Recognitive alginate nanoparticles for protein therapeutics

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Background

Tissue injuries include bone, tendon, muscle, skin, nerves and cartilages. Depending on the cause of the damage, they can become acute or chronic. Initial therapies were based on same-donor transplantation, yet in trauma, burned, or deep wounded patients the alternatives were very limited. Current strategies used to enhance tissue regeneration include scaffolds, gels, sheets or implants.

The aforementioned strategies have evolved with the surge and development of new synthetic materials. These approaches offer improved control, and the ability to fabricate novel systems. However, they lack complex structures that mimic the natural cellular environment.

These substitutes can however cause reduced vascularization, scarring, absence of cellular differentiation, or lack the biomechanical properties necessary to have proper function.

Hydrogel scaffolds

New-age materials are based on the combination of natural materials present in the body (taking advantage of their complex architecture) and include synthetic polymers to confer specific properties (mechanical, chemical or biological).

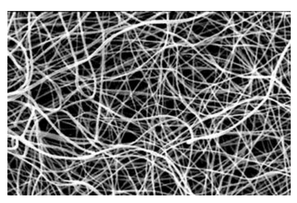


Figure 1. Biomaterials in tissue engineering.[1,2] Scaffolds and synthetic polymers are commercially available for regenerative applications.

- There are multiple approaches that have been explored to improve tissue regeneration, however, the main basic strategy involves the use of a scaffold (structural device that defines the geometry of the replacement tissue) that provides environmental cues for tissue regeneration.

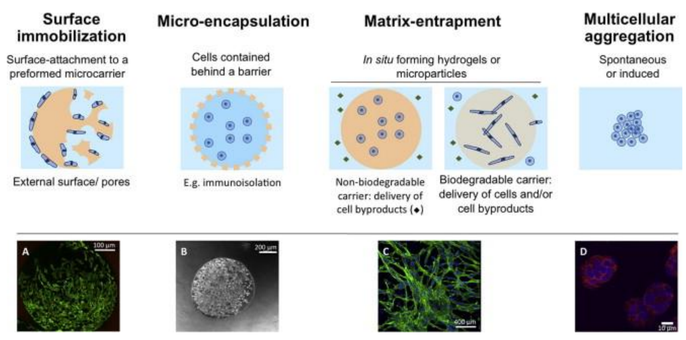


Figure 2. Hydrogel scaffolds in tissue engineering.[3] Among the multiple scaffold strategies are surface-immobilization, micro-encapsulation, matrix-entrapment, and multi-cellular aggregation. Depending on their application, cellular environment and targeted tissue, scaffold materials can be modified.

- One of the new-age tissue engineering strategies is the use of molecular recognitive polymers.
- These materials are an alternative to natural recognition elements, since they improve stability and lower technology costs.

Molecular imprinting

Molecular imprinting is based on the use of a macromolecule as a template (>1500 Da) polymeric matrices are imprinted to enhance specific interactions with particular biomolecules.

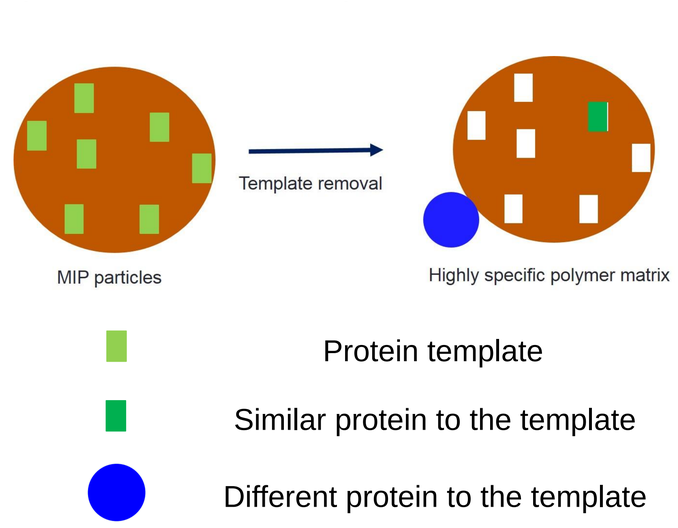


Figure 3. Molecular imprinting scheme. Protein templates are used to create nanocavities with specific charge and size within polymers by crosslinking them in their presence.

Natural polymers

- Natural materials were the first strategy used to develop regenerative technologies. Among them are included:
  - Collagen
  - Hyaluronic Acid
  - Alginate
- Alginates are promising candidates for tissue engineering since they are bioresorbable, biocompatible, and non –immunogenic.
- In addition, the presence of carboxyl and hydroxyl groups in alginate allow for a variety of chemical modifications to provide alginates with specific desirable characteristics.

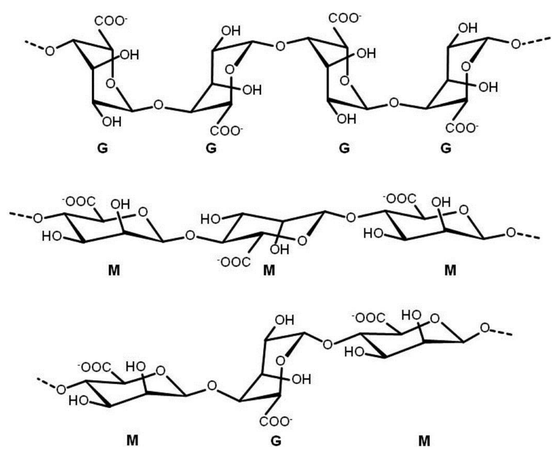
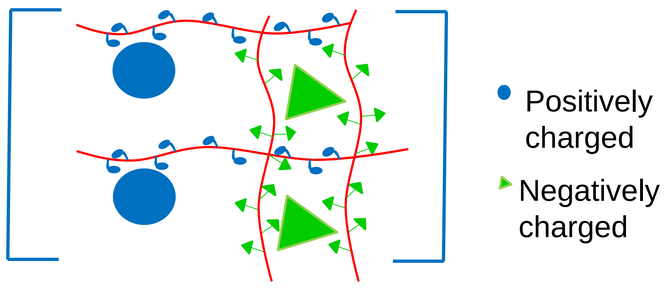


Figure 4. Alginate chemical structures.[4] Alginates are anionic polymer produced by brown algae and bacteria. They are formed by α-L-guluronic acid (G blocks) and β-D-mannuronic acid (M blocks).

Project Goal

To design and develop an alginate-based molecularly recognitive nanoparticle system for tissue engineering



Alginate nanoparticles

- Alginate microparticles have been previously used as protein and drug delivery carriers.
- Alginate nanoparticles have higher surface area, allowing imprinting with less amount of template.

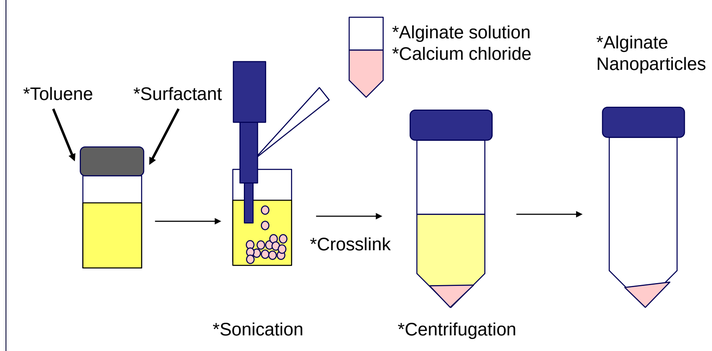
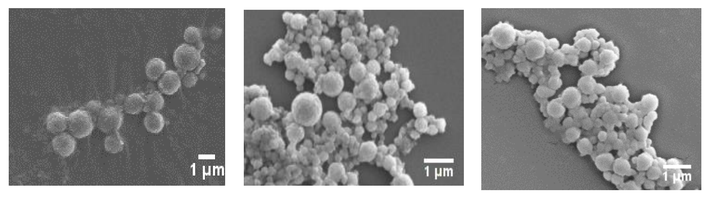


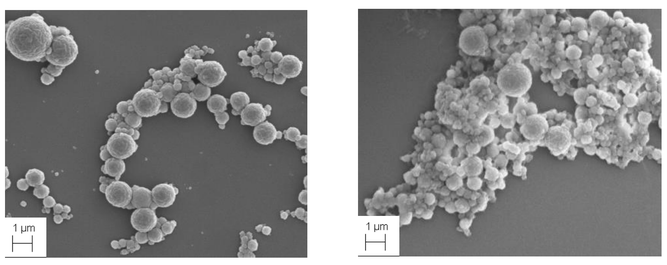
Figure 5. Alginate nanoparticles are fabricated using water in oil nanoemulsions with surfactant. Ionic crosslinking was performed using $CaCl_2$ solution.

Nanoparticle characterization



*0.5 % Alginate *1 % Alginate *2% Alginate

Figure 6. Photomicrographs of nanoparticles with different alginate content. Alginate solutions (20% v/v) were emulsified in toluene with 5% (w/w) Span® 80. Resulting particles were dropcasted and coated with 12 nm of Pt/Pd and imaged using scanning electron microscopy. Scale bar= 1 µm.



* Hemoglobin-loaded nanoparticles *Cytochrome C-loaded nanoparticles

Figure 7. Photomicrographs of model protein-loaded alginate particles. Hemoglobin and cytochrome C loaded alginate particles were fabricated using water in oil microemulsions. Alginate solutions containing 1% (w/w) hemoglobin and 1% (w/w) cytochrome C, respectively, were emulsified (20% v/v) in toluene. Resulting particles were imaged using scanning electron microscopy. Scale bar= 1 µm.

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Acknowledgments

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