Negative templating method to form internal microstructures in polymers through the use of a nanostructured carbohydrate network as a sacrificial scaffold

Nicola Muzzin, Kelli-anne Johnson, David Latulippe and Todd Hoare

Department of Chemical Engineering, McMaster University, Hamilton, Ontario, Canada

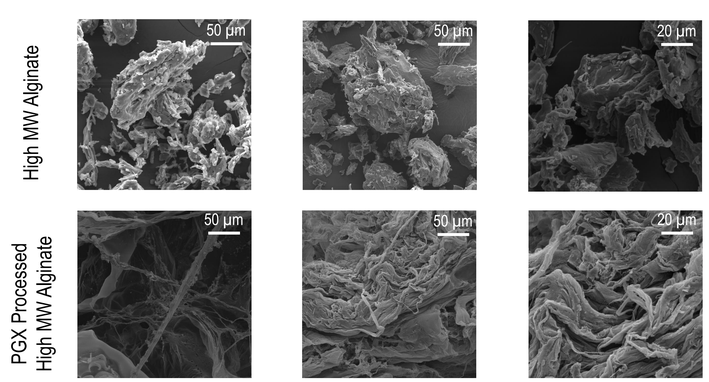
Phone: 1-905-525-9140 ext. 24701 | E-mail: muzzinn@mcmaster.ca, hoaretr@mcmaster.ca | Website: http://hoarelab.mcmaster.ca

Motivation

- Polymer monoliths are continuous porous networks fabricated from a polymeric scaffold. [1] While they hold promise as an alternative to classical chromatography techniques for use in bio-separations due to their high surface area, the current limitation is the high cost of production.
- Polymer monoliths are currently fabricated using techniques such as gas foaming, lyophilisation, and solvent casting. These techniques often require long processing times to remove solvents, reagents and surfactants and have low control over the size, shape, and connectivity of the internal porosity [2], resulting in irreproducible or ineffective separations in bioseparations applications and poor cell-cell communication in tissue engineering applications.
- Herein, we aim to apply a sacrificial micro/nanoporous carbohydrate network to create an interconnected pore structure within a hard polymer scaffold as an inexpensive alternative to traditional separation methods for high volume bio-therapeutics and/or hard tissue scaffolds

PGX Technology

- Ceapro's Pressurized Gas eXpanded (PGX) liquid technology is a technique used to process carbohydrate polymers with tunable internal structures and high internal surface areas, typically with the goal of facilitating easy re-dispersion of the materials in water.
- The carbohydrate is precipitated into a pressure vessel under supercritical conditions. The solvent is removed, and upon release of the pressure, the polymer undergoes rapid expansion to create macro and mesopores within the dry polymer. [3]
- PGX can form a variety of structures such as particles, fibres, flakes and interconnected networks. Alginate was chosen for this project since it is highly water soluble (and thus easily extractable from the hard matrix) and PGX processing forms a highly interconnected network structure.



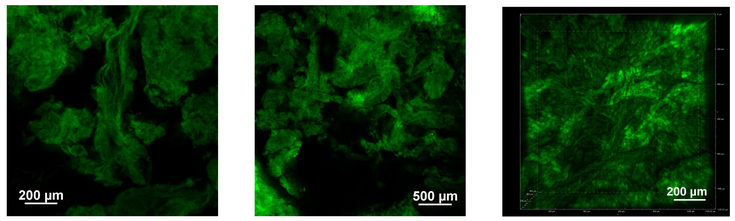
Monolith Composition Options

Monomer	Rationale for Use
Methyl Methacrylate (MMA)	Creates a hard continuous phase with good mechanical strength under pressure/force loading
Butyl Methacrylate (BMA)	Lower T_g polymer; some malleability at room temperature
Ethylene Glycol Dimethacrylate (EGDMA)	Creates an elastic but hydrated continuous phase that enhances the ease of alginate extraction.
Methacrylic Acid (MAA)	Incorporates functional groups for the attachment of ligands for affinity separations/growth factor tethering

Negative Templating

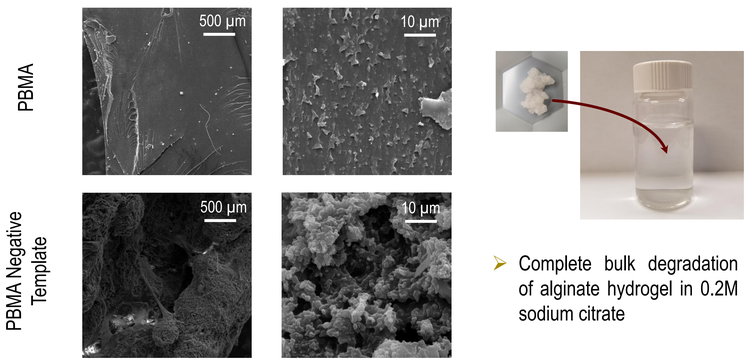
Internal Structure

- The carbohydrate was labelled with fluorescein isothiocyanate (FITC) before PGX processing and MMA was polymerized around the labelled network. Confocal microscopy confirms that the continuous micro/nanoporous structure is maintained following the templating reaction.



Removal of Alginate

- Efficacy of templating scaffold removal depends on mass transfer of sodium citrate into the polymerized monolith, facilitated by the continuity of the network prior to polymerization



- Complete bulk degradation of alginate hydrogel in 0.2M sodium citrate

Conclusions

- The PGX processed alginate network contains macro and mesopores, useful for bio-separations applications.
- Polymers can be polymerized around a templating PGX material by free radical polymerization without collapsing or substantially altering the carbohydrate structure.
- The polymer composition of the continuous monolith can be altered via copolymerization to have different mechanical properties and water penetration.
- Templating alginate PGX hydrogels can be removal from the polymer monolith by soaking in an aqueous complexation buffer to remove calcium crosslinks.

Future Directions

- The polymer composition should be optimized for the appropriate functionality and mechanical integrity for bio-separations and/or engineering hard tissues (e.g. bone, cartilage).
- Ligand conjugation to the functional comonomer included in the monolith will be explored to enhance the selectivity of potential bioseparation processes.
- Osteoblasts will be seeded in the monolith to evaluate its potential as a scaffold for bone regeneration, both with and without bioadhesive ligands conjugated to the functional tags.

Acknowledgements and References

Special thanks to the PGX team at Ceapro, a collaboration made possible by the NSERC strategic grant program.

[1] Groarke R.J., and Brabazon D., Monolithic Materials for Bio-Separations. In: Saleem Hashmi (editor-in-chief), Reference Module in Materials Science and Materials Engineering. Oxford: Elsevier; 2016. pp. 1-25.
[2] G. Y. Huang, L. H. Zhou, Q. C. Zhang, Y. M. Chen, W. Sun, F. Xu, and T. J. Lu, "Microfluidic hydrogels for tissue engineering," *Biofabrication*, vol. 3, no. 1, p. 12001, 2011.
[3] F. Temelli and B. Seifried, "Supercritical Fluid Treatment of High Molecular Weight Biopolymers," US Patent Application 20130101849A1, 2013.

THE HOARE LAB
Laboratory for Engineered Smart Materials

CEAPRO
Nature Enhancing Life™