MEDICO & ENGINEERING FUTURE

Bridging Medical Science and Engineering for a Healthier Tomorrow

Volume: 2
ISSUE: 1

SUMMER 2025

DOI:10.5281/zenodo.16018839

ISSN: Pending

Editor-in-Chief

Dr. A. Mirani

MEDICO & ENGINEERING FUTURE

Orginal Article

Receive: 06/12/2024
Acceptance: 10/04/2025
Publish: 15/07/2025

Investigation and application of electrospun nanofibers in tissue repair and engineering

Seyyed Hossein Sajjadifar [a*] , Hamideh Barghamadi [b*]

[a] epartment of Medical Engineering, South Tehran Branch, Islamic Azad University, 15847/43311, Tehran, Iran.

Abstract

The ability of electrospun nanofibers to mimic the structure and composition of specific extracellular matrix (ECM) components has been widely utilized in constructing scaffolds for tissue regeneration. As a biophysical signal from the ECM, bioelectrical communication mediated by endogenous electric fields and currents also plays a crucial role in the repair and regeneration of damaged tissues. To achieve this objective, it is crucial to develop electroactive electrospun nanofibers for tissue engineering. Here, we briefly summarize the commonly developed electroactive electrospun nanofibers and their advances in tissue engineering, particularly for cardiac repair, nerve injury treatment, wound healing, and skeletal muscle and bone regeneration. We also discuss their potential applications as biosensors and drug delivery platforms. We then specifically focus on future directions in the design and functionalization of electroactive electrospun nanofibers for tissue engineering. Finally, we suggest some promising strategies to make the framework smarter, more portable, easier to monitor, and safer.

Keywords: ***Electrospun, nanofibers, specific extracellular matrix, bioelectrical, tissue engineering***

VOLUME (1), ISSUE(2) (SUMMER)
DOI:**10.5281/ZENODO.16018758**

* Corresponding e-mail: H a. Barghamadi@iau.ac.ir

1-Introcdution

The aim of tissue engineering is to facilitate the process of repairing and reconstructing damaged tissues by developing biological substitutes based on biomaterials [1-2]. Scaffolds are a key component of tissue engineering because they provide a supportive environment to regulate and control cell proliferation and matrix synthesis, thereby promoting the formation of new tissues [3]. The microenvironment provided by the scaffold must be rich in biochemical and physical signals to achieve long-term signaling exchange between cellular activities and tissues/organs, essential for the reconstruction of defective tissues [4]. Electrospun nanofibers have been widely used to construct scaffolds for tissue regeneration due to their ability to mimic the structure and components of the extracellular matrix (ECM) [5-7]. The morphology and components of individual nanofibers and nanofiber-based scaffolds can be tailored to manipulate cellular behaviors, such as cell adhesion, migration, proliferation, differentiation, and apoptosis [4-10]. In combination with biochemical and external biophysical signals, various types of two-dimensional and three-dimensional electrospun nanofiber scaffolds have been developed to promote the repair of defective tissues [11-16]. In addition to the well-known biochemical signals provided by bioactive factors, bioelectrical communication mediated by endogenous electric fields (EFs) and currents also plays an important role as biophysical signals [17-20]. In the human body, many functions are controlled by electrical signals, as various types of tissues exhibit conductive and/or sensitive properties, such as piezoelectricity and ferroelectricity. As shown in Figure 1, these tissue types include the nervous system, heart, bone, muscle, and skin, which are involved in the activities of neurotransmission [11-28], cardiac activity [15-33], bone regeneration [17-37], muscle contraction [38-40], and wound healing [39-43]. The nervous system, heart and other muscles are the electrically active tissues/organs of the human body. The strongest electrical activity among them is the nervous system, where signals from neurons are transmitted to the desired parts through synapses. Cardiomyocytes (CMs) are the pacemaker cells of the heart and are responsible for sending rhythmic impulses. These rhythmic electrical impulses travel throughout the heart and finally reach the ventricular muscle cells, where mechanical activity occurs. h. Until the heart beats. Bones and skin also use EF and even piezoelectricity to regenerate new tissues [18]. Endogenous bioelectrical signals are one of the most important cues for determining tissue function in electrosensitive tissues and therefore play a key role in tissue regeneration processes [17]. Electrotherapy and related devices based on electrical stimulation have been established in the clinic [44-45], such as electrical nerve stimulators, cardiac pacemakers, bone growth stimulators [46-47] and electrical muscle stimulators [48]. These devices have shown good results in treating neurodegenerative diseases, recovering from nerve injuries and promoting healing of musculoskeletal tissues. Electrical stimulation has also been proposed as a less invasive treatment option. For example, epidurally implanted bipolar electrodes can achieve similar effects as deep brain stimulation in animal models of Parkinson's disease and restore motor function [49]. Similarly, subcutaneous nerve stimulation not only shows satisfactory analgesic effects but also potential modulation of spasticity [50]. However, most of these devices require a power source, which requires replacing batteries or connecting cables, thus increasing the risk of infection after implantation [51-53]. At the same time, poor interaction between the electrode and tissue interface and lack of correspondence with the mechanical properties of tissues make the application of electrical stimulation more difficult. To improve the versatility and ease of use of electrical signals for tissue regeneration, efforts have been made to design and fabricate electroactive electrospun nanofiber scaffolds (EENFS) that interact with electrically active tissues [54-56]. These smart scaffolds can transmit electrical signals or convert stimuli (e.g., mechanical stimuli, light, heat) into electricity, allowing efficient and precise delivery of electrical stimuli to the desired cells and tissues. EEFS can also function as biosensors for disease diagnosis and monitoring the process of tissue regeneration [57-60]. The release of

bioactive factors can also be triggered by well-designed EENFS through stimulation with external electrical stimuli. In addition to electroactive properties, the scaffold should also have good biocompatibility, biodegradability, and mechanical properties, and should be able to mimic the target ECM to modulate cell behavior [18]. EENFS have made satisfactory progress in various tissues, such as cardiac, neural, bone, skin, and muscle, by manipulating cell alignment, proliferation, and even differentiation [17-20]. We share our perspective on EENFS and its recent applications based on our understanding of the electrophysiological properties of human tissues. In the current perspective, we first discuss piezoelectric and conductive nanofibers and their advances in the tissue engineering field, especially their use as cardiac patches, nerve guidance conduits, skin wound dressings, controlled bone regeneration membranes, drug delivery platforms, and sensing devices. Although EENFS has made certain progress in the above fields, EENFS will play a more important role in the future intelligent medical system and integrated diagnosis and treatment. Here we look forward to the development of EENFS and electrical signal sources, the development of multifunctional diagnostic and therapeutic devices based on EENFS interfaces, and the consideration of biological safety. It is expected that electrical signals can be generated/collected to promote tissue repair (electrical stimulation, morphology control, controllable drug release), combined with intelligent monitoring of the recovery process of various tissues, while precisely controlling electrical stimulation within a safe range. To be achieved. The device should be designed to be flexible, simple, reasonably degradable, and multifunctional. Ultimately, this perspective aims to provide a future vision for the introduction of scaffold-based devices into clinical practice.

1-1 NANOFIBERS AS FUNCTIONAL SCAFFOLDS FOR TISSUE ENGINEERING

Electrospun nanofibers had been notably explored as scaffolds for tissue engineering due to their capacity to imitate the hierarchical structure of an extracellular matrix (ECM). Our organization has evolved a lot of scaffolds primarily based totally on electrospun nanofibers for the law of mobiliary behaviors and tissue regeneration. Several terrific examples are highlighted as follows.

1-2Mimicking the Alignment of the ECM To Manipulate Cell Morphology

In the human body, some tissues, such as tendons, muscles, nerves, and hearts, are characterized by highly ordered structures. For example, tendons are highly anisotropic tissues in which collagen fibrils are uniaxially aligned and arranged parallel to each other. Electrospun nanofibers, when collected as uniaxially aligned arrays, can be used for tendon regeneration. As the fluorescence microscopy images in Figure 1A, B show, the uniaxially aligned nanofibers provide contact guidance to tendon fibroblasts, aligning the cells and organizing their ECM into a highly ordered structure. Furthermore, to better mimic the anatomical structure of collagen fibrils in tendon tissue, we fabricated uniaxially aligned nanofibers with a curled morphology. The changes in cell morphology induced by nanofiber alignment could also be effectively translated into cytoskeleton remodeling. For example, Schwann cells seeded on random nanofibers exhibited a disorganized actin network (Figure 1C), whereas cells seeded on uniaxially aligned nanofibers exhibited an aligned actin network along the long axis of the underlying nanofiber (Figure 1D). Human pluripotent stem cell-derived cardiomyocytes were also shown to exhibit anisotropic and isotropic orientation when cultured on scaffolds composed of uniaxially aligned and random PCL nanofibers, respectively.

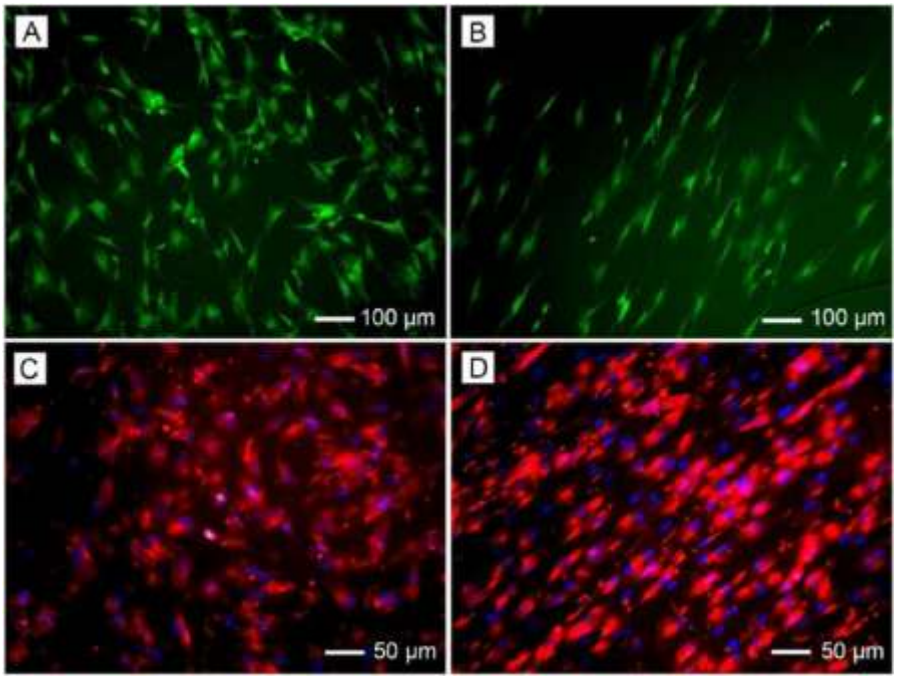

Figure 3: Fluorescence micrographs showing (A, B) tendon fibroblasts seeded on random and uniaxially aligned PCL nanofibers and stained with fluorescein diacetate and (C, D) Schwann cells seeded on random and uniaxially aligned PCL nanofibers stained with rhodamine phalloidin (red) and 4',6-diamidino-2-phenylindole (blue), respectively.

1-3 Directing Cell Migration for Dural Tissue Regeneration

A suitable scaffold for dural tissue regeneration must promote the migration of dural fibroblasts from the periphery toward the center of the wound. To this end, our group developed a new class of scaffolds based on radially aligned nanofibers.

1-4 Guiding and Promoting the Outgrowth of Neurites

Scaffolds based on uniaxially aligned nanofibers have enabled the design of nerve guidance conduits to better recapitulate the anisotropic structure of nerves.45,48 It is well-established that the physical cue offered by the aligned nanofibers can direct the extension of neurites derived from various cell phenotypes, including dorsal root ganglia (DRG) and embryonic bodies (EBs).

2.4. Mimicking the Tendon-to-Bone Insertion Site

Repairing the interface between soft and hard tissues has been one of the major clinical challenges. For the repair of tendon-to-bone insertion, we developed "aligned-to-random" nanofiber scaffolds to mimic the orientational changes of the collagen fibers in enthesis. Cells cultured on different portions of the scaffolds presented different structures of the cytoskeleton. We also fabricated a nonwoven mat of electrospun nanofibers with a continuously graded coating of calcium phosphate.

2- Conclusion

As a simple and widely available technique, electrospinning allows for the rapid production of fibrous nanomaterials from a wide range of materials. Furthermore, many strategies have been demonstrated to develop the composition, structure, porosity, surface area, and orientation of nanofibers. These features allow the properties of nanofibers to be tailored for different applications. Although electrospun nanofibers have shown great potential in applications ranging from heterogeneous catalysis to biomedical research, they still face many challenges. For ceramic nanofibers, their mechanical strength and flexibility need to be

improved so that they can be used as free-standing structures over large areas. In addition to precise control of the microstructure of ceramic nanofibers, the fabrication of surface-functionalized nanofiber sponges provides an effective way to develop flexible and reusable catalytic systems. For polymer nanofibers to be used as scaffolds for tissue regeneration, their design, including composition and structure, should be further optimized for in vivo applications. Future research should aim to fabricate three-dimensional scaffolds with integrated cells and growth factors to improve cell infiltration and viability. By closely mimicking the complex spatial distribution of natural tissues, three-dimensional scaffolds with functionally graded variations in composition, orientation, porosity, and pore size could lead to significant improvements in tissue regeneration. The ultimate goal is to bring electrospun nanofibers from the laboratory to industry and from bench to bedside.

3- Acknowledgments

We thank Medico & Engineering Future and its Editor-in-Chief, Dr. A. Mirani, for their expert guidance and support during the publication process. We also appreciate the constructive feedback from the reviewers, which improved our manuscript.

References

1. Tahmasebifar, A., Kayhan, S. M., Evis, Z., Tezcaner, A., Çinici, H., & Koç, M. (2016). Mechanical, electrochemical and biocompatibility evaluation of AZ91D magnesium alloy as a biomaterial. Journal of Alloys and Compounds, 687, 906-919.
2. B.D. Ratner and B.S. An, "Biomaterials Science: An Introduction to Materials in Medicine," vol. 26, p. 5093, 2005.
3. Wu S., Liu X., Yeung K.W.K., Guo H., Li P., Hu T., Chung C.Y., Chu P.K. Surf. Coat. Technol., 233 (2013), pp. 13-26
4. A. Biesiekierski, "A New Look at Biomedical Ti-based Shape Memory Alloys," no. January 2012, 2012.
5. Chen Y., Xu Z., C. Smith, J. Sankar Acta Biomater., 10 (11) (2014), pp. 4561-4573.
6. S.V. Dorozhkin Acta Biomater., 10 (7) (2014), pp. 2919-2934.
7. N.E.L. Saris, E. Mervaala, H. Karppanen, J.A. Khawaja, A. Lewenstam Clin. Chim. Acta, 294 (1–2) (2000), pp. 1-26.
8. A. Biesiekierski, Wang J., M. Abdel-Hady Gepreel, Wen C. Acta Biomater., 8 (5) (2012), pp. 1661-1669.
9. Li J., Tan L., Wan P., Yu X., Yang K. Mater. Sci. Eng. C, 49 (June) (2015), pp. 422-429.
10. Zheng Y.F., Gu X.N., F. Witte Mater. Sci. Eng. R Rep., 77 (2014), pp. 1-34.
11. Cheng J., Liu B., Wu Y.H., Zheng Y.F. J. Mater. Sci. Technol., 29 (7) (2013), pp. 619-627.
12. J. Lévesque, H. Hermawan, D. Dubé, D. Mantovani Acta Biomater., 4 (2) (2008), pp. 284-295.
13. M. Peuster, C. Hesse, T. Schloo, C. Fink, P. Beerbaum, C. von Schnakenburg Biomaterials, 27 (28) (2006), pp. 4955-4962.
14. J.M. Seitz, A. Lucas, M. Kirschner JOM, 68 (4) (2016), pp. 1177-1182.
15. H. Ibrahim, S.N. Esfahani, B. Poorganji, D. Dean, M. Elahinia Mater. Sci. Eng. C, 70 (2016), pp. 870-888.
16. Li N., Zheng Y. J. Mater. Sci. Technol., 29 (6) (2013), pp. 489-502.
17. W. Schmidt, P. Behrens, C. Brandt-Wunderlich, S. Siewert, N. Grabow, K.P. Schmitz Cardiovasc. Revascularization Med., 17 (6) (2016), pp. 375-383.
18. H. Windhagen, K. Radtke, A. Weizbauer, J. Diekmann, Y. Noll, U. Kreimeyer, R. Schavan, C. Stukenborg-Colsman, H. Waizy. Biomed. Eng. Online, 12 (1) (2013), p. 62.
19. Xie G., H. Takada, H. Kanetaka Mater. Sci. Eng. A, 671 (2016), pp. 48-53.
20. A.K. Chaubey, S. Scudino, M. Samadi Khoshkhoo, K.G. Prashanth, N.K. Mukhopadhyay, B.K. Mishra, J. Eckert J. Alloys Compd., 610 (2014), pp. 456-461.

21. Xiong G., Nie Y., Ji D., Li J., Li C., Li W., Zhu Y., Luo H., Wan Y. Curr. Appl. Phys., 16 (8) (2016), pp. 830-836.
22. Feng J., Sun H., Li X., Zhang J., Fang W., Fang W. Adv. Powder Technol., 27 (2) (2015), pp. 550-556.
23. M. Rashad, Pan F., Guo W., Lin H., M. Asif, M. Irfan Mater. Charact., 106 (2015), pp. 382-389.
24. Yang D., Hu Z., Chen W., Lu J., Chen J., Wang H., Wang L., Jiang J., Ma A. J. Manuf. Process., 22 (2016), pp. 290-296.
25. Kang M.H., Do Jung H., Kim S.W., Lee S.M., Kim H.E., Y. Estrin, Y.H. Koh Mater. Lett., 108 (2013), pp. 122-124.
26. H. Asgharzadeh, Yoon E.Y., Chae H.J., Kim T.S., Lee J.W., Kim H.S. J. Alloys Compd., 586 (SUPPL. 1) (2014), pp. S95-S100.
27. Zhou Y.L., Li Y., Luo D.M., Ding Y., P. Hodgson Mater. Sci. Eng. C, 49 (2015), pp. 93-100.
28. Li X., Liu X., Wu S., Yeung K.W.K., Zheng Y., Chu P.K. Acta Biomater., 45 (2016), pp. 2-30.
29. Bi Y., Zheng Y., Li Y. Mater. Lett., 161 (2015), pp. 583-586.
30. Z.S. Seyedraoufi, S. Mirdamadi J. Mech. Behav. Biomed. Mater., 21 (2013), pp. 1-8.
31. M. Yazdimamaghani, M. Razavi, D. Vashaee, K. Moharamzadeh, A.R. Boccaccini, L. Tayebi Mater. Sci. Eng. C (71) (2016), pp. 1253-1266.
32. R. del Campo, B. Savoini, A. Muñoz, M.A. Monge, G. Garcés J. Mech. Behav. Biomed. Mater., 39 (2014), pp. 238-246.
33. S. Cabeza, G. Garcés, P. Pérez, P. Adeva J. Mech. Behav. Biomed. Mater., 46 (2015), pp. 115-126.
34. S.Z. Khalajabadi, M.R. Abdul Kadir, S. Izman, M. Marvibaigi J. Alloys Compd., 655 (2016), pp. 266-280.
35. A. Tahmasebifar, S.M. Kayhan, Z. Evis, A. Tezcaner, H. Çinici, M. Koç J. Alloys Compd., 687 (2016), pp. 906-919.
36. S.M. Kayhan, A. Tahmasebifar, M. Koc, Y. Usta, A. Tezcaner, Z. Evis Mater. Des., 93 (2016), pp. 397-408.
37. Xia X.C., Chen X.W., Zhang Z., Chen X., Zhao W.M., Liao B., Hur B. J. Magnes. Alloy., 1 (4) (2013), pp. 330-335.
38. M. Yazdimamaghani, M. Razavi, D. Vashaee, L. Tayebi Mater. Sci. Eng. C, 49 (2015), pp. 436-444.
39. M. Wolff, J.G. Schaper, M.R. Suckert, M. Dahms, T. Ebel, R. Willumeit-Römer, T. Klassen JOM, 68 (4) (2016), pp. 1191-1197.
40. B. Ratna Sunil, C. Ganapathy, T.S. Sampath Kumar, U. Chakkingal J. Mech. Behav. Biomed. Mater., 40 (2014), pp. 178-189.
41. Zhang J., Kang Z., Wang F. Mater. Sci. Eng. C, 68 (2016), pp. 194-197.
42. R. Viswanathan, N. Rameshbabu, S. Kennedy, D. Sreekanth, K. Venkateswarlu, M. Sandhya Rani, V. Muthupandi Mater. Sci. Forum, 765 (Jul. 2013), pp. 827-831.
43. Kang M.-H., Jang T.-S., Kim S.W., Park H.-S., Song J., Kim H.-E., Jung K.-H., Jung H.-D.
Mater. Sci. Eng. C, 62 (2016), pp. 634-642.
44. Cheng W., Ma S., Bai Y., Cui Z., Wang H. J. Alloys Compd., 731 (2017), pp. 945-954.
45. Y. Lu, A.R. Bradshaw, Y.L. Chiu, and I.P. Jones, “Effects of secondary Phase and Grain Size on the Corrosion of Biodegradable Mg–Zn–Ca alloys,” vol. 48, pp. 480–486, 2015.
46. J.J. Ramsden, D.M. Allen, D.J. Stephenson, J.R. Alcock, G.N. Peggs, G. Fuller, G. Goch
CIRP Ann. – Manuf. Technol., 56 (2) (2007), pp. 687-711.
47. Zhang X., Yuan G., Niu J., Fu P., Ding W. J. Mech. Behav. Biomed. Mater., 67 (2012), pp. 74-86.
48. Zhang X., Yuan G., Mao L., Niu J., Fu P., Ding W. J. Mech. Behav. Biomed. Mater., 7 (2012), pp. 77-86
49. Zhao C., Pan F., Zhang L., Pan H., Song K., Tang A. Mater. Sci. Eng. C, 70 (2017), pp. 1081-1088.
50. A. Gil-Santos, I. Marco, N. Moelans, N. Hort, O. Van der Biest Mater. Sci. Eng. C, 71 (2017), pp. 25-34.
51. Ai Y., Luo C., Liu J., Huang Y. Jinshu Xuebao/Acta Metall. Sin., 41 (1) (2005), pp. 49-54.

52. A. Gil-Santos, G. Szakacs, N. Moelans, N. Hort, O. Van der Biest J. Alloys Compd., 694 (2017), pp. 767-776.
53. Chen Y., Gao J., Song Y., Wang Y. Mater. Sci. Eng. A, 671 (2016), pp. 127-134.
54. Zhang Y., Huang X., Ma Z., Li Y., Guo F., Yang J., Ma Y., Hao Y. Mater. Sci. Eng. A, 686 (2017), pp. 93-101.
55. S. Bauer, P. Schmuki, K. von der Mark, Park J. Prog. Mater. Sci., 58 (3) (2013), pp. 261-326.
56. Y. Shibata, Y. Tanimoto J. Prosthodont. Res., 59 (1) (2015), pp. 20-33.
57. D. Deligianni Biomaterials, 22 (11) (2001), pp. 1241-1251.
58. A.F. van Tol, J.E. Tibballs, N. Roar Gjerdet, P. Ellison J. Mech. Behav. Biomed. Mater., 28 (2013), pp. 254-262.
59. T. Scheerlinck, P.-P. Casteleyn J. Bone Joint Surg. Br., 88–B (11) (2006), pp. 1409-1418.
60. H.J. Rønold, S.P. Lyngstadaas, J.E. Ellingsen Biomaterials, 24 (25) (2003), pp. 4559-4564.