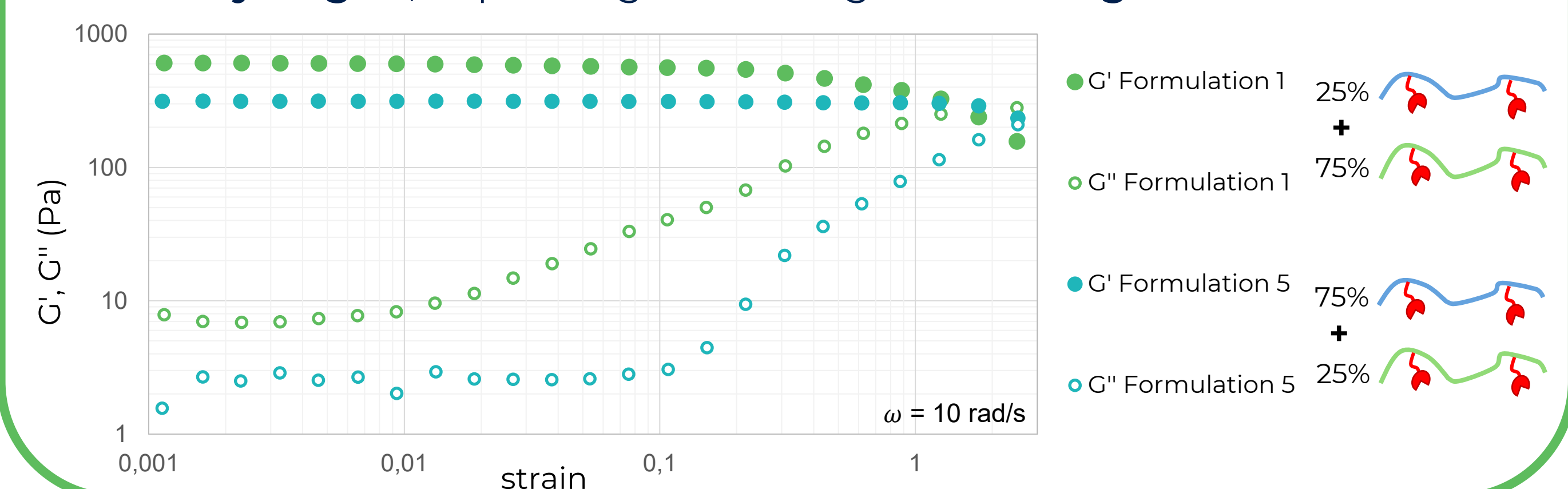


- Both synthesis processes have shown great robustness, scalability and lead to wide **custom polymer platforms**.

Crosslinking

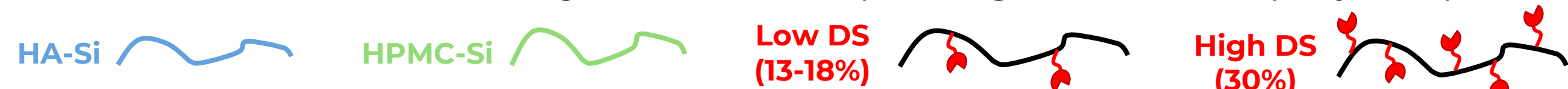


- By combining **HA-Si** and **HPMC-Si** through a **unique crosslinking protocol** (based on pH-driven condensation), we are able to formulate blended **tuned hydrogels**, depending on the targeted **rheological characteristics**.

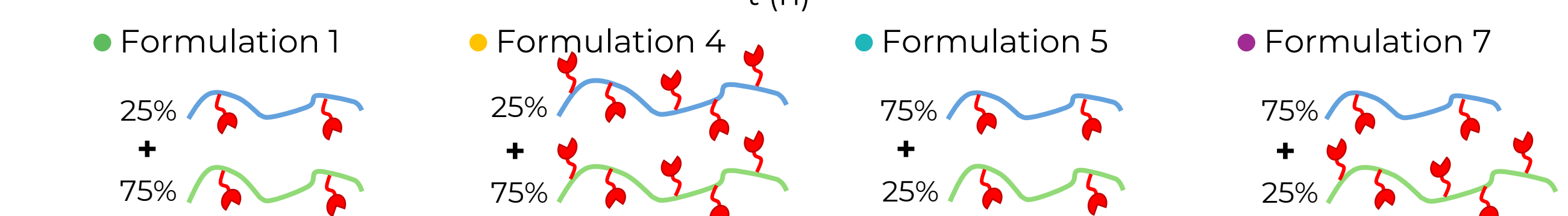
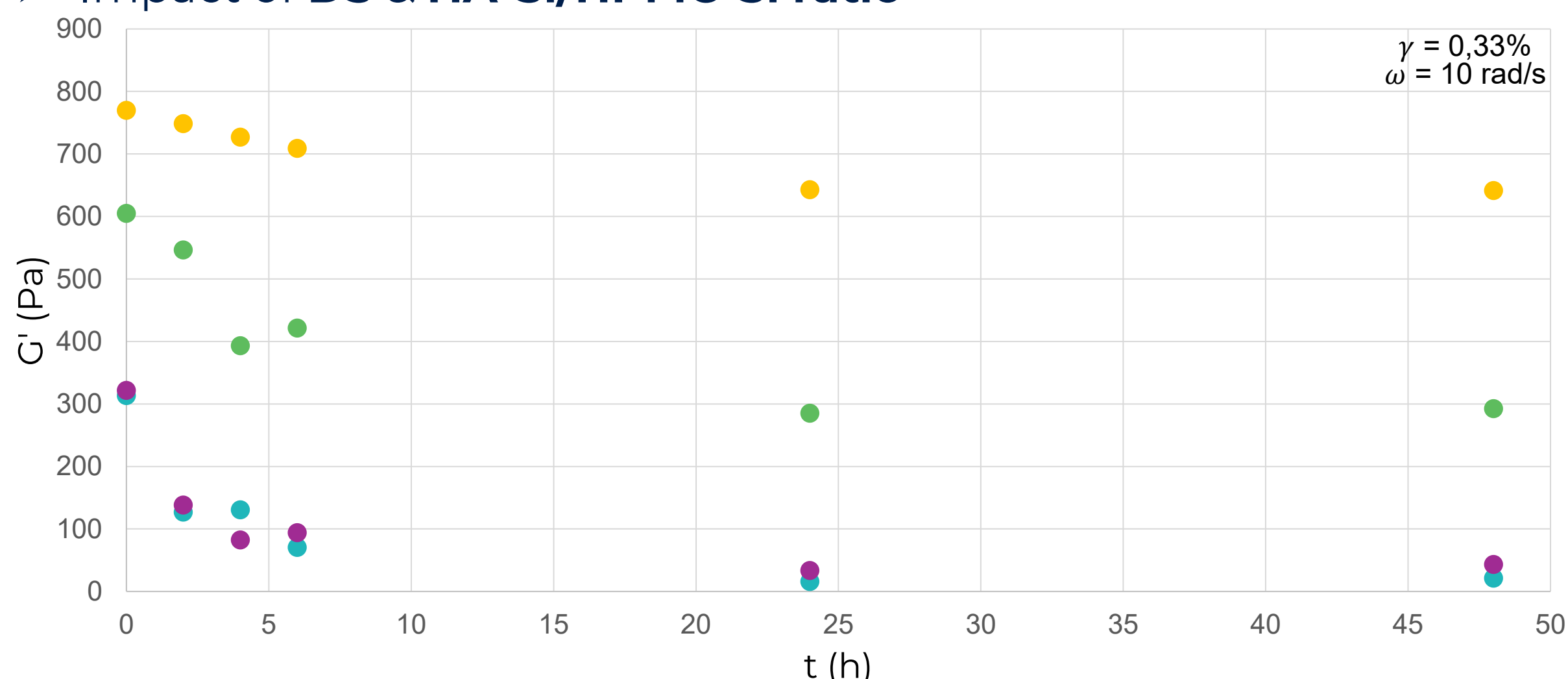


Degradability

- **Formulation & test:** all hydrogels are prepared at 24 mg/mL (total) and then, mixed with **hyaluronidase** (1 U/mg of silanized polymer)



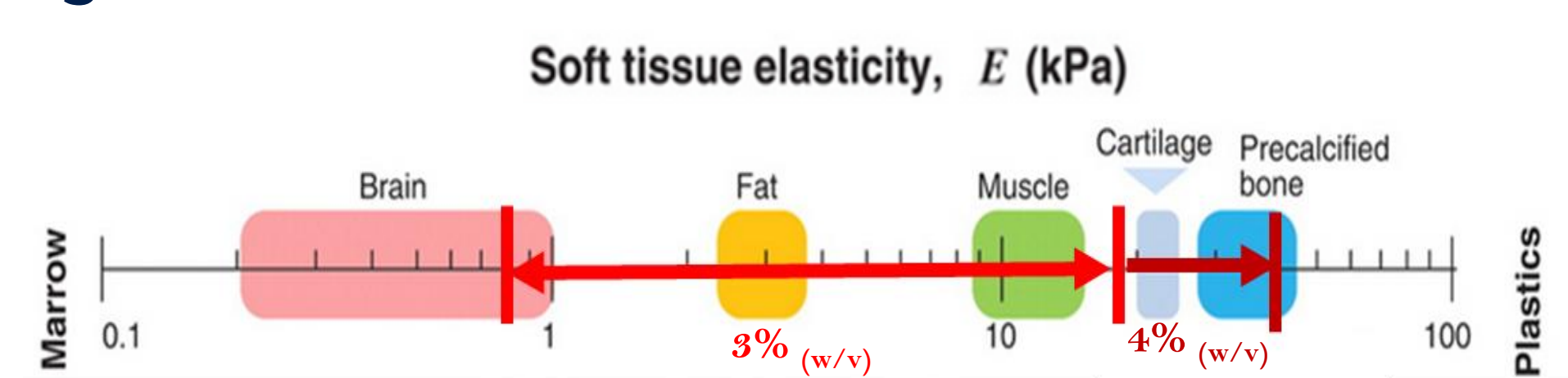
- Impact of **DS & HA-Si/HPMC-Si ratio**



- **Degradability kinetics** can be totally **adjusted** to fit the needed properties.

Applications

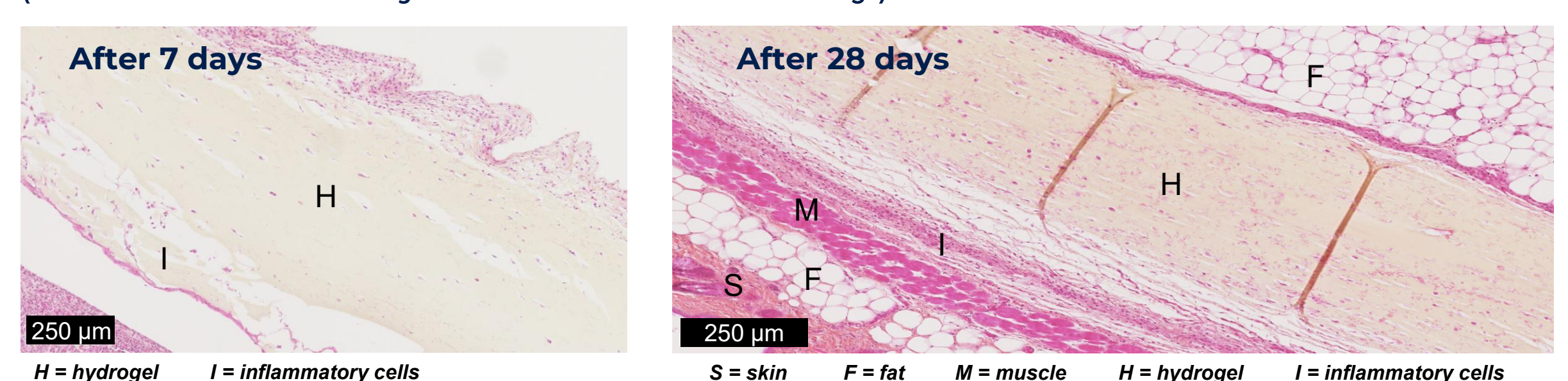
- **Silanized polymer family** can target a very **wide spectrum of tissues to be regenerated...**



- ...through **different applications:** **Tissue regeneration** and **Drug delivery**



- **HA-Si** hydrogels reveal impressive results for **skin regeneration** (subcutaneous injection – in vivo study):



- **Very nice implant integration** in dermal layers: **low inflammation & colonization by cells**

Conclusion & perspectives

- The development of **silanized polymer platforms** and their custom formulations offer infinite possibilities for tissue regeneration, thanks to a total tuning of the **rheological, mechanical** and **degradability** properties of the hydrogels.
- These **tailor-made scaffolds** can thus be integrated for **soft or hard tissue repairs**, from skin to bone, to propose a medicine that is increasingly tailored to the specific needs of patients.

References

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- A. Fatimi *et al.* The rheological properties of silylated hydroxypropylmethylcellulose tissue engineering matrices. *Biomaterials*, 29 : 533-543, 2008.
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