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Paper 1 – Particle Hydrogels on Hyaluronic acid building blocks

Materials and Mechanics in Medicine HS 2019

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Jack Kendall

Today

- **15.15-15.30:** Paper Overview
- **15.30-16.00:** Solve the Quiz (optional)

Paper 1

Particle Hydrogels Based on Hyaluronic Acid Building Blocks

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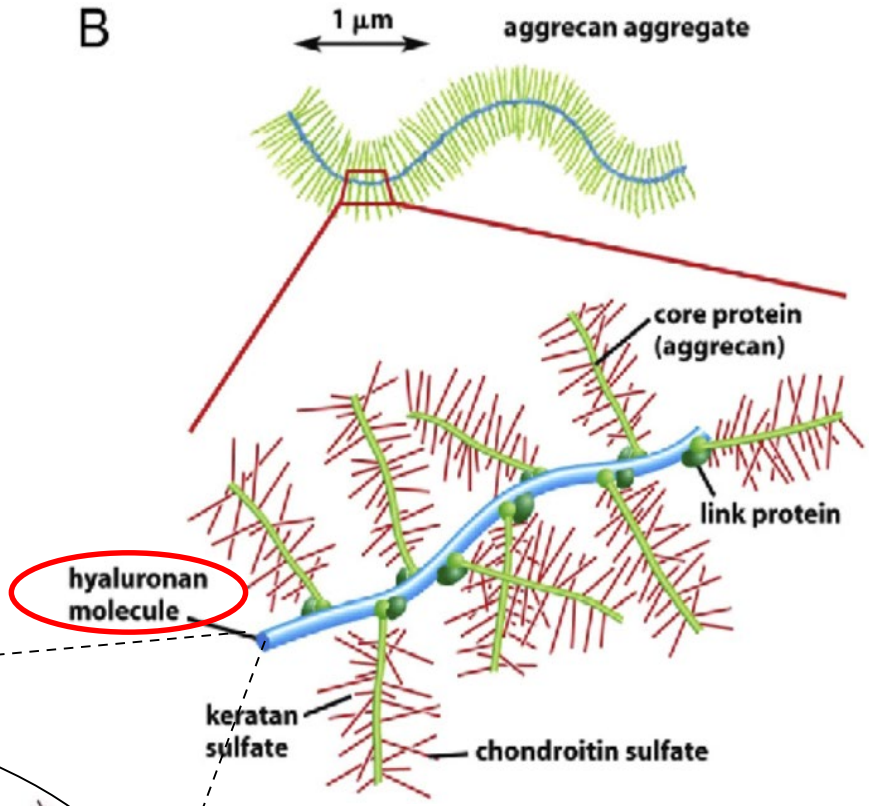
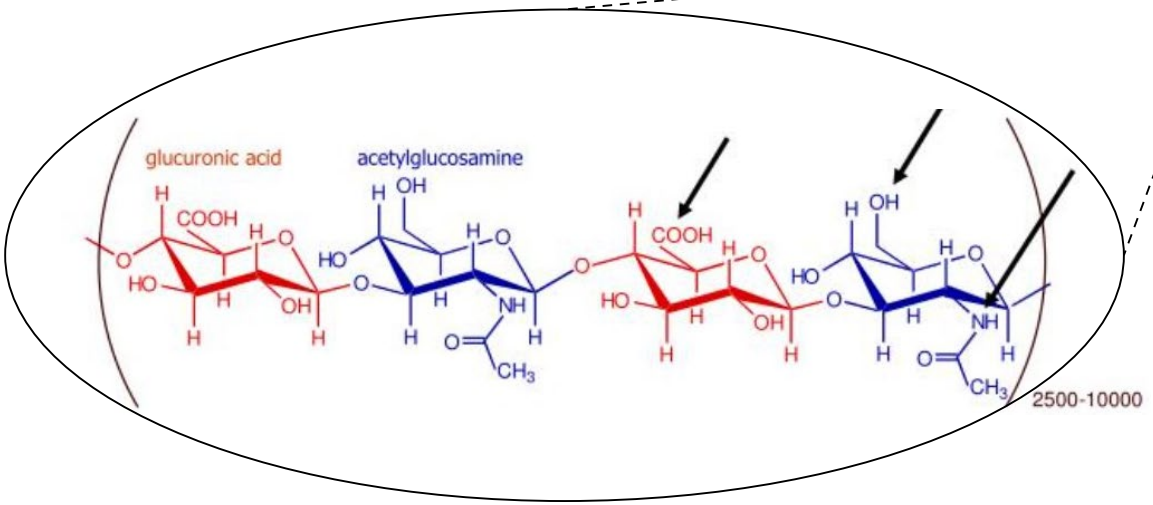
Hyaluronic Acid (HA) = Hyaluronan

- Linear, non sulfated GAGs
- Natural ECM component

→ biodegradable, non-immunogeneic

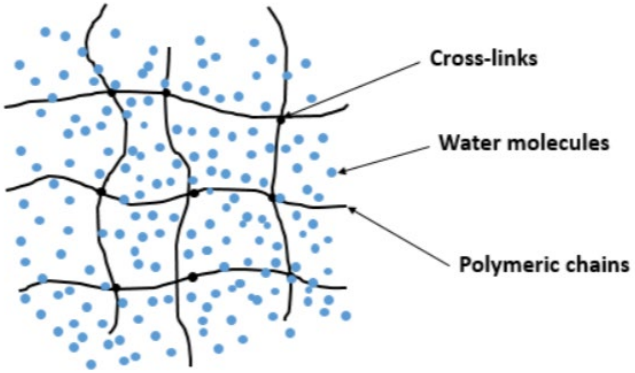
- Multiple sites for modification:
  - Carboxyl and hydroxyl groups

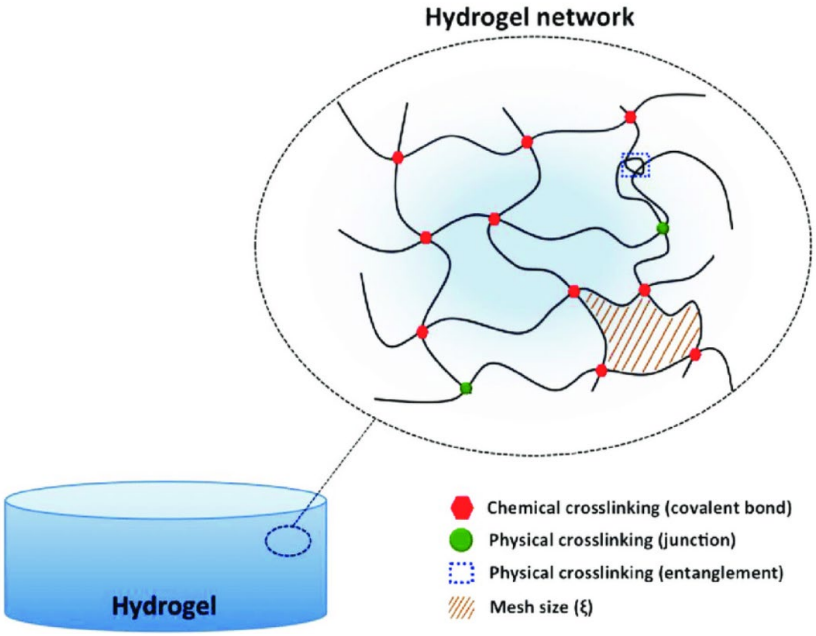




Hydrogels

- Hydrophilic crosslinked polymers
- Natural/synthetic polymeric building blocks
  - **For example:** Hyaluronic acid, Chitasan, Alginate, PEG,…





Why polymeric hydrogels?

- Mimic ECM
- 3D structural framework
- Moldable
- Tunable mechanical properties
- Water-based
- Swollen mesh (mesh size: 10-100nm)

  →Degradation is required for cellular infiltration.

Why?

Degradation rate

- How to modulate it?
  a) Integration of degradation sites
  b) Noncovalent bonds→ Stress relaxing

- Challenge:
  - Too slow degradation → no cell infiltration, fibrotic encapsulation
  - Too fast degradation→ no mechanical support

→Need for balance between degradability and long-term mechanical support

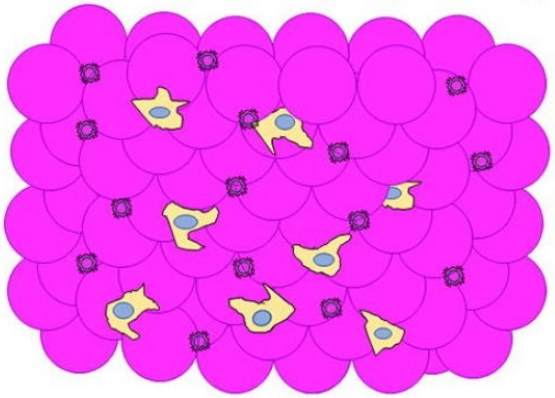
Why is cellular infiltration essential?

Why is cellular infiltration essential?

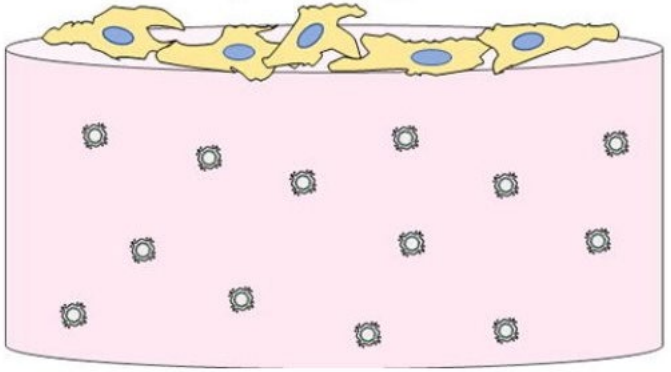
→To allow endogeneous tissue integration

Hydrogel (Paper)

Microporous annealed particle (MAP) hydrogel



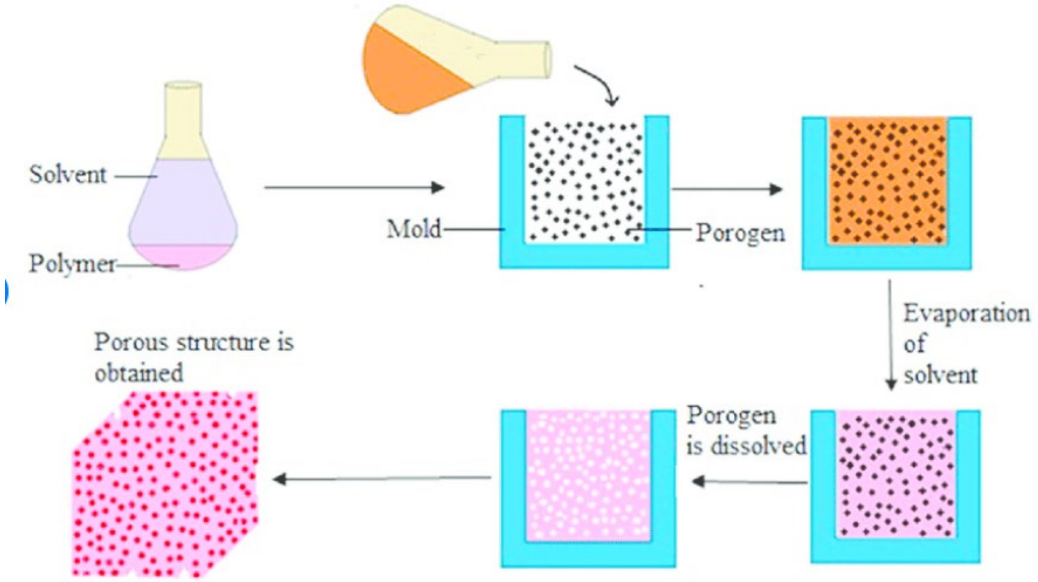
Standard bulk hydrogel



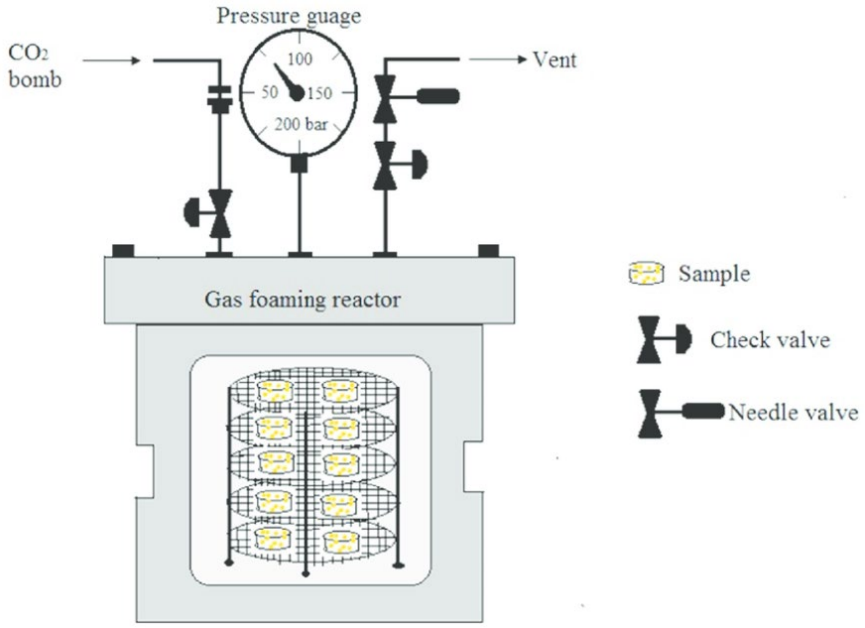
Methods to produce microporous scaffolds

- Salt leaching
- Gas foaming
- Lyophilization
- Sphere templating

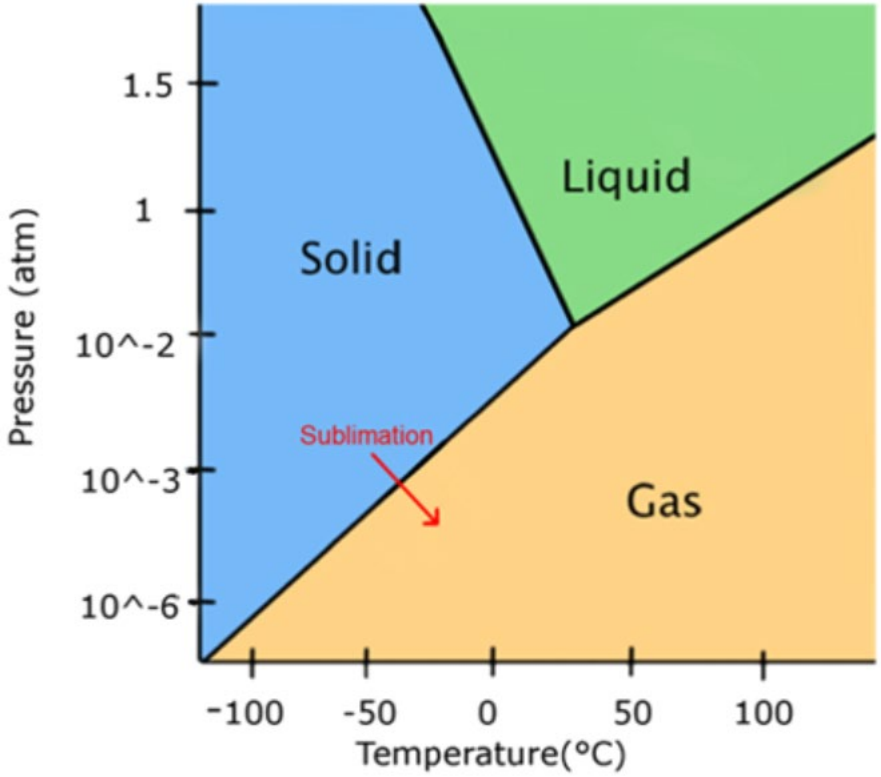
Salt leaching



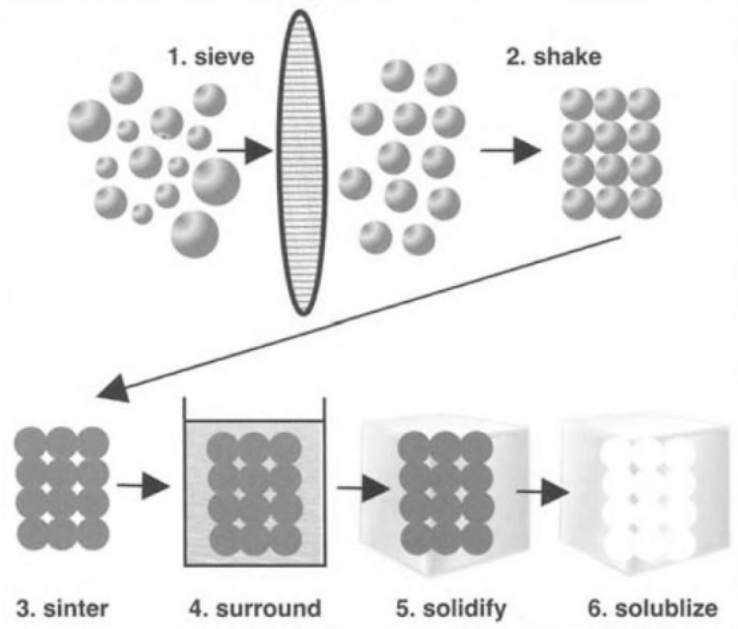
Gas foaming


Pressure guage
CO2 bomb
100
50
150
200 bar
Vent
Gas foaming reactor
Sample
Check valve
Needle valve

Lyophilization (=Freeze drying)



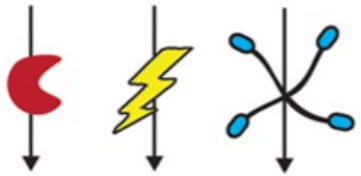
Sphere templating



Aim (Paper)

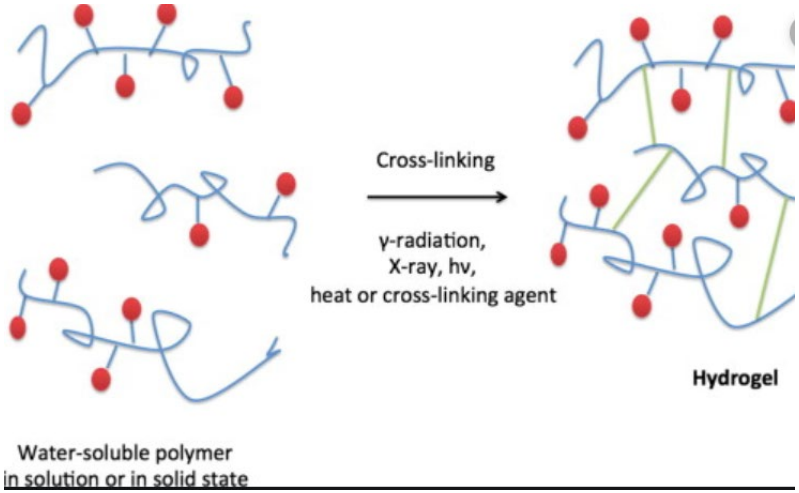
- Deeper characterization of HA MAP gels
- Generation of particle hydrogels using 3 different annealing approaches
- Demonstrate the versality of those 3 approaches by exploration of physical differences:
  - Pores connectivity
  - Pore area/void fraction
  - Mechanical properties of the scaffold
  - Cell spreading

3 Orthogonal annealing chemistries



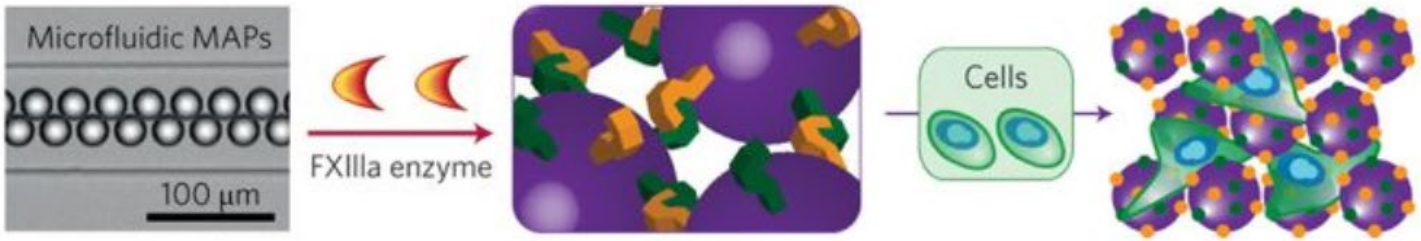
- Enzymatic reaction
  - FXIIIa
- Light-based radical polymerization
  - Eosin Y
- Amine/carboxylic acid-based cross-linking
  - PEG-NHS

→All three leads to the formation of a stable 3D scaffold

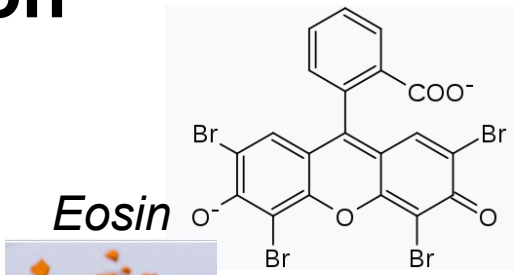


Enzymatic reaction

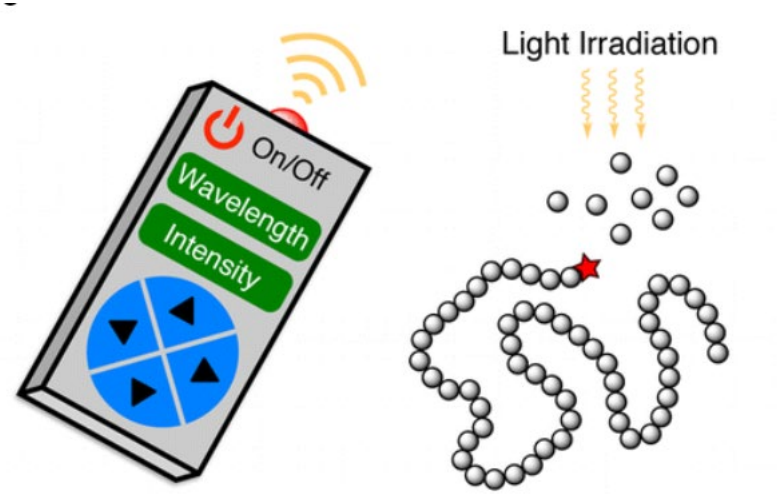
- FXIIIa
  - A coagulation factor



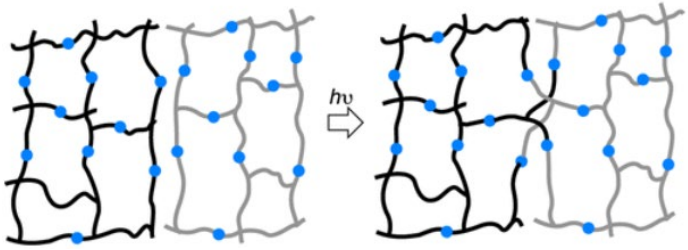
Light-based radical polymerization (Eosin Y)



Eosin

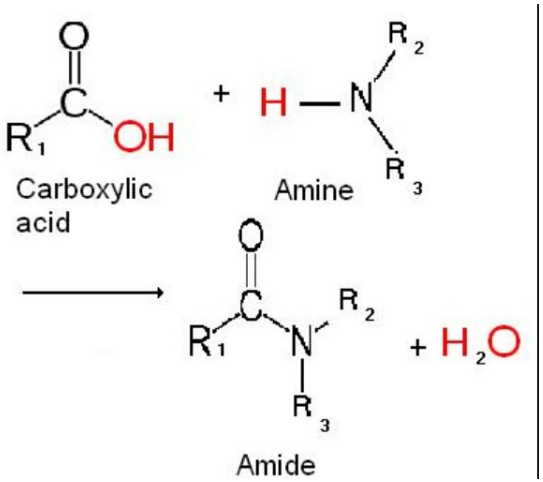


- Ease of Control On/Off, Wavelength, Light Intensity, etc.
- Functional Group Tolerance
- Orthogonal to Other Methods

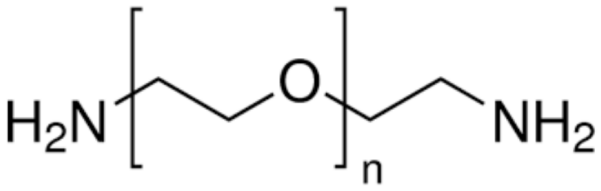


Amine/carboxylic acid-based cross-linking

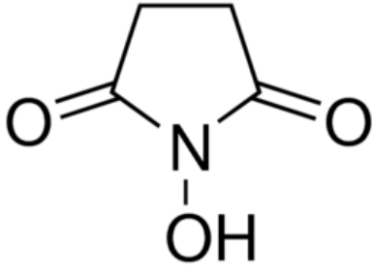
- PEG-NHS



PEG



NHS



Key Findings (Paper)

In HA based MAP Hydrogel:

- Pore sizes are smaller than in other scaffolds
- Annealing of the beads is required
- Pore diameter depends on the packing density
- Cells loading during scaffold formation is possible
- Pores are interconnected
- HDFs cells spread in HA within 2 days

References and further reading

- *https://parjournal.net/article/view/2342*
- https://pubs.rsc.org/en/content/articlehtml/2013/cs/c3cs60040h
- https://www.sciencedirect.com/science/article/pii/S1742706119304003
- https://pubs.acs.org/doi/pdf/10.1021/acs.chemrev.5b00671
- https://www.intechopen.com/books/emerging-concepts-in-analysis-and-applications-of-hydrogels/in-situ-forming-cross-linking-hydrogel-systems-chemistry-and-biomedical-applications

Quiz