3D bioprinting hydrogels using “click” chemistry

Brian Huang
brh125@terpmail.umd.edu
Science, Discovery and the Universe
Bioengineering

ABSTRACT

Utilizing click reactions in bioprinting processes can be advantageous. Click reactions can provide favorable characteristics to bioprinting methods, such as maintaining biomaterial functionality and quick construction of desired structure.

In my investigation, I will be determining methods to bioprint common hydrogels using click reactions.

INTRODUCTION

Bioprinting technology is an invaluable resource in many important applications in the field of tissue engineering.[1] The technology allows for the formation of three-dimensional structures of biomaterials that allow for growth of cells. This technology can be applied to create organs and tissues for implantation.

Click chemistry refers to a group of strong linking reactions that are simple, fast, and high yielding.[2] The “click” refers to the relatively simple joining of molecular building blocks.

Combining click reactions with bioprinting processes can be advantageous. Click reactions can provide instant formation of the desired structure and maintain mechanical integrity while keeping the functionality of the biomaterials.[3] Functionality of biomaterials is especially important in bioprinting processes to maintain biocompatibility of the structure for host implantation and cell viability.

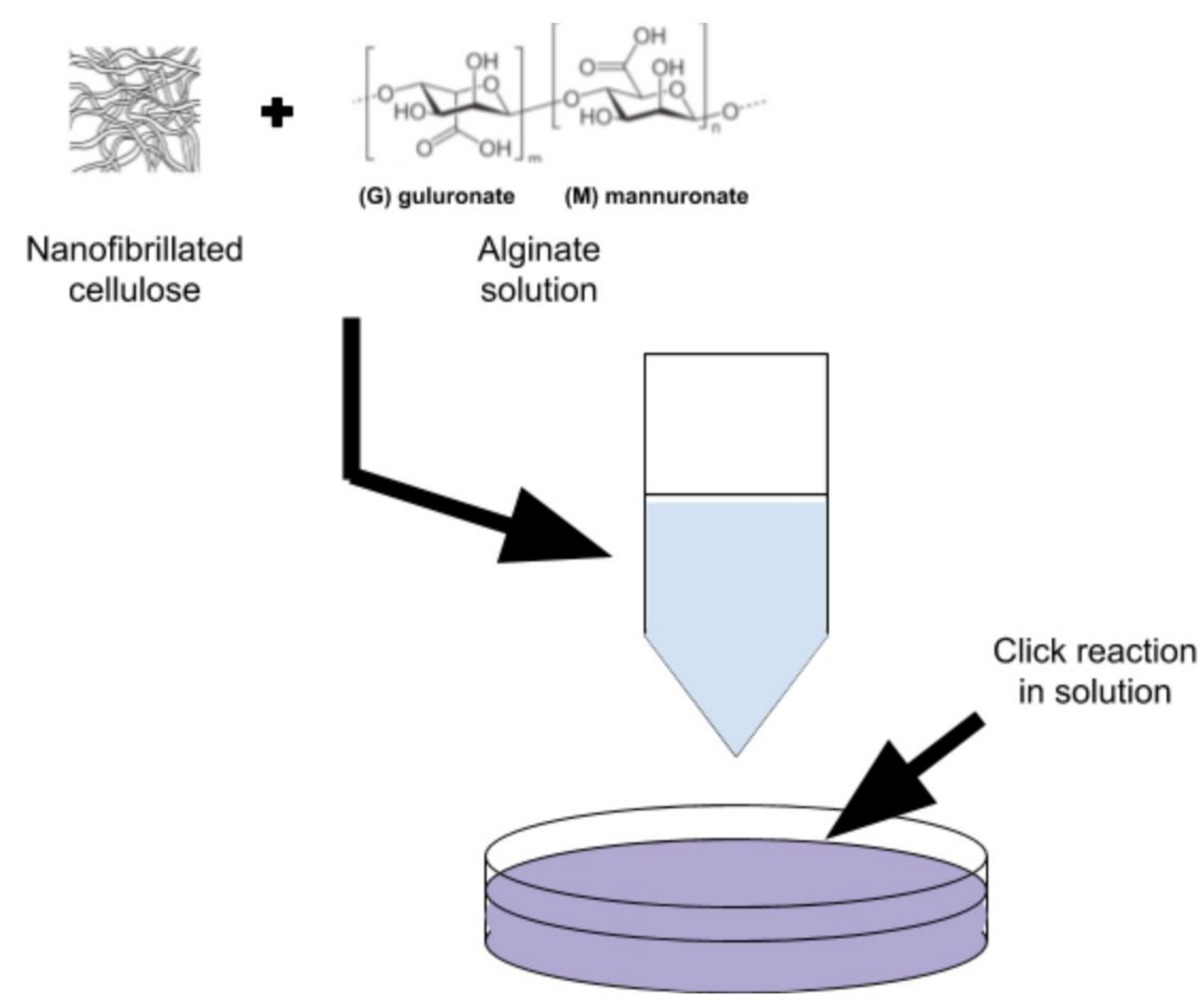

Figure 1. Method of bioprinting nanocellulose and alginate bioink into solution to undergo gelling via a click reaction.

Hydrogels, such as alginate, chitosan, and hyaluronic acid, are considered good base materials for bioprinting due to their innate biocompatibility. However, their poor rheological properties, such as low viscosity at low shear rates, often presents a challenge for extrusion printing.[4]

Recently, in Markstedt, K. *et al. Biomacromolecules* 2015, low viscosity alginate solution was found to have excellent printability and maintained biocompatible properties when combined with nanocellulose.[4]

Utilizing viscosity modifiers, such as nanocellulose, and click reactions to maintain favorable biological characteristics can potentially create an excellent method for bioprinting applications.

Future Work

In order to determine the effectiveness of this method, there are several aspects that need to be investigated.

The first is the characterization of the bioink. Flow curves are commonly used to gauge the rheological properties and printability of bioinks. Other rheological data that can be useful includes storage modulus, loss modulus, and Tan δ of the bioink formulations. Stress-strain curves are commonly used to observe mechanical strength. Other mechanical measurements include stiffness.

The second aspect that must be investigated is shape fidelity. The printed construct must maintain their shape and not collapse during printing. First, printed 2D structures must be controlled. Then larger constructs can be printed and observed.

Cytotoxicity is another aspect that should also be analyzed to ensure cell viability in the bioink.

Bioprinting is a valuable method in biomedical applications. Different biomedical applications require different bioinks with different properties. Determining the potential of click reactions in bioprinting can result in the discovery of more suitable methods of bioprinting for different applications.

REFERENCES

1. Seol YJ, Kang HW, Lee SJ, Atala A, Yoo J. Bioprinting technology and its applications. *European Journal of Cardio-Thoracic Surgery*. 2014 Sep; 46(3):342–348.
2. Hein CD, Liu XM, Wang D. Click chemistry, a powerful tool for pharmaceutical sciences. *Pharm Res.* 2008 Oct; 25(10): 2216–2230.
3. Gopinathan J, Noh I. Click chemistry-based injectable hydrogels and bioprinting inks for tissue engineering applications. *Tissue Eng Regen Med.* 2018 Oct; 15(5): 531–546.
4. Markstedt K, Mantas A, Tournier I, Avila HM, Hagg D, Gatenholm P. 3D bioprinting human chondrocytes with nanocellulose–alginate bioink for cartilage tissue engineering applications. *Biomacromolecules.* 2015 Mar; 16(5): 1489–1496.