A Review of Soft Electronic Devices Based on Flexible and Stretchable Materials for Cardiac Monitoring

Minkyung Sung
American International School of Johannesburg, Knopjeslaagte, Midrand, 1682, South Africa.
Email: msung@aisj-jhb.com

Keywords
Soft Bioelectronics, Cardiovascular Healthcare, Wearable and Implantable Device, Cardiac Monitoring, Flexible and Stretchable Materials.

Article History
Received on 29th December 2022
Accepted on 26th February 2023
Published on 27th February 2023

Cite this article
Sung, M. (2023). A Review of Soft Electronic Devices Based on Flexible and Stretchable Materials for Cardiac Monitoring. *International Journal of Students' Research in Technology & Management*, *11*(1), 15-22. https://doi.org/10.18510/ijsrtm.2023.1113

Abstract

Purpose of the study: The number one killer, cardiovascular disease, has sharply increased in recent years. For early diagnosis and prevention, continuous cardiac monitoring is crucial, and flexible, stretchable electronic devices have become essential instruments to record cardiac activity. Bioelectronics has greatly improved from recent developments in soft, ultrathin bioelectronics that have been made possible by breakthroughs in soft materials and novel device designs.

Methodology: This study focuses on flexible and stretchable materials as well as design strategies for current developments in soft electronics-based wearable and implantable devices for cardiac monitoring.

Main Findings: The mechanical deformability in soft bioelectronics has enabled researchers to obtain high-quality bio-signals and reduce long-term negative effects *in vivo*. They provide close, long-term integration with cardiac tissues due to their thin and soft characteristics, allowing for continuous, high-quality, and wide coverage in cardiac monitoring.

Applications of this study: This review is anticipated to provide timely and significant information for prospective audiences in the fields of material science and biomedical engineering, who seek a concise summary of key technologies, as well as biomedical fields who may be interested in the clinical implications of soft bioelectronics for cardiac healthcare.

Novelty/Originality of this study: The materials, fabrication techniques, and device designs for flexible and stretchable electronics are reviewed with a particular emphasis on flexible and soft materials.

INTRODUCTION

The heart is a crucial organ that distributes blood which carries out essential metabolic processes vital to our life. Cardiovascular diseases, which impact the heart and blood vessels are a concerning problem with high numbers of deaths.(Ershad et al., 2019a) Constant monitoring is needed to manage cardiovascular diseases, as it is substantially beneficial when diagnosed early. Abnormal heart activities or heart failure can be detected through multiple methods such as monitoring electrocardiogram patterns, blood pressure, or blood oxygen saturation.(Hong et al., 2019)

Electrocardiogram (ECG) monitoring is especially important as it indicates the heart's condition through a simple setup. (Rigatelli et al., 2012) Looking at ECG waves can lead to the detection of cardiac abnormalities such as myocardial ischemia. Apart from detecting cardiac abnormalities, ECG waves can also provide information related to the patient such as prognostic estimation, mental stress, and the risk of sudden cardiac death.(Savoji et al., 2019)

Currently, the Holter monitor, a portable ECG device is used to assess the heart in long-term.(Hong et al., 2019) However, these monitors have limitations such as the complicated setup and gels that can reduce the signal qualities over a period of time which can also cause skin irritation. (Yoder et al., 2018) Additionally, the equipment used for monitoring must be retrieved, resulting in frequent visits by the patient to the clinic, and that time lag will occur, leading to a delayed response to cardiac emergencies. Cardiac monitoring devices must not only obtain clinic-grade ECG but should also be comfortable for the patients.(Gutbrod et al., 2014)

Continuous research into flexible and stretchable electronics has enabled the development of wearable and implantable devices based on soft and ultrathin materials, hence improving the interface between the device electrode and biological tissue.(Koo et al., 2020) An enhanced device interface will decrease interfacial resistance and increase mechanical stability in the case of monitoring electrophysiological signals. (Liu et al., 2016) Some devices comprised of exceptionally soft materials can completely cover the heart and blood vessels in three-dimensional space without interfering with the heart function. Unlike current cardiac implants, soft and ultrathin electronic device enable high-resolution spatiotemporal mapping of the heart.(Viventi et al., 2010) Therefore, it is important to create monitoring devices that can monitor the cardiovascular system efficiently and accurately, using innovative materials and designs.

This review discusses advances in soft bioelectronics for cardiac monitoring. First, the significance of matching the mechanical behavior of device materials to biological tissue is emphasized by providing actual damages associated with conventional, stiff, and bulky medical equipment. In addition, the thickness of the device affects device performance, such as signal-to-noise ratio, which is dependent on conformal contact with heart tissue. The next section discusses some of the flexible and stretchable materials and design strategies for making devices stretchable. Lastly, recent advancements in soft bioelectronic devices to monitor cardiac activity in the form of wearable and implantable devices are discussed. The implementation of soft bioelectronic technology in cardiac devices has substantially enhanced the capability and quality of cardiac monitoring, as well as made numerous potentials for future advancement.

Conventional rigid and bulky medical devices

In the 1980s, the electrode heart "socks" were developed as an implantable cardiac device for monitoring and identifying the conduction and mechanisms of the heart.(Gutbrod et al., 2014) These devices could wrap the heart entirely and record cardiac activity. The initial sock devices were constructed using electrodes connected to synthetic cloth and loosely stitched to a ventricle. These devices allowed for the enhancement of recording pattern resolution. A nylon sock has also been used to perform cardiac resynchronization treatment (CRT) for mechanical resynchronization, as part of studies aiming to examine atrial activity patterns.(Kim et al., 2012) Fabricating these socks device is complicated, considering the spatial resolution of electrode array and scalable production.

In addition, several cardiac implants, such as pacemakers, consisted of massive pumps attached to the left ventricle to aorta, which were located below the diaphragm. (Spittell & Hayes, 1992) They were connected to an external power source by a percutaneous cable, which is comparable to the modern setup. Patients were unsatisfied with the implants' size, noise, risk of infection, and poor durability. (Rogers et al., 2010) Furthermore, it is challenging for the device to maintain enhanced interface with the heart when the heart is beating. Due to their rigid and bulky form factors, conventional cardiac devices may cause various negative effects. Most significantly, these devices can induce discomfort to patients/users.

Side effects derived from mechanical mismatch in device materials

The incompatibility of device components, such as the mechanical properties of the materials, with heart tissue is a key challenge in current bioelectronics. Long-term biocompatibility and user-friendliness of conventional bioelectronics have been significant obstacles to the widespread implementation of such bio-integrated electronic systems due to their considerable size and rigidity. Young's modulus, which reflects a material's susceptibility to deformation under strain, differs between the rigid bioelectronics and soft heart tissues. (Sunwoo et al., 2019) In addition to influencing the bending stiffness, thickness of the electrode, the overall size, and design of the electrode will also influence on achieving high-quality device performance in soft bioelectronics. Major organs, particularly the brain (1-4 kPa) and heart (10-15 kPa), have a significant modulus (mechanical stiffness) difference from conventional rigid electronic materials and devices (100 GPa; Figure 1). (Shim et al., 2021) These inconsistencies hinder the biomedical device's monolithic conformal integration with the human body and cause a range of side effects, especially when the bulky, stiff devices must be continuously implanted in or in interface with the target tissue and organ. Due to this mismatch, stiff bioelectronics may harm cardiac tissue and the device, resulting in the functional failure of both components.

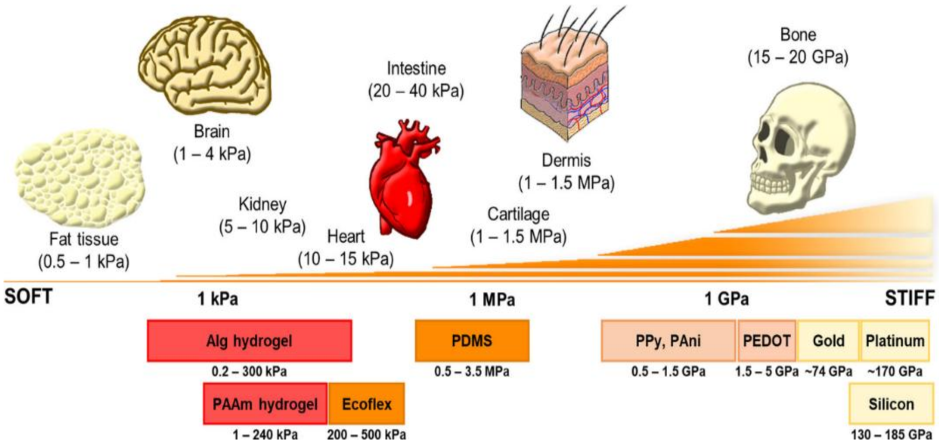

Figure 1: Elastic moduli of biological tissue and electronic materials.

Reproduced with permission from ref.(Cho et al., 2022) Copyright 2021 American Chemical Society.

Implantation of medical devices can result in both immediate and long-term damages on tissue and implant. (Cho et al., 2022) This can lead to increased electrical impedance, poor electrical signals, and the formation of fibrous scar tissue. The size and geometry of the implant as well as the implant's ongoing exposure to mechanical stress can influence the severity of the damage. In cardiac implantation, symptoms such as high blood pressure and hemorrhage might develop, and nonfunctional cells can obstruct the heart-electrode contact. The use of strong wire electrodes can result in blood vessel abrasion and damage, leading to thrombosis and stenosis. (Spittell & Hayes, 1992) (Figure 2A) Hard devices implanted on soft cardiac tissue with dynamic movement, can induce fibrosis and potential ruptures (Roubelakis et al., 2015) (Figure 2B), while rigid subcutaneous implants can also trigger inflammatory responses during device retrieval at the end of diagnosis.(Buch et al., 2011) (Figure 2C) Due to mechanical stress and *in vivo* circumstances, bioelectronics materials can degrade, releasing metal ions and causing electrical current leakage or loss of conductivity.(Pang et al.,

2014) (Figure 2D).

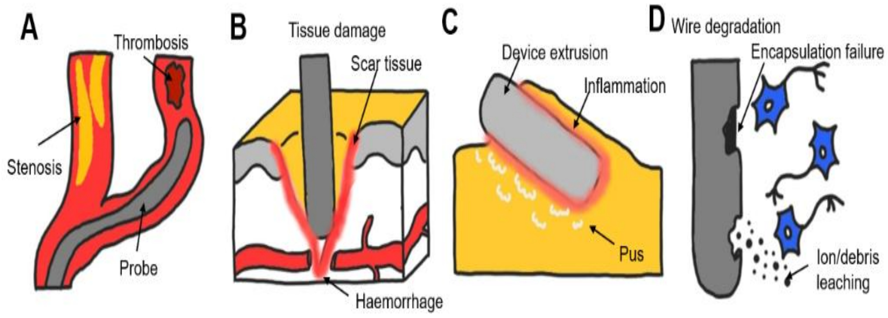

Figure 2: Schematic illustrations of side effects induced by conventional rigid bioelectronics including (A) stenosis and thrombosis, (B) tissue damage by wire implantation, (C) pus and pain due to subcutaneous implantation, and (D) wire degradation by body fluids.

Electrode-tissue bio-interface

The interface between the electrode and skin is a critical component in the performance of bioelectronic devices, such as wearable and implantable electrodes. (Wu et al., 2021) The stability, efficiency, and biocompatibility of these devices depend on the quality of the interface between the electrode and the skin. This interface is where electrical signals are transmitted between the device and the body, making it crucial for the proper functioning of the device.

For wearable ECG measurement devices, the main challenge is to maintain conformal contact between the electronics and the skin in the long-term. Current electrodes cannot perfectly conform to the wrinkled skin. Repetitive stretching of elastic skin can also lead to the electrodes to fall off of them. Non-conformal contact of the device onto tissue surface leads to increase in contact impedance and decrease the signal-to-noise ratio.(Koo et al., 2021) Having rigid electrodes attached to the skin in the long-term can also lead to skin irritation, which is why soft and ultrathin bioelectronics are much needed. (Figure 3)

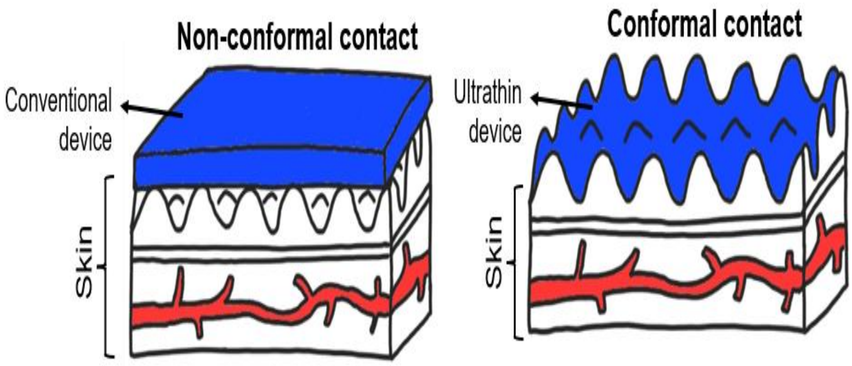

Figure 3: Schematic illustration of interface between electrode and skin.

Flexible and stretchable materials

Materials are a great factor that impacts stretchable electrode performance. The two factors to consider for selection of device materials are compatibility in material properties to the target application in fabricating the flexible and stretchable electronic device, and mechanical properties that can withstand various mechanical deformations such as bending and stretching. (Figure 4) Structural engineering of rigid materials to yield mechanical softness has been an important strategy in the fabrication of soft cardiac devices. Nanoscale materials play an important role in developing stretchable electrodes. The nanoscale materials have been reduced from their bulk materials, leading to fabrication of ultrathin device having an extremely low rigidity.

Flexible and stretchable device fabrication is mostly based on semiconductor fabrication techniques including thin-film deposition, photolithography, and transfer-printing technology which transfers the ultrathin device from the donor substrate onto the soft target substrate, *i.e.*, elastomers. The concept of epidermal electronics gave rise to skin-conforming dry and soft surface electrodes.(Kim et al., 2011) Au was the material of choice for epidermal electrodes because to its biocompatibility, high conductivity, and chemical stability. A nanometer-thick Au on polyimide (PI) was patterned into mesh design on a rigid wafer and transfer printed onto a 30 µm thick soft Ecoflex substrate. As the thickness, Young's modulus, and stretchability of these electrodes closely resemble the skin, they are referred to as epidermal electrodes. The surface ECG has been successfully measured with epidermal electrodes.

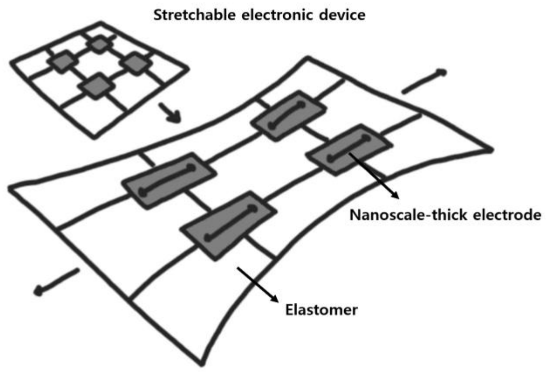

Figure 4: Schematic illustration of stretchable electronic device

Another method to develop stretchable electrodes is to utilize intrinsically soft conducting materials. Combining different materials which results in nanocomposites can lead to enhanced performance of electrodes. Electrically conductive nanoparticles, for example, could be used to construct surface electrodes. Electrohydrodynamic printing was used to fabricate Ag nanowire (AgNW)-based electrodes, which allows the printing of conductive inks on a various distinct substrate such as paper and polymers (PET and polydimethylsiloxane (PDMS)).(Cui et al., 2018) When AgNWs were mixed into an elastomeric matrix, the nanocomposite recovers its mechanical characteristics and electrical conductivity within seconds even under mechanical deformation.

Because of its biocompatibility, mechanical robustness, and chemical inertness, an atomically thin graphite layer known as graphene is also a viable electrode material. Transparent graphene e-tattoos have been successfully created utilizing the "cut-and-paste" method since graphene is also mechanically cuttable.(Ferrari et al., 2018) Organic conductors such as poly(3,4-ethylene dioxythiophene):poly(styrene sulfonate) (PEDOT:PSS) can be inkjet-printed onto nanomembranes as skin-conformable electrodes with long-term stability.(Chiolerio et al., 2014)

Design strategies to fabricate stretchable electronics

A suitable design of the electrode can relieve the stress applied to the electrode and minimize the strain at a specific point, allowing the electrode to be stretchable without impacting its performance. A widely used design is the serpentine structure to form stretchable electrodes and systems as well. The serpentine-shaped thin film metal ribbons on a stretchable PDMS substrate alleviate the mechanical stress from external forces, such as stretching condition. The stretchability of such structures is influenced by geometrical properties of bioelectronic system.

A wrinkled nanoscale film is developed by placing ultrathin films on pre-strained elastomers and releasing the pre-applied strain.(Zhang et al., 2013) The wrinkled electrode can withstand high amounts of mechanical stress under deformation. Kirigami, a paper cutting strategy can be adopted as a new strategy for designing and producing stretchable electrodes. (Ma et al., 2018) This approach is aided with the precise etching technology using photolithography especially for devices that are consisted of deformable nanopatterns. Stretchable graphene sheets have been designed using this kirigami approach with an in-plane spring shape pattern utilizing etching and photolithography. This graphene sheet could be stretched substantially without any mechanical failure.

3-D architecture designs have also been used to design new types of stretchable electrodes. (Ma et al., 2018) The out-of-plane pop-up strategy of 2-D nanomembranes with 2-D nanopatterns can be used to produce multiple 3-D architectural designs. 3-D helical coil structures were applied to electrical intercepts, which showed stretching mechanics like those of a spring when external forces were applied. (Kim et al., 2012)

Soft bioelectronics for monitoring cardiac activity

High-resolution ECG recording is needed to observe activation and repolarization patterns in both clinical and research contexts. In 1999, there was an algorithm developed to estimate the epicardial activation from electrograms on the surface of the body.(Ershad et al., 2019) However, this technique is expensive, requires body surface electrodes at very accurate positions, and does not provide a real-time mapping solution. A potential substitute is using endovascular mapping catheters. However, it must be acknowledged that it is difficult to achieve a high-quality tissue-electrode contact due to the incompatibility in mechanical properties of sequential probes. The limitations for both methods challenge the reliability of recordings obtained from these devices. Neither technology provides the opportunity the monitor the patient throughout the entire day, even in their daily lives.

Soft bioelectronics offers this possibility to achieve high-resolution ECG mapping. For instance, thin-film flexible electronics based on ultrathin silicon on a polymer film have been used to spatially map electrophysiological activities. Even rigid materials like Au can be implemented in epicardial patches as stretchable device by changing the device design into open-mesh structure, providing overall mechanical stretchability and deformability under dynamic beating condition of heart. An alternative route is to use intrinsically soft materials. Soft conductive composites of silver nanowires (AgNWs)/styrene–butadiene–styrene (SBS) have been developed into a cardiac wrap for preserving diastolic relaxation, mechanically supporting the heart and improving cardiac contractility through electrical stimulation. (Park et al., 2016) (Figure 5) While recording and interpreting the patterns of ECGs is major strategy to diagnose cardiac healthcare, monitoring blood oxygen saturation as well as blood pressure is also common practice. Low level in blood oxygen saturation and elevated blood pressure are important risk factors in acute hear failure.(Chung et al., 2020)

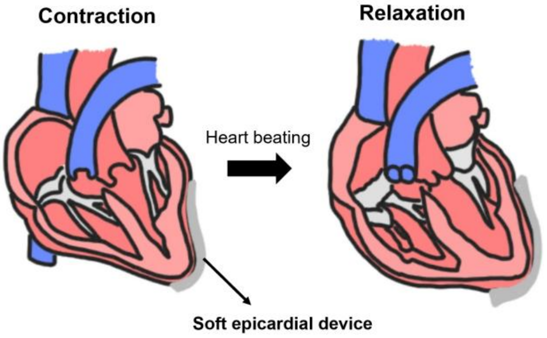

Figure 5: Schematic illustration of soft epicardial device conformally attached onto cardia tissue under deformation of heart beating.

Wearable electronic device

Because of its flexibility and elasticity, the epidermal ECG sensor may be intimately attached to biological tissue *via* van der Waals force. Ultrathin Au electrodes are flexible and even stretchable. As a flexible substrate, Au electrodes have been inkjet-printed on a 50 mm-thick Kapton sheet. And this Kapton sheet can be directly soldered with integrated circuit (IC) to fabricate Bluetooth System-on-Chip ICs. Also, 3D design was utilized to create a completely skin-conformal and stretchable wireless ECG sensor. Due to homogeneous stress distribution, rigid ICs developed by 3D helical structures on an Ecoflex elastomer exhibited high stretchability.

Yamamoto et al. reported a real-time cardiac monitoring patch with a compact design that separates reusable and disposable components in response to cost and risk of infection issues.(Yamamoto et al., 2016) The device consisted of three Ag electrodes imprinted on a PET film with a thickness of 38 mm. However, the device must be linked to an external power source and data link for data processing because signal processing components, amplifiers, and filters are not integrated together. Also, the PET substrate cannot provide sufficient conformability on skin, hence extra conductive medicinal grease was used to improve electrode contact with skin.

To expand functionality, a single-layer circuit's limited area becomes a key obstacle. To overcome such limitation, 3D stacking of soft circuits has been suggested. The laser-fabricated 3D flexible circuit utilized soft elastomer as the interlayer dielectric layer. Through laser ablation of the elastomer layers, vertical connection accesses can be created. The stretchable patch with 3D stacking may broadcast real-time ECG and motion through Bluetooth when powered by an external battery.

While a continuous ECG has been measured from skin, continuous measurement of the blood oxygen saturation (SpO_2) on the wrist can be achieved by using flexible pulse oximeters.(Elgendi et al., 2019) In the blood, O_2 is dissolved and selectively binds to hemoglobin, resulting in the formation of oxyhemoglobin (binding and carrying oxygen, HbO2) and deoxyhemoglobin (without bound oxygen, Hb). A conventional rigid pulse oximeter is attached to a fingertip *via* a clip. It is composed of a photodetector (PD) and two rapidly alternating light-emitting diodes (LEDs) with different wavelengths, such as infrared (940 nm) and red (660 nm) or green (530 nm). PD and LEDs are positioned vertically as light from LEDs passes through arterial and venous blood, and absorb the light *via* PD. The signal composed of a pulsing alternating-current (AC) signal and a non-pulsating direct-current (DC) is utilized to determine SpO_2. In conjunction with the pulse, SpO_2 is an effective parameter for detecting abnormal cardiovascular activity.

Commercial pulse oximeters that are rigid and bulky to wear are inapplicable for continuous SpO_2 sensing. Consequently, more "skin-like," flexible and stretchable pulse oximeters shows conformal contact to the skin due to their ultrathin dimension along with the utilization of flexible and stretchable materials. Organic LEDs (OLEDs) and organic photodiodes (OPDs) that are flexible have become promising active materials for flexible oximeters. (Lochner et al., 2014) Lochner et al. employed polyfluorene derivatives as the emissive layers of OLEDs, and the active layer of OPDs was printed using a blade-coating approach on a planarized polyethylene naphthalate substrate. (Lochner et al., 2014) Red and green OLEDs with peak wavelengths of 626 and 532 nm, respectively, were developed for long-term recording of SpO_2 with high stability and device performance.

Implantable electronic device

Implantable epicardial sensors are capable of cardiac mapping with high spatiotemporal resolution. Real-time mapping and modulating electrophysiology of *in vivo* cardiomyocytes could have significant impacts on monitoring cardiac activity for early diagnosis of cardiac disorders. Soft mapping devices such as 2D sheet, sleeve, and mesh have been demonstrated for recording a multitude of sites on the heart. For example, an electronic sensor system conforming to the epicardium *via* surface tension, composed of 288 multiplexed silicon nanomembrane channels, was configured to measure cardiac activity. (Xu et al., 2014) (Figure 6)

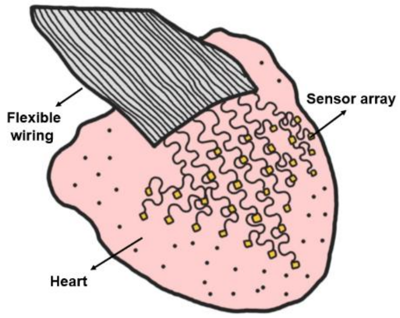

Figure 6: Schematic illustration of soft implantable device conformally attached to heart for ECG mapping.

Flexible arrays of 2D sheet-like mapping devices, however, have limitations such as spatial resolution and stability of conformal contact to cardiac surface. The development of 3D-multifunctional integumentary membranes (3D-MIMs) has been the first time to map cardiac activity in full coverage, both anterior and posterior surface, with high spatiotemporal resolution.(Xu et al., 2015) 3D-MIMS is integrated with high-density electrical, pH, and temperature sensors, which allows to record ECG, pH, and temperature mapping. Also, *in vivo* investigations on rabbit hearts demonstrates the spatiotemporal mapping capability of the 3D-MIMs.

Due to inherent physiological differences between small and big animals,(Viventi et al., 2010) it is difficult to extend the validity of these devices to human cardiac models based on *in vivo* investigations on small animal models. Recently, *in vivo* experiments on large animal, swine heart, was conducted with large-area conductive nanocomposite mesh. The cardiac mesh was composed of Au-coated AgNWs in SBS elastomer, designed into fan shape with 42 electrodes array. This nanocomposite could encapsulate the ventricle surface of a swine heart with high conductivity (41,850 S cm^{-1}) and stretchability (266 %).

pH is a reliable way to provide information on the cardiac tissue metabolically. However, monitoring pH fluctuations, especially on a beating heart, at high spatiotemporal resolution is difficult. Researchers observe pH in a cell culture environment and *ex vivo* tissue experiments utilizing glass electrodes which are stiff, cumbersome, and only allow a single measurement channel. Chung et al., however, successfully achieved high-density pH mapping on epicardial surface of explanted rabbit heart during ischemia-reperfusion.(Chung et al., 2014) The device consisted of an array of Au electrodes encapsulated by polyimide layers, which act as insulator. IrO2 was electrochemically deposited as an active layer at the point of pH sensing electrode. The system was designed into island-bridge configuration to reduce material strain as well as interfacial stress on curvilinear rabbit heart. Information regarding pH is relatively easier to analyze compared to ECG, yet pH data provides valuable parameters in which physician can diagnose cardiac condition.

CONCLUSION

Due to their life-threatening impact, acute and chronic heart disorders have attracted great interest and generated large study fields in cardiac monitoring. Flexible and stretchable devices are suitable for cardiac diagnostics due to their numerous benefits including multifunctional characteristics, conformal contacts to soft tissue, soft properties, and enhanced bio-interface. Advancements in electrode materials, design, and fabrication techniques are needed to achieve these soft bioelectronics, especially for wearable devices that record high-quality bio-signals such as ECG and blood oxygen saturation without causing discomfort to patients. In addition, implantable electronic devices such as epicardial electrode array are required to be mechanically soft to obtain bio-signals with high-precision and high spatiotemporal resolution. Consequently, continued efforts to develop multifunctional and effective monitoring devices by using soft bioelectronics hold great promise for managing cardiac health.

ACKNOWLEDGEMENT

I would like to thank Calvin Cho for his guidance and encouragement during the process of this review.

REFERENCES

1. Buch, E., Boyle, N. G. & Belott, P. H. (2011). Pacemaker and Defibrillator Lead Extraction. *Circulation*, *123*(11), e378–e380. https://doi.org/10.1161/CIRCULATIONAHA.110.987354
2. Chiolerio, A., Rivolo, P., Porro, S., Stassi, S., Ricciardi, S., Mandracci, P., Canavese, G., Bejtka, K. & Pirri, C. F. (2014). Inkjet-printed PEDOT:PSS electrodes on plasma-modified PDMS nanocomposites: quantifying plasma treatment hardness. *RSC Adv.*, *4*(93), 51477–51485. https://doi.org/10.1039/C4RA06878E
3. Cho, K. W., Sunwoo, S.-H., Hong, Y. J., Koo, J. H., Kim, J. H., Baik, S., Hyeon, T. & Kim, D.-H. (2022). Soft Bioelectronics Based on Nanomaterials. *Chemical Reviews*, *122*(5), 5068–5143. https://doi.org/10.1021/acs.chemrev.1c00531
4. Chung, H.-J., Sulkin, M. S., Kim, J.-S., Goudeseune, C., Chao, H.-Y., Song, J. W., Yang, S. Y., Hsu, Y.-Y., Ghaffari, R., Efimov, I. R. & Rogers, J. A. (2014). Stretchable, Multiplexed pH Sensors With Demonstrations

on Rabbit and Human Hearts Undergoing Ischemia. *Advanced Healthcare Materials*, *3*(1), 59–68. https://doi.org/10.1002/adhm.201300124

5. Chung, H. U., Rwei, A. Y., Hourlier-Fargette, A., Xu, S., Lee, K., Dunne, E. C., Xie, Z., Liu, C., Carlini, A., Kim, D. H., Ryu, D., Kulikova, E., Cao, J., Odland, I. C., Fields, K. B., Hopkins, B., Banks, A., Ogle, C., Grande, D., … Rogers, J. A. (2020). Skin-interfaced biosensors for advanced wireless physiological monitoring in neonatal and pediatric intensive-care units. *Nature Medicine*, *26*(3), 418–429. https://doi.org/10.1038/s41591-020-0792-9
6. Cui, Z., Han, Y., Huang, Q., Dong, J. & Zhu, Y. (2018). Electrohydrodynamic printing of silver nanowires for flexible and stretchable electronics. *Nanoscale*, *10*(15), 6806–6811. https://doi.org/10.1039/C7NR09570H
7. Elgendi, M., Fletcher, R., Liang, Y., Howard, N., Lovell, N. H., Abbott, D., Lim, K. & Ward, R. (2019). The use of photoplethysmography for assessing hypertension. *Npj Digital Medicine*, *2*(1), 60. https://doi.org/10.1038/s41746-019-0136-7
8. Ershad, F., Sim, K., Thukral, A., Zhang, Y. S. & Yu, C. (2019a). Invited Article: Emerging soft bioelectronics for cardiac health diagnosis and treatment. *APL Materials*, *7*(3), 031301. https://doi.org/10.1063/1.5060270
9. Ferrari, L. M., Sudha, S., Tarantino, S., Esposti, R., Bolzoni, F., Cavallari, P., Cipriani, C., Mattoli, V. & Greco, F. (2018). Ultraconformable Temporary Tattoo Electrodes for Electrophysiology. *Advanced Science*, *5*(3), 1700771. https://doi.org/10.1002/advs.201700771
10. Gutbrod, S. R., Sulkin, M. S., Rogers, J. A. & Efimov, I. R. (2014a). Patient-specific flexible and stretchable devices for cardiac diagnostics and therapy. *Progress in Biophysics and Molecular Biology*, *115*(2–3), 244–251. https://doi.org/10.1016/j.pbiomolbio.2014.07.011
11. Hong, Y. J., Jeong, H., Cho, K. W., Lu, N. & Kim, D.-H. (2019). Wearable and Implantable Devices for Cardiovascular Healthcare: from Monitoring to Therapy Based on Flexible and Stretchable Electronics. *Advanced Functional Materials*, *29*(19), 1808247. https://doi.org/https://doi.org/10.1002/adfm.201808247
12. Kim, D.-H., Ghaffari, R., Lu, N., Wang, S., Lee, S. P., Keum, H., D'Angelo, R., Klinker, L., Su, Y., Lu, C., Kim, Y.-S., Ameen, A., Li, Y., Zhang, Y., de Graff, B., Hsu, Y.-Y., Liu, Z., Ruskin, J., Xu, L., … Rogers, J. A. (2012). Electronic sensor and actuator webs for large-area complex geometry cardiac mapping and therapy. *Proceedings of the National Academy of Sciences*, *109*(49), 19910–19915. https://doi.org/10.1073/pnas.1205923109
13. Kim, D.-H., Lu, N., Ma, R., Kim, Y.-S., Kim, R.-H., Wang, S., Wu, J., Won, S. M., Tao, H., Islam, A., Yu, K. J., Kim, T. -i., Chowdhury, R., Ying, M., Xu, L., Li, M., Chung, H.-J., Keum, H., McCormick, M., … Rogers, J. A. (2011). Epidermal Electronics. *Science*, *333*(6044), 838–843. https://doi.org/10.1126/science.1206157
14. Kim, Dae-Hyeong, Ghaffari, R., Lu, N. & Rogers, J. A. (2012). Flexible and Stretchable Electronics for Biointegrated Devices. *Annual Review of Biomedical Engineering*, *14*(1), 113–128. https://doi.org/10.1146/annurev-bioeng-071811-150018
15. Koo, J. H., Song, J. K., Kim, D. H. & Son, D. (2021). Soft Implantable Bioelectronics. *ACS Materials Letters*, *3*(11), 1528–1540. https://doi.org/10.1021/acsmaterialslett.1c00438
16. Koo, J. H., Song, J., Yoo, S., Sunwoo, S., Son, D. & Kim, D. (2020). Unconventional Device and Material Approaches for Monolithic Biointegration of Implantable Sensors and Wearable Electronics. *Advanced Materials Technologies*, *5*(10), 2000407. https://doi.org/10.1002/admt.202000407
17. Liu, Y., Norton, J. J. S., Qazi, R., Zou, Z., Ammann, K. R., Liu, H., Yan, L., Tran, P. L., Jang, K.-I., Lee, J. W., Zhang, D., Kilian, K. A., Jung, S. H., Bretl, T., Xiao, J., Slepian, M. J., Huang, Y., Jeong, J.-W. & Rogers, J. A. (2016). Epidermal mechano-acoustic sensing electronics for cardiovascular diagnostics and human-machine interfaces. *Science Advances*, *2*(11), e1601185. https://doi.org/10.1126/sciadv.1601185
18. Lochner, C. M., Khan, Y., Pierre, A. & Arias, A. C. (2014). All-organic optoelectronic sensor for pulse oximetry. *Nature Communications*, *5*(1), 5745. https://doi.org/10.1038/ncomms6745
19. Ma, R., Wu, C., Wang, Z. L. & Tsukruk, V. V. (2018). Pop-Up Conducting Large-Area Biographene Kirigami. *ACS Nano*, *12*(10), 9714–9720. https://doi.org/10.1021/acsnano.8b04507
20. Pang, B. J., Lui, E. H., Joshi, S. B., Tacey, M. A., Alison, J., Senevirante, S. K., Cameron, J. D. & Mond, H. G. (2014). Pacing and Implantable Cardioverter Defibrillator Lead Perforation As Assessed by Multiplanar Reformatted ECG-Gated Cardiac Computed Tomography and Clinical Correlates. *Pacing and Clinical Electrophysiology*, *37*(5), 537–545. https://doi.org/10.1111/pace.12307
21. Park, J., Choi, S., Janardhan, A. H., Lee, S.-Y., Raut, S., Soares, J., Shin, K., Yang, S., Lee, C., Kang, K.-W., Cho, H. R., Kim, S. J., Seo, P., Hyun, W., Jung, S., Lee, H.-J., Lee, N., Choi, S. H., Sacks, M., … Hwang, H. J. (2016). Electromechanical cardioplasty using a wrapped elasto-conductive epicardial mesh. *Science Translational Medicine*, *8*(344), 344ra86. https://doi.org/10.1126/scitranslmed.aad8568
22. Rigatelli, G., Santini, F. & Faggian, G. (2012). Past and present of cardiocirculatory assist devices: A comprehensive critical review. *Journal of Geriatric Cardiology*, *9*(4), 389–400. https://doi.org/10.3724/SP.J.1263.2012.05281
23. Rogers, J. A., Someya, T. & Huang, Y. (2010). Materials and Mechanics for Stretchable Electronics. *Science*, *327*(5973), 1603–1607. https://doi.org/10.1126/science.1182383
24. Roubelakis, A., Rawlins, J., Baliulis, G., Olsen, S., Corbett, S., Kaarne, M. & Curzen, N. (2015). Coronary Artery Rupture Caused by Stent Infection. *Circulation*, *131*(14), 1302–1303. https://doi.org/10.1161/CIR20CULATIONAHA.114.014328

25. Savoji, H., Mohammadi, M. H., Rafatian, N., Toroghi, M. K., Wang, E. Y., Zhao, Y., Korolj, A., Ahadian, S. & Radisic, M. (2019). Cardiovascular disease models: A game changing paradigm in drug discovery and screening. *Biomaterials*, *198*(May 2018), 3–26. https://doi.org/10.1016/j.biomaterials.2018.09.036
26. Shim, H. J., Sunwoo, S., Kim, Y., Koo, J. H. & Kim, D. (2021). Functionalized Elastomers for Intrinsically Soft and Biointegrated Electronics. *Advanced Healthcare Materials*, *10*(17), 2002105. https://doi.org/10.1002/adhm.202002105
27. Spittell, P. C. & Hayes, D. L. (1992). Venous Complications After Insertion of a Transvenous Pacemaker. *Mayo Clinic Proceedings*, *67*(3), 258–265. https://doi.org/10.1016/S0025-6196(12)60103-7
28. Sunwoo, S. H., Lee, J. S., Bae, S., Shin, Y. J., Kim, C. S., Joo, S. Y., Choi, H. S., Suh, M., Kim, S. W., Choi, Y. J. & Kim, T. (2019). Chronic and acute stress monitoring by electrophysiological signals from adrenal gland. *Proceedings of the National Academy of Sciences*, *116*(4), 1146–1151. https://doi.org/10.1073/pnas.1806392115
29. Viventi, J., Kim, D.-H., Moss, J. D., Kim, Y.-S., Blanco, J. A., Annetta, N., Hicks, A., Xiao, J., Huang, Y., Callans, D. J., Rogers, J. A. & Litt, B. (2010). A Conformal, Bio-Interfaced Class of Silicon Electronics for Mapping Cardiac Electrophysiology. *Science Translational Medicine*, *2*(24), 24ra22. https://doi.org/10.1126/scitranslmed.3000738
30. Wu, H., Yang, G., Zhu, K., Liu, S., Guo, W., Jiang, Z. & Li, Z. (2021). Materials, Devices, and Systems of On-Skin Electrodes for Electrophysiological Monitoring and Human–Machine Interfaces. *Advanced Science*, *8*(2), 2001938. https://doi.org/10.1002/advs.202001938
31. Xu, L., Gutbrod, S. R., Bonifas, A. P., Su, Y., Sulkin, M. S., Lu, N., Chung, H.-J., Jang, K.-I., Liu, Z., Ying, M., Lu, C., Webb, R. C., Kim, J.-S., Laughner, J. I., Cheng, H., Liu, Y., Ameen, A., Jeong, J.-W., Kim, G.-T., … Rogers, J. A. (2014). 3D multifunctional integumentary membranes for spatiotemporal cardiac measurements and stimulation across the entire epicardium. *Nature Communications*, *5*(1), 3329. https://doi.org/10.1038/ncomms4329
32. Xu, L., Gutbrod, S. R., Ma, Y., Petrossians, A., Liu, Y., Webb, R. C., Fan, J. A., Yang, Z., Xu, R., Whalen, J. J., Weiland, J. D., Huang, Y., Efimov, I. R. & Rogers, J. A. (2015). Materials and Fractal Designs for 3D Multifunctional Integumentary Membranes with Capabilities in Cardiac Electrotherapy. *Advanced Materials*, *27*(10), 1731–1737. https://doi.org/10.1002/adma.201405017
33. Yamamoto, Y., Harada, S., Yamamoto, D., Honda, W., Arie, T., Akita, S. & Takei, K. (2016). Printed multifunctional flexible device with an integrated motion sensor for health care monitoring. *Science Advances*, *2*(11). https://doi.org/10.1126/sciadv.1601473
34. Yoder, M. A., Yan, Z., Han, M., Rogers, J. A. & Nuzzo, R. G. (2018). Semiconductor Nanomembrane Materials for High-Performance Soft Electronic Devices. *Journal of the American Chemical Society*, *140*(29), 9001–9019. https://doi.org/10.1021/jacs.8b04225
35. Zhang, Y., Xu, S., Fu, H., Lee, J., Su, J., Hwang, K.-C., Rogers, J. A. & Huang, Y. (2013). Buckling in serpentine microstructures and applications in elastomer-supported ultra-stretchable electronics with high areal coverage. *Soft Matter*, *9*(33), 8062. https://doi.org/10.1039/c3sm51360b