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Cell Electrospinning: Revolutionising Cell Scaffolding for Healthcare

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Electrospinning is a century-old technology, which has recently found its vast applicability to many areas of research and development and its utility in industry. In the context of the life and health sciences, electrospinning for many years has been explored as a unique approach to scaffolding, on which cells are manually or through automated means seeded with cells. Unfortunately, this approach has seen little being achieved, as the voids generated between fibers within a scaffold negate cell infiltration throughout the entire scaffold. This limitation is a bottleneck for electrospinning in its true applicability to the healthcare and medical sciences.

In 2004, electrospinning for its utility in the biological and medical sciences was reimagined and investigated for directly mixing a biopolymer with cells and exposing this cell suspension to electrospinning. Those investigations demonstrated the cells with the biopolymer being electrospun, did not undergo any damage from a molecules level upwards, despite using applied voltages in the several thousands of volts. It was later uncovered; the accompanied applied current was generally in the nanoamperes. Hence looking sideways into another such electric field-driven approach, in the medical and clinical sciences, namely electroporation, which operates with voltages of a few hundred volts but with a current in the several tens of milliamperes, is reported to damage and kill cells. The current in the case of electroporation is required for making the cell's membrane permeable, allowing the genetic constructs into the cells. Unfortunately, in the process, a large majority of cells have been found to be incapable of repairing their leaky membranes and thus die. This is a tradeoff, that most geneticists have learned to live with, thus generating low-viable populations of transfected cells.

In 2006, the ability to directly electrospin cells was coined, and is now well-known as "cell electrospinning". To date, cell electrospinning has been explored to handle over 600 different cell types ranging from prokaryotic to eukaryotic, mammalian, and other cell types including stem cells and whole fertilized embryos. The uniqueness of this technology lays not only in its ability to generate living scaffolds as thick sheets and vessels (**Figure 1**), but its ability to process large volumes of cells either as singular or multiple cell types with the addition of biomolecules and/or other advanced materials, to the ease of scaling up.

It's worth thinking about and appreciating, when the first cell electrospinning studies were carried out, not many biopolymers were available in the market. This obstacle in 2023, is a thing of the past, with many biopolymers (some of which are already approved by FDA), now available, and a whole raft of new ones constantly entering the market and accessible for its utility with cell electrospinning.

Since 2006 cell electrospinning, has been investigated by many independent research groups around the world. Therefore, in this special section of *Advanced Biology*, some of these contributions are highlighted, further demonstrating the technologies reach into the biomedical sciences. We start with Hoare et al.,[1] demonstrating the ability to explore cell electrospinning as a reactive strategy, allowing the creation of nanofibrous hydrogel scaffolds with controllable local cell gradients. Thus, offering the ability to form co-cultures leading to the reconstruction of complex model tissues. He et al.[2] applied the technology as a cell printing approach, coupled with a specially formulated electro-conductive cell-bearing hydrogel, which was used to bioprint living tissues, with a micrometer scale resolution. The above articles demonstrate the technological capability to reconstruct a living tissue, mimicking a native tissue, on the microscale, which could be explored in many areas of research and development. In fact, architectures such as these have recently paved the way, for the FDA to state, they no longer require data generated from animal models, as read-outs, and data generated from tissues in a dish have shown great promise.[3] Maver et al.[4] reviewed the field of functional tissue engineering and demonstrates the use of cell electrospinning with particular emphasis on the materials explored in electrospinning of cells. They further go on to discuss the applications of cell electrospinning. Pranke et al.[5] performed a comprehensive overview of the materials and methodologies explored for cell electrospinning, while also elucidating their biomedical applications in tissue engineering and in general to the vast field of regenerative medicine. Following on, Wang et al.,[6] provided a concise but interesting review on bottom-up biofabrication methodologies, and materials explored for fabricating cell fibers, while focusing on electrospinning. Their review goes on to elucidate how these cell electrospun fibers mimic those native

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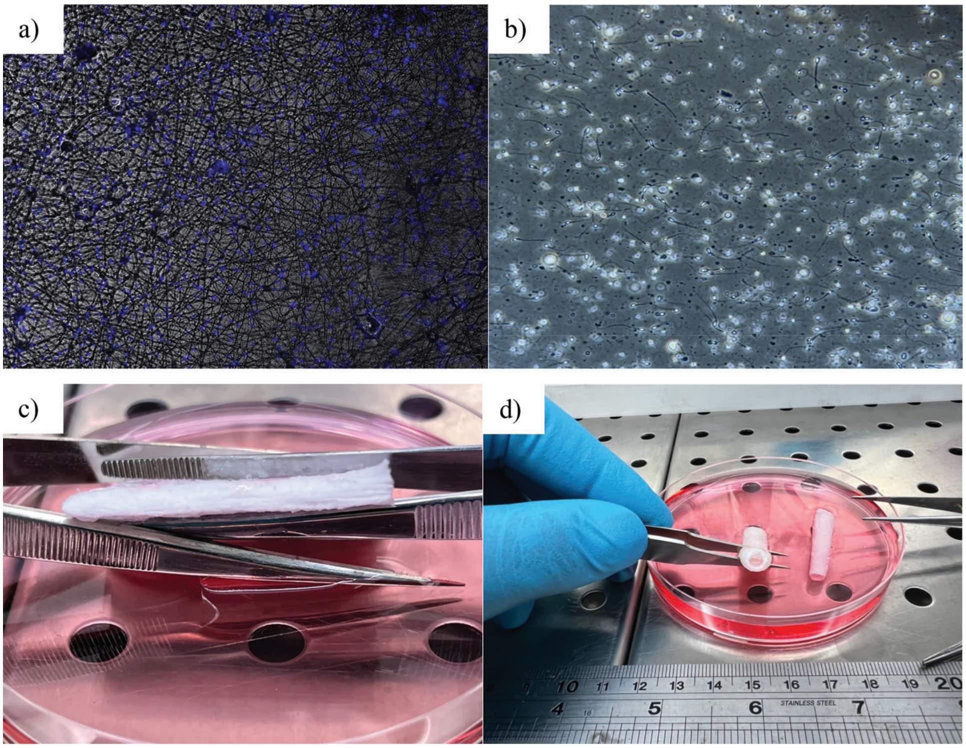

Figure 1. Characteristic digital a) fluorescent (human sperm labeled with Hoechst 33342) overlay image showing the immobilized human sperm within fibers, b) frozen sperm recovery from thawed scaffolds, post-scaffold dissolution (remnants of dissolved scaffold appear as debris). Panels (c) and (d) depict representative cell bearing, a thick scaffold sheet, and vessels generated by way of cell electrospinning.

fibrous tissues and have a plethora of utility in the biomedical and clinical sciences. Last but certainly not least, a critical but balanced review by Nosoudi et al.,[7] discusses articles in this field, while highlighting each article's, specific contribution. With each summarised article the authors review their thoughts on how those particular studies contribute to the wider implications of these cell deposition approaches while focussing on the end goal, namely the reconstruction of a 3D functional tissue.

Interestingly, the author's articles and opinions in the special section demonstrate the research carried out to date on cell electrospinning, while demonstrating the far-reaching implications this platform biotechnology will have to wider areas of research, ranging from 3D cell preservation, culture, and expansion, reconstructing tissues from repair, replacement to rejuvenation (cell therapy), to tissues (3D biological models) in a dish that would be useful for testing and developing personalized drugs to screening vaccines to name a few. Looking outside the healthcare envelope, this platform will have implications for the fast-growing in vitro meat and meat substitute industries, to those ranging from agriculture to aquaculture areas.

In coda, and in brief, the future is both promising and exciting for cell electrospinning, we look forward to seeing the advancements as this technology matures.

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Conflict of Interest

The author declare no conflict of interest.

Keywords

3D functional tissues and organs, biological models, cell electrospinning, personalised medicines, tissue engineering, regenerative biology/medicines

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