# Memorandum

**Date: 10/8/2017**
**To: Research Division Chief Michael Scott – Miltenyi Biotec**
**From: Kevin Nguyen**
**Subject: Electrospinning Improves Pore Design of Biomimetic Scaffolds**

## Introduction:

The purpose of this memo is to introduce a technology that allows for greater control in the creation of pores in biomimetic scaffolds. Many conventional techniques are unable to produce porous biomimetic scaffolds that meet all of the extremely precise life-sustaining conditions that cells require. However, by using a relatively new technique called electrospinning, one can "produce the ultra fine fibers with special orientation, high aspect ratio, high surface area, and having control over pore geometry" (Subia, Kundu, & Kundu, 2010), which meet most of those conditions. As you are aware, tissue damage, repair and regeneration is a very serious clinical problem which accounts for countless health issues all over the world every year. While there are many different approaches to tissue regeneration, many of them come with drawbacks, which is why it is important to research for better tissue regeneration techniques. In this memo I will explain the following: what a biomimetic scaffold is, what factors are considered in pore design, what electrospinning is, how electrospun scaffolds compare to other scaffolds, and where we can see this technology in other fields of healthcare.

## Background:

### What Is a Biomimetic Scaffold?

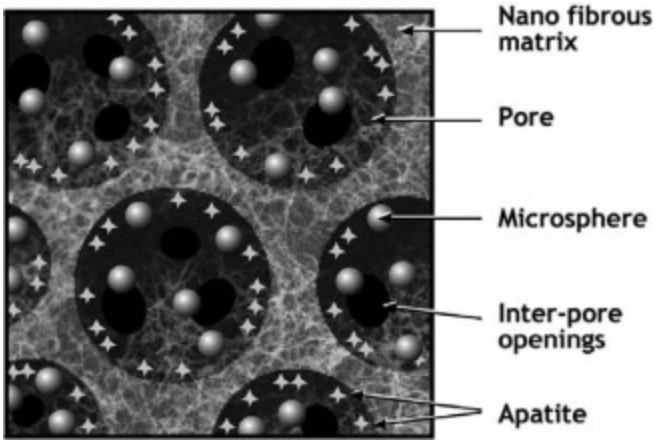
As the Research Division Chief, I am sure you are familiar with many tissue regeneration techniques. But perhaps you aren't as familiar with the new emerging approaches to tissue engineering. The frontier of regenerative medicine is changing from synthetic implants and tissue grafts to a biomimetic scaffold approach.

Biomimetic scaffolds are used to fill anatomical defects and assist in the tissue regeneration process. The scaffolds are implanted during a surgical operation and essentially act as a house for stem cells, protecting them and nurturing their growth. During the regeneration process, the scaffold slowly degrades away until the tissue on the site fully regenerates. (Nigam & Mahanta, 2014)

### What Factors Are Considered in Pore Design?

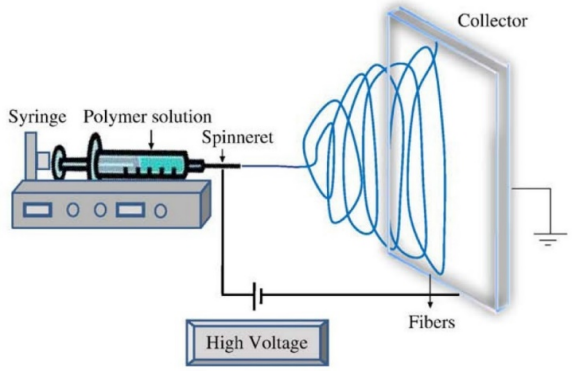
- Porosity – The percentage of the ratio between the empty pores to the total volume of a structure. Cells need porous environments to proliferate.
- Interconnectivity – Whether the pores are connected or not. Cells needs interconnected environments to migrate and communicate.
- Pore size – How big each individual pore is on average.

- Pore geometry – What is the shape of the pore? Cells have different geometries.
- Inter-pore openings – Are there pores within the pores? (Visual included below for better understanding).
- Surface area – Is there enough surface that cells can attach and proliferate?




**What is Electrospinning?**

Electrospinning is a technique that uses a strong electric field to produce polymeric fibers with diameters ranging from a few nanometers to a few micrometers. Using a high-voltage power supply that's connected to a syringe, we can induce a strong electric field between the syringe and a charged collector plate. Passing an electric current through the droplet forces the droplet to form a conical shape known as a Taylor cone. When you increase the voltage of the power supply past a certain degree, the electric force overcomes the strength of the surface tension of the droplet. This results in a thin jet of polymer solution ejected from the Taylor cone. The solvent in the polymer jet evaporates during its travel to the collecting screen, increasing the surface charge on the jet, which results in a spinning force. The formation of nanofibers results from the action of the spinning force on the polymer droplets. Nanofibers are deposited layer-by-layer on the metal target plate, forming a non-woven nanofibrous mat. (Li & Tuan, 2009). The setup is illustrated in the image below.



## Discussion:

## How Electrospun Scaffolds Compare to Its Predecessors

**Particulate-Leeching:**

Approach: Salt, wax or sugars known as porogens are used to create the pores or channels. Here salt is grounded into small particles and those particles that have desired size are poured into a mold and filled with the porogen. The polymer solution is poured onto said mold, water washes away the salt crystals, and a biomimetic scaffold is created.

Problem: You cannot precisely control pore shape, because pore shape is dependent on the grounded porogens that are used to create the mold. In addition, you have no method to control the creation of inter-pore openings, which are essential in cell migration (Subia et al., 2010).

**Freeze-Drying:**

Approach: "This technique is based upon the principle of sublimation. Polymer is first dissolved in a solvent to form a solution of desired concentration. The solution is frozen and solvent is removed by lyophilization under the high vacuum that fabricate the scaffold" (Subia et al., 2010).

Problem: Small pore size. Pores need to be big enough that cells can proliferate freely and be able to migrate.

**Gas-Foaming:**

Approach: "During the gas foaming process, molded biodegradable polymers are pressurized at high pressures with gas-foaming agents, such as CO2 and nitrogen, water, or fluoroform, until the polymers are saturated. This results in nucleation and growth of gas bubbles with sizes ranging between 100 and 500 μm in the polymer." (Zhu & Chen, 2013)

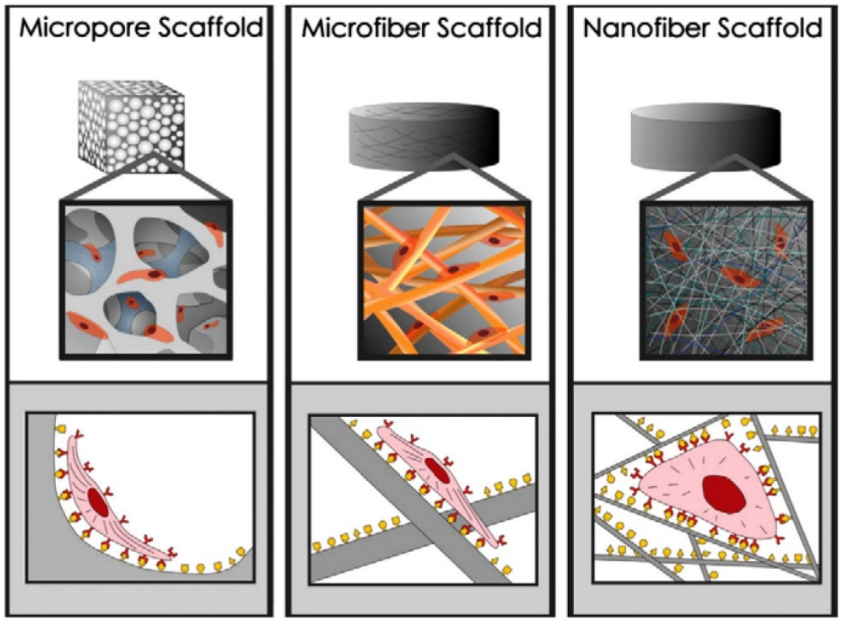
Problem: For the most part, the pores made by gas-foaming lack interconnectivity, and the external surface has a chance of being non-porous.

**Electrospinning:**

The benefits of electrospun scaffolds originates from the properties that are inherent to nanofibers. Nanofibers are very porous, with a high surface area to volume ratio, which make them an ideal candidate to create biomimetic scaffolds from. By changing parameters in the polymer, environment, and electrical set up, we can be in control of many of the drawbacks that the conventional methods suffer from.

The big idea here is that electrospun scaffolds do not suffer from most of the drawbacks as the other the techniques.

Furthermore, not only do they not suffer from as many drawbacks, they do a better job of promoting cell growth. “Nanofibrous architectures can positively affect cell binding and spreading compared to micropore and microfibrous architectures. Nanofibrous scaffold architectures have larger surface areas to adsorb proteins than micro-architectures, presenting more binding sites to cell membrane receptors”(Zhu & Chen, 2013). Refer to the image below for the binding site comparison.




## Future Implications:

In the pharmaceutical industry, nanofibers can be a promising tool for the controlled delivery of drugs, therapeutics, or molecular medicine. Since nanofibers are created from polymers, we can use special polymers that target and bind to a certain cell-receptor, and have that polymer deliver drugs directly into a cell upon meeting certain conditions.

Or, we can use the nanofiber polymers as a gradual-release medication. We can coat the nanofiber polymers in a biological or chemical ligand, that responses to certain physiological changes. For example, if a ligand detects low levels of insulin in a diabetes patient, this will trigger a release of some insulin stored in the polymer.

## Conclusion:

Many past scaffold creation techniques are unable to produce porous biomimetic scaffolds that meet all of the extremely precise life-sustaining conditions that cells require. Conventional techniques, such as gas-forming, particulate-leaching, and freeze drying do not offer much ability to precisely control pore size, pore geometry, pore interconnectivity, inter-pore openings, and spatial distribution of pores (Zhu &

Chen, 2013). Using the electrospinning technique, we can produce nanofibers with high surface areas and porosity that are ideal for cell function and survivability in order to make better biomimetic scaffolds. We can control factors that contribute to the drawbacks of conventional methods. I've touched upon only but one other future implication. However, there is so much more that electrospun nanofibers are capable of in the field of medicine. That is why I urge you Mr. Scott, as Research Division Chief, to invest in a team of researchers that can further explore the uses of nanofibers, or further improve it. The future of tissue regeneration lies within electrospun nanofibers.

Please contact me via email for any questions or concerns.

# References


Li, W.-J., & Tuan, R. S. (2009). Fabrication and Application of Nanofibrous Scaffolds in Tissue Engineering. *Current Protocols in Cell Biology / Editorial Board, Juan S. Bonifacino ... [et Al.]*, *CHAPTER*, Unit-25.2. https://doi.org/10.1002/0471143030.cb2502s42

Nigam, R., & Mahanta, B. (2014). An Overview of Various Biomimetic Scaffolds: Challenges and Applications in Tissue Engineering. *Journal of Tissue Science & Engineering*, *5*(2), 1, 1–5. https://doi.org/10.4172/2157-7552.1000137

[Schematic of a 'biomimetic nano scaffold'.]. (2004, May). Retrieved October 14, 2017, from http://www.sciencedirect.com/science/article/pii/S1369702104002330#FIG10

Subia, B., Kundu, J., & Kundu, S. C. (2010). Biomaterial Scaffold Fabrication Techniques for Potential Tissue Engineering Applications. https://doi.org/10.5772/8581

Zhu, N., & Chen, X. (2013). Biofabrication of Tissue Scaffolds. https://doi.org/10.5772/54125

Zhu, N., & Chen, X. (2013, March 27). [Schematic of electrospinning apparatus.]. Retrieved October 9, 2017, from https://www.intechopen.com/books/advances-in-biomaterials-science-and-biomedical-applications/biofabrication-of-tissue-scaffolds

Zhu, N., & Chen, X. (2013, March 27). [Scaffold architecture affects cell binding and spreading.]. Retrieved October 9, 2017, from https://www.intechopen.com/books/advances-in-biomaterials-science-and-biomedical-applications/biofabrication-of-tissue-scaffolds