Chapter

Piezoelectric/Triboelectric Nanogenerators for Biomedical Applications

Panpan Li, Jeongjae Ryu and Seungbum Hong

Abstract

Bodily movements can be used to harvest electrical energy via nanogenerators and thereby enable self-powered healthcare devices. In this chapter, first we summarize the requirements of nanogenerators for the applications in biomedical fields. Then, the current applications of nanogenerators in the biomedical field are introduced, including self-powered sensors for monitoring body activities; pacemakers; cochlear implants; stimulators for cells, tissues, and the brain; and degradable electronics. Remaining challenges to be solved in this field and future development directions are then discussed, such as increasing output performance, further miniaturization, encapsulation, and improving stability. Finally, future outlooks for nanogenerators in healthcare electronics are reviewed.

Keywords: nanogenerator, biomedical application, self-powered healthcare devices, energy harvester

1. Introduction

The ongoing development of nanogenerators in recent years has enabled the design of self-powered systems that can operate without external power supplies. Nanogenerators have the ability to harvest mechanical energy in different forms from a variety of sources, including human body motion and activities. This makes them particularly suitable for applications in the biomedical field. Nanogenerators can convert the tiny mechanical energy in body motion, muscle contraction/relaxation, bone strain, and respiration into electrical energy [1–4]. The generated electrical energy can be used as a sustainable energy source for implantable biomedical devices, which would both reduce the volume of the powering unit and eliminate the need for battery replacement [5–7].

A great deal of work has been invested in the study of biomedical applications of nanogenerators, including self-powered sensors, pacemakers, and stimulators, and the results have shown that nanogenerators can be very promising in the biomedical field [8–15].

In this chapter, we first introduce the required characteristics of nanogenerator materials that can be used in the biomedical field. Generally, there are two main types of biomedical nanogenerators, piezoelectric nanogenerators (PENG) and triboelectric nanogenerators (TENG), which have different operating mechanisms. PENG are based on piezoelectric materials, such as polyvinylidene fluoride (PVDF) [8], poly(vinylidenefluoride-co-trifluoroethylene) [P(VDF-TrFE)] [9], $BaTiO_3$ (BTO) [10], ZnO [11], $Pb(Zr_xTi_{1-x})O_3$ (PZT) [12], and $(1 - x)Pb(Mg_{1/3}Nb_{2/3})O_3$-$xPbTiO_3$ (PMN-PT) [13]. While TENG are based on triboelectric charges which are generated when dissimilar materials are in contact [14, 15], their operating mechanism is a combination of tribo-electrification and electrostatic induction between the two contacted materials [14, 15]. A broad range of materials exhibiting these effects can be selected, which make TENG ideal for biomedical applications. Besides the PENG and TENG nanogenerators, there are also other types of biomedical nanogenerators using biofuel cells (BFCs) or photovoltaics. BFCs transform chemical energy into electrical energy from molecules present in human body [16], which are very promising since there is >100 W of chemical energy in our body [17]. Flexible photovoltaic materials can meet the conformability requirements of e-skin, thus showing the possibility of solar-powered e-skin [18, 19].

Next, we will provide some examples of important biomedical nanogenerator applications, including self-powered human activity sensors; pacemakers; cochlear implants; simulators for cells, tissues, and brain; and biodegradable electronics. After that, we will also discuss challenges and future outlooks for biomedical nanogenerators, including their miniaturization, stability, encapsulation, and output performance. We hope this book chapter will provide insight and inspiration to people who are interested in biomedical devices and nanogenerator development.

2. Nanogenerator materials for biomedical applications

Self-powered biomedical devices require nanogenerators that can directly harvest energy from their surroundings, in this case, from activities in the human body. This also requires the nanogenerators to have specific designs that respond to different mechanical stimuli with high sensitivity, since many bodily activities are subtle.

The materials used in biomedical nanogenerators should also be biocompatible. The primary conventional piezoelectric material is lead zirconate titanate (PZT). PZT has a high piezoelectric coefficient; however, the toxicity of Pb makes it unsuitable for application in the human body. Scientists have been searching for other materials in efforts to develop alternatives to lead-based nanogenerators. One of the emerging lead-free piezoelectric materials, $0.5Ba(Zr_{0.2}Ti_{0.8})O_3$-$0.5(Ba_{0.7}Ca_{0.3})TiO_3$ (BZT-BCT), has a piezoelectric coefficient comparable to PZT and also good biocompatibility, which makes it a promising candidate for applications in the biomedical field [10]. ZnO has also attracted great interest because of its favorable characteristics, which include piezoelectricity, biocompatibility, transparency, and large-area fabrication [11].

In many cases, nanogenerators based on nanowires, nanobelts, and nanorods can be placed into specific structures to fit inside the body. Nanostructures, nanocomposites, or piezoelectric polymers specifically designed with superior flexibility and elasticity are particularly preferred for biomedical applications. For example, poly(vinylidenefluoride-co-trifluoroethylene) [P(VDF-TrFE)]-based nanogenerators have demonstrated good piezoelectric coefficient, flexibility, and biocompatibility [20–24].

Finally, nanogenerators used in the biomedical field should have high sensitivity and efficiency because many bodily activities, such as respiration, heartbeat, muscle stretching, or blood circulation, are very gentle and render a small amplitude. Nanogenerators need high energy conversion efficiency and sufficient output power to be used in devices with comparable size [25–27].

Piezoelectric materials	Characteristics	Biomedical applications
PZT	High piezoelectric coefficient, toxicity	Energy harvesting from body motion, including the heart, lung, and diaphragm [4, 28] Cochlear implant [29] Eye fatigue detection [30]
PMN-PT	High piezoelectric coefficient, toxicity	Cardiac pacemaker [13, 31]
(Na, K)NbO_3	Piezoelectric, biocompatible	Cardio-mechanical electric sensor [32]
$BaTiO_3$-based	High piezoelectric coefficient, biocompatible	Implantable medical devices [10, 32]
ZnO	Piezoelectric, low toxicity, biodegradable, transparency	Biosensors [33]
PVDF	Piezoelectric, flexibility, elasticity, biocompatibility	In vivo biomechanical energy harvesting [8, 27] Cochlear implant [34]
PVDF-TrFE	Piezoelectric, flexibility, biocompatibility	Energy harvesting [9, 20–24] Pressure sensor [26] Bone tissue engineering [35]
Poly-L-lactic acid	Piezoelectric (shear piezoelectricity in particular), shape-adaptable, biodegradable, biocompatible	Energy harvesting [36] Biodegradable implants [37]

Table 1.
Piezoelectric materials can be used for nanogenerators in biomedical field.

There are many nanogenerator materials that have been reported thus far. Some representative piezoelectric materials that can be used for nanogenerators in biomedical applications are shown in **Table 1**.

In the future, it will be critical to further develop nanogenerator materials with more precise conformity to medical principles and the requirements of clinical applications.

3. Examples of nanogenerator applications in the biomedical field

Energy harvesting systems based on irregular body motions or mechanical deformation are promising candidates for self-powered biomedical devices [1–4]. Using nanogenerators inside the human body is of great medical interest because they can scavenge inexhaustible biomechanical energy from muscle contraction/relaxation, blood circulation, respiration, and cardiac motion and convert it into electrical energy [5–10]. Several examples of the applications of nanogenerators in the biomedical field are illustrated in the following text.

3.1 Nanogenerators can be used as self-powered pressure sensors

Human healthcare monitoring is becoming increasingly significant because of the need for early disease diagnosis and daily health assessments. Conventional monitoring systems are usually powered by batteries, which have limited lifespan and can cause many problems [38]. Self-powered nanogenerators can solve the power supply issue and can be easily integrated into the healthcare system [38]. Some examples are listed below.

A cardiac sensor, used for heart-rate monitoring, is a critical component in personal healthcare management. Self-powered nanogenerators have been employed in self-powered cardiac sensors, as shown in **Figure 1** [5]. Besides the merit of self-powered, they are non-invasive, cost-effective and user-friendly. These implantable cardiac sensors can detect a number of arrhythmic symptoms and provide real-time feedback spontaneously [5]. Compared to current wearable heartbeat monitoring systems, the implantable cardiac sensors can provide both higher accuracy and greater reliability [39]. Self-powered wireless cardiac sensors have a great potential in the future heart healthcare monitoring market.

Physiological parameters such as respiration rate, blood pressure, and pulse rate are major concerns in clinical practice [40]. Failure to detect these signals timely can result in life-threatening conditions [40]. Scientists recently fabricated self-powered TENG-based pressure sensors with a high sensitivity of 150 mV/Pa [41]. When the flexible pressure sensor was attached to the human body, respiration and pulse were accurately and spontaneously monitored [41]. The sensitivity, flexibility, and robustness of nanogenerators allow them to be used in wearable and wrist-based pulse wave detectors [40–43].

3.2 Nanogenerators can be used in pacemakers

When a heart's natural pacemaker is not working properly, resulting in a heart-rate that may be too fast, too slow, or irregular, a doctor may implant a device called pacemaker to restore the heart's nature rhythm. Implantable battery-powered pacemakers, which use electrical impulses to stimulate the heart muscles and regulate heartbeat, have been in clinical use for more than 50 years [13, 15]. Pacemakers have made significant contributions to the treatment of heart diseases such as sick sinus syndrome, heart blockage, and abnormal heart rate [13, 15]. However, every 7–10 years, surgery is needed to replace the pacemaker battery [44, 45]. Self-powered devices can prolong the pacemaker's operation and eliminate battery replacement surgery.

Both PENG and TENG have been investigated for cardiac pacemakers [46, 47]. Generally, PENG are more robust and durable, but their outputs are relatively low.

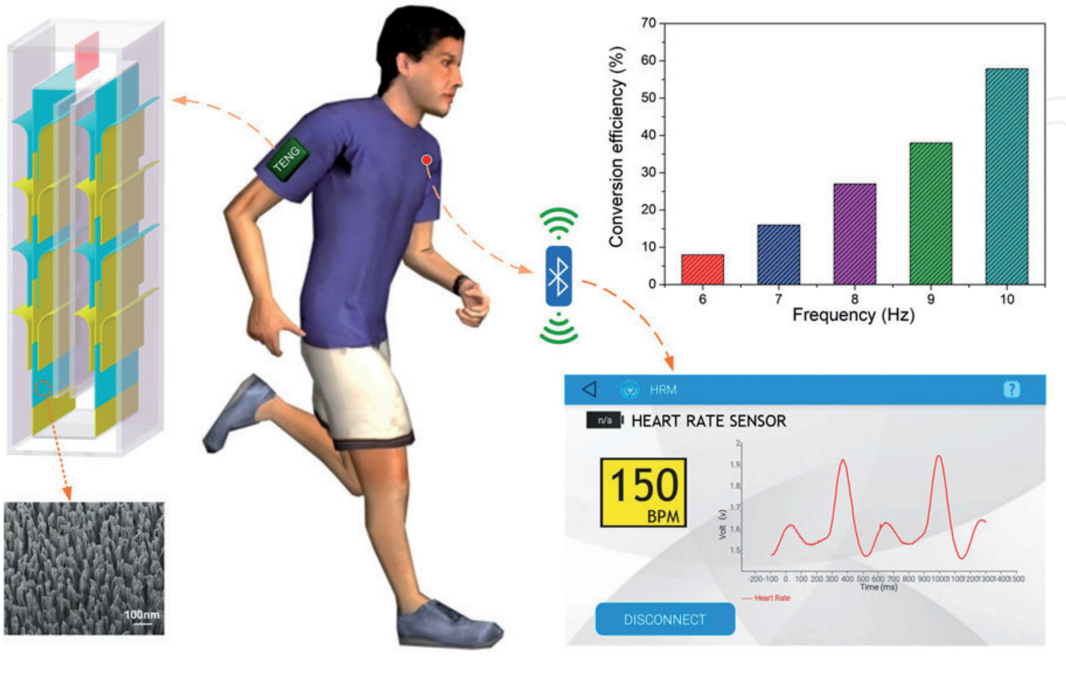

Figure 1.
Illustration of heart-rate monitoring by a wireless self-powered cardiac sensor. Reprinted with permission from [5]. Copyright (2017) American Chemical Society.

TENG materials show a higher output, but they need to be well encapsulated to prevent leakage. A schematic diagram of cardiac pacemaker without battery that can pace the porcine heart is shown in **Figure 2** [31].

3.3 Nanogenerators can be used in cochlear implants

Cochlear implants are neural prosthetic devices that can restore a sense of hearing to people with hearing disability. Cochlear implants work by picking up sound using a microphone located externally above the pinna, and with an external processor, convert the microphone output into electrical pulses that are transmitted internally using a transmitter or receiver to finally stimulate the auditory neurons using an array of electrodes implanted in the cochlea [34]. The conceptual schematics of the cochlear and the basilar membrane are shown in **Figure 3**. However, current cochlear implants have limitations, because they require external components, which are inconvenient for patients. A totally implantable cochlear implant powered by a nanogenerator would address this issue [48]. Scientists have reported the fabrication and characterization of a prototype polyvinylidene

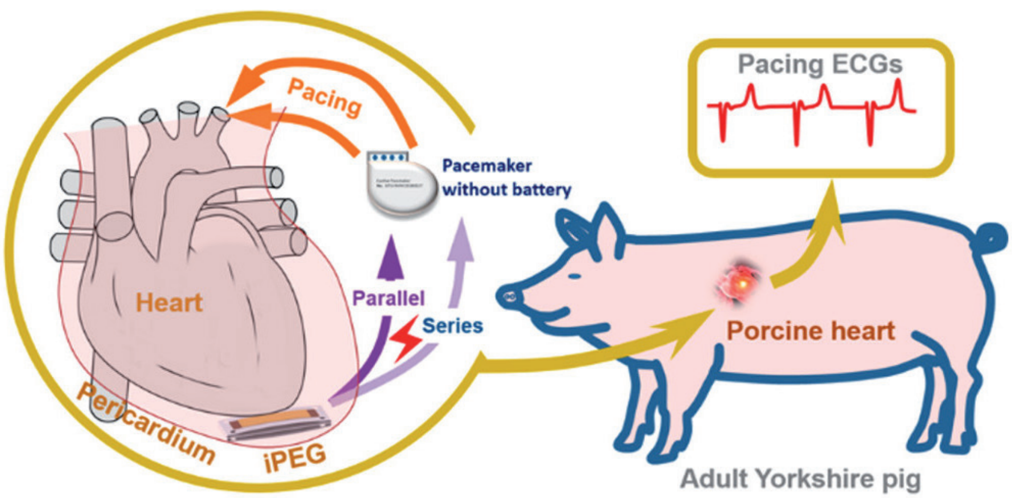

Figure 2.
Schematic diagram of self-powered cardiac pacemaker that pace the porcine heart in vivo. Reprinted with permission from [31]. Copyright (2019) American Chemical Society.

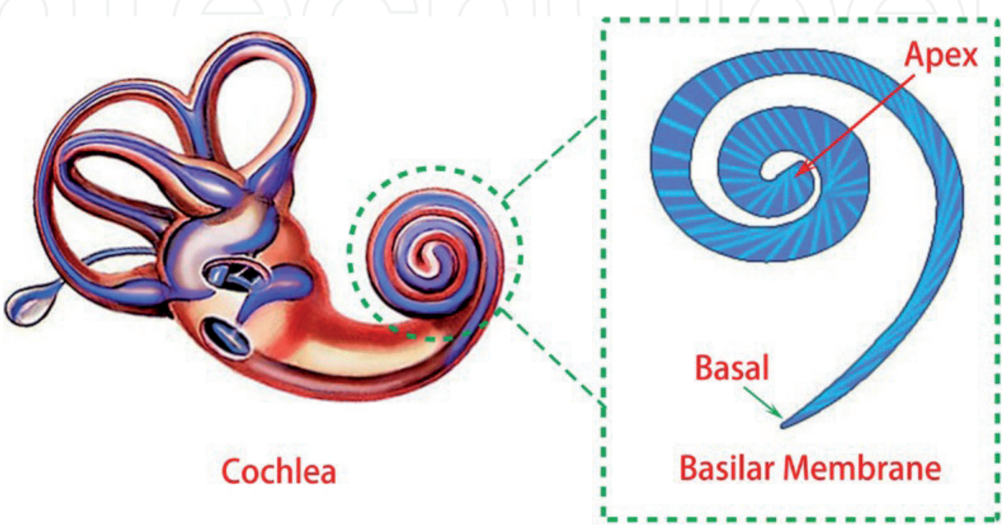

Figure 3.
Conceptual schematics of the cochlear and the basilar membrane. Reprinted with permission from [48]. Copyright © Yudong Liu, et al. 2018.

Cells and tissues	Required electrical fields	Reference
Migration of nerve cells	7 mV/mm	[49]
Migration of embryonic cells	150 mV/mm	[50]
Migration of neural crest cell	150 mV/mm	[51]
Migration of human keratinocytes	10–100 mV/mm	[52]
Wound healing	40–180 mV/ mm	[53, 54]
Cultivation of human bone marrow mesenchymal stem cells	10–600 mV/mm	[55]
Proliferation of osteoblastic cells	20 mV/cm	[56]
Proliferation, migration, and differentiation of muscle precursor cells	Several to tens of nA/cm^2	[57]
Cardiac adipose tissue-derived progenitor cells	5 mV/mm	[58]
Muscle stimulation	mA-level current	[59]

Table 2.
Required electrical fields for cellular and tissue behaviors.

fluoride polymer-based implantable microphone for detecting sound inside gerbil and human cochleae [34]. These results demonstrate the feasibility of the prototype devices as implantable microphones for the development of completely implantable cochlear implants. For patients, this will improve sound reception by utilizing the outer ear and will improve the use of cochlear implants. It should be noted that the development of nanogenerators in cochlear implants field is at the very early stage. They will need further design and innovation to achieve miniaturization, low-power electronics, and an implantable microphone, before they meet the requirements of clinical applications.

3.4 Nanogenerators as stimulators for cells and tissues

Electrical signals play an instructive role in many cellular behaviors, including cell proliferation, differentiation and migration, and tissue wound healing and regeneration. Several examples and their required electrical fields are shown in **Table 2**.

Nanogenerators can provide electrical stimulation for cells and tissues [60–63]. A recent report shows that a self-powered well-aligned P(VDF-TrFE) piezoelectric nanofiber nanogenerator can be used as a piezoelectric stimulator for bone tissue engineering, as shown in **Figure 4** [35]. The well-aligned piezoelectric P(VDF-TrFE) nanogenerators encouraged the MC3T3 cells to proliferate in vitro under a sustainable piezoelectric stimulus. This provides insights into the application of P(VDF-TrFE) piezoelectric nanofiber nanogenerators as a self-powered electrical stimulation system to assist tissue repair and regeneration.

Electrical muscle stimulation is clinically employed for rehabilitative and therapeutic purposes [60]. **Figure 5** illustrates recent research using a stacked-layer triboelectric nanogenerator (TENG) through a flexible multiple-channel intramuscular electrode, which permitted electrical muscle stimulation [60]. Such a self-powered system could be potentially used for rehabilitative and therapeutic purposes to treat muscle function loss.

Nanogenerators have also been developed for skin wound healing. Scientists reported an efficient electrical bandage for accelerated skin wound healing [61]. From in vitro studies, they showed that accelerated skin wound healing could

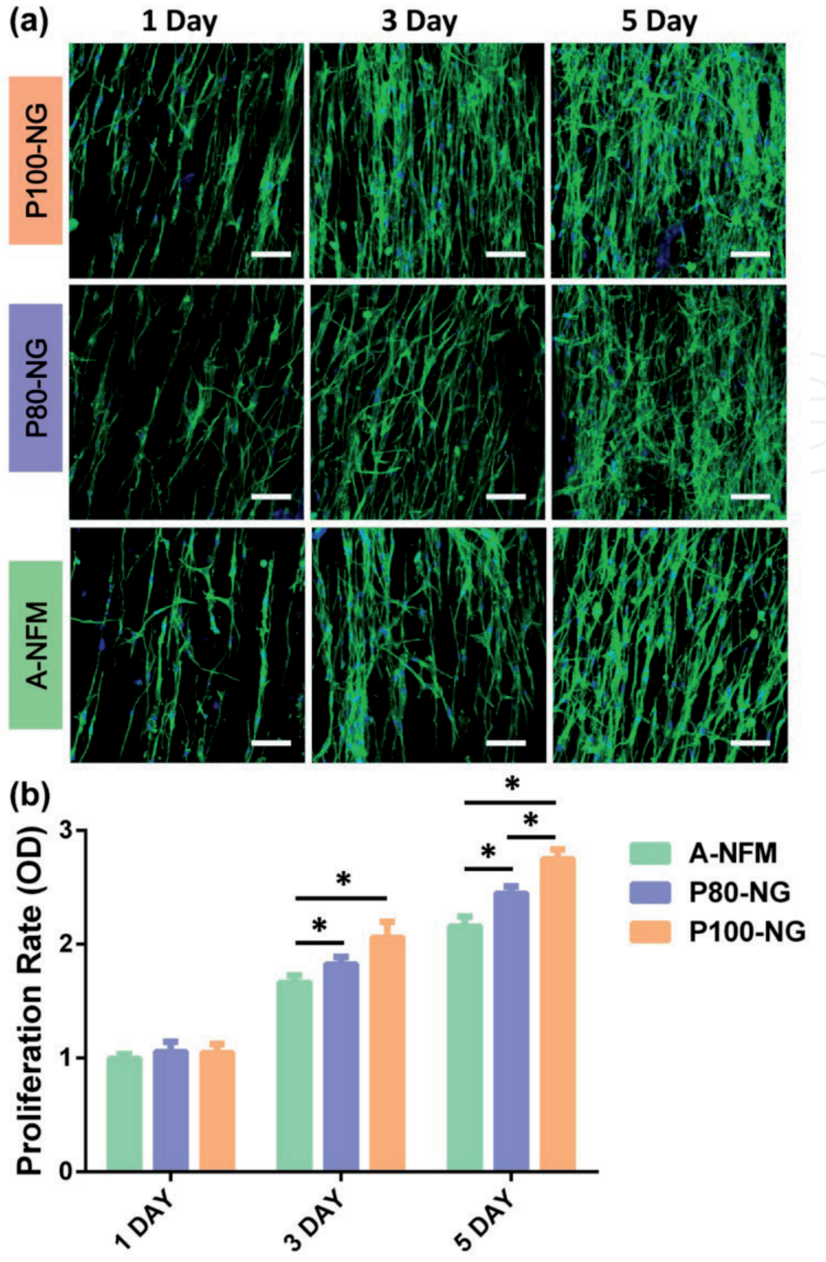

Figure 4.
Proliferation of MC3T3 cells on P80-NG, P100-NG, and control A-NFM. (a) Fluorescence microscopy images of MC3T3 cells on A-NFM, P80-NG, and P100-NG. (b) MC3T3 cells proliferation after 1, 3, and 5 days of culture. The scale bar is 100 μm. The P(VDF-TrFE) nanofiber membranes (NFMs) poled with the electric field of 80 MV/m and 100 MV/m were labeled as P80-NG and P100-NG, respectively. The samples treated by annealing were coded as A-NFM. Reprinted with permission from [35]. Copyright, © 1996–2019 MDPI.

be attributed to electric field-facilitated fibroblast migration, proliferation, and transdifferentiation [61]. This research could lead to a facile therapeutic strategy for nonhealing skin wound treatment.

3.5 Nanogenerators can be used in deep brain stimulators and neural stimulators

Deep brain stimulation is an effective treatment for a variety of neurological disorders, including Parkinson's disease, essential tremor, and epilepsy [64–66]. At present, it involves administering a train of pulses with constant frequency via electrodes implanted in the brain [67]. However, the implantable brain stimulator requires surgery to replace the battery every 3 to 5 years [68]. Self-powered deep brain stimulation is a future technology which does not need external power supply.

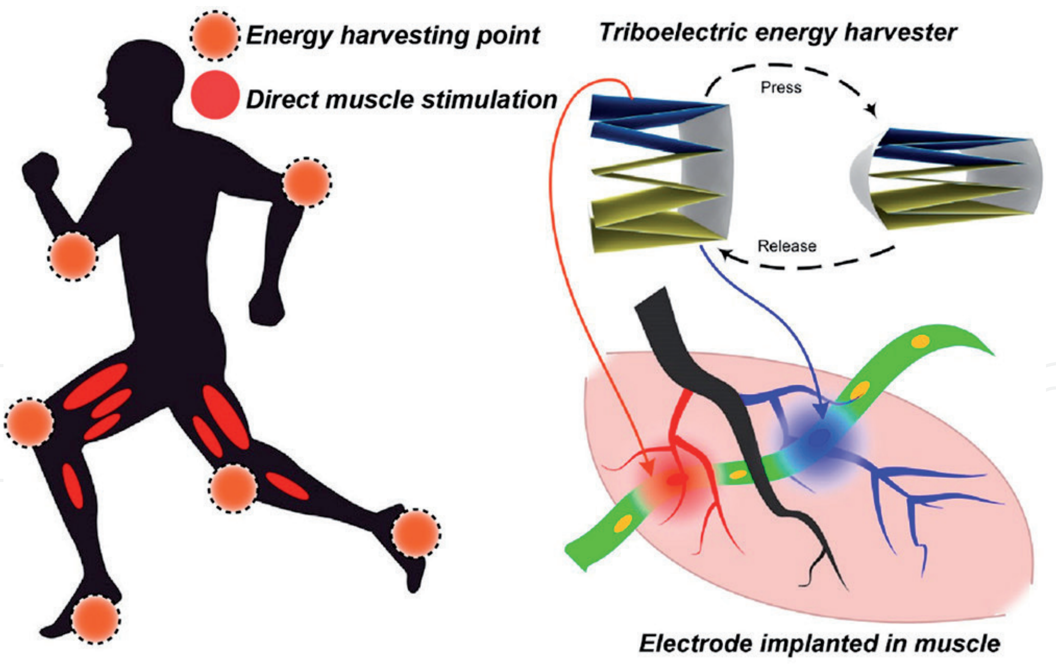

Figure 5.
Schematic illustration of direct electrical muscle stimulation powered by a triboelectric nanogenerator. Reprinted with permission from [60]. Copyright (2019) American Chemical Society.

Scientists have developed a flexible $Pb(In_{1/2}Nb_{1/2})O_3–Pb(Mg_{1/3}Nb_{2/3})O_3–PbTiO_3$ (PIMNT) energy harvester that can be used in a self-powered deep brain stimulator [68]. More researches in this field open a new avenue for future deep brain stimulation using self-powered deep brain stimulator.

Modulation of neural signals using implantable bioelectronics is an emerging field in fields such as neuroprosthesis and bioelectronic medicine [69–72]. Triboelectric nanogenerators (TENGs) show a promising performance as a power source for neuro-stimulators. Recently, scientists have developed a novel water/air-hybrid TENG that can be used for force-controlled direct stimulation [69]. In another research, scientists present an implanted vagus nerve stimulation system that is battery-free and can spontaneously respond to stomach movement [70]. These provide a concept in therapeutic technology using artificial nerve signal generated from coordinated body activities.

3.6 Nanogenerators as biodegradable electronics

Biodegradable electronics are quite a new scientific term but also an emerging area of research. The general goal is to create human-friendly electronics and enable the integration of electronic circuits with living tissue [73]. Biodegradable electronics, also called transient electronics, are built with degradable organic and inorganic materials, so that they can be integrated with living tissue and used for diagnostic and/or therapeutic purposes during certain physiological processes [74–77]. Once the therapeutic or diagnostic process is completed, the transient devices can be left behind in the body and will degrade and be absorbed gradually without any residue.

Reports show that a biodegradable triboelectric nanogenerator can degrade and be absorbed by the human body after completing its work cycle, so no operation is needed to remove them, leaving no long-term effects [76, 77]. This demonstrates the potential of nanogenerators as a power source for transient medical devices.

Scientists have recently introduced a fully biodegradable nanogenerator based on gelatin film and electro-spun polylactic acid nanofiber membrane, which is fully biodegradable in water [75]. The TENG are disposable and do not harm or pollute the environment.

In general, biodegradable triboelectric nanogenerators offer a promising green micro-power source for biomedical implants, by harvesting energy from body movements, and then dissolve with no adverse effect. The biodegradable medical device field is an emerging area, which shows a great potential for in vivo sensors and therapeutic devices.

4. Future development

The development of nanotechnologies can greatly advance healthcare systems. Nanogenerators can provide complementary or alternative power to traditional batteries in healthcare electronics. Autonomous biomedical devices might be realized with the development of nanogenerators, which will revolutionize the biomedical device and healthcare systems. We expect that autonomous self-powered biomedical systems with active sensing properties are the future development direction of medical devices.

Currently, the key challenges that need to be solved in the field of self-powered implantable medical devices are miniaturization, encapsulation, and stability. There is a strong demand for implantable medical devices with reduced size and weight, to minimize impact on daily activities and increase patient comfort. Also, TENG performance is greatly affected if moisture or liquid leaks into the device when applied in vivo. To avoid corrosion by body fluids, it will be necessary to develop durable and flexible encapsulation to protect the stability and working efficiency of TENG [5, 6].

Future nanogenerator developments in this field are expected to address the following three aspects. Firstly, output performance and energy conversion efficiency should be increased to meet clinical requirements. Secondly, to be used in the human body, nanogenerators need to be highly flexible, sensitive, and durable. For example, many in vivo movements are gentle, and their amplitude is very small, so the nanogenerator must be sensitive enough to exploit small scale motion [7, 14]. Thirdly, since the in vivo environment can be very complex and challenging, careful packaging is needed using biocompatible and soft materials.

In general, nanogenerators have many advantages, including high efficiency, low cost, light weight, and easy fabrication. Nanogenerators have an excellent potential for application in a variety of uses, to provide a sustainable power source for self-powered biomedical electronics and healthcare monitoring systems. With further cutting-edge research and development in this field, a revolution in biomedical devices and healthcare system will be realized in the future.

5. Conclusion

In this chapter, we introduced typical nanogenerator materials that have been developed for biomedical applications. We summarized several examples of how nanogenerators can be used in the biomedical field. We included recent research on nanogenerators in self-powered pressure sensors; pacemakers; cochlear implants; stimulators for cells, tissues, and the brain; and biodegradable electronics. We also pointed out the challenges facing current research and future research directions for nanogenerators in medical devices. We hope this work provides insights and inspiration for future biomedical device and nanogenerator research.

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Conflict of interest

The authors declare no conflict of interest.

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