Trends in Graphene-Based E-Skin and Artificial Intelligence for Biomedical Applications—A Review

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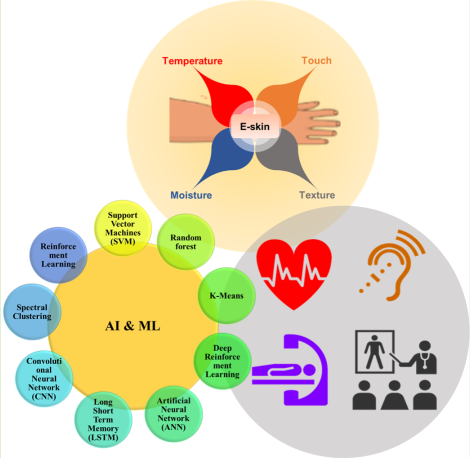
***Abstract*—Electronic skin (e-skin) mimics human skin and is an indispensable part of wearable technology with widespread applications ranging from robotics to health care. Designing and fabricating e-skins equipped with multifunctionality is the focus of current research that amalgamates materials with a variety of structures and unique properties. Several attempts toward various mechanisms and materials that make e-skin flexible, stretchable, and sensitive have been reported. At the material level, graphene is the most suitable material for e-skin owing to its excellent electronic, electrical, and mechanical properties. Although remarkable progress has been made in this field over the years, fabricating multifunctional smart e-skin is still a challenge. This perspective article explores the recent advances in e-skin through graphene as a material example and the use of artificial intelligence (AI) in wearable technology. In this study, an emphasis has been laid on the applications of AI in wearable devices along with a brief insight into the advantages, and limitations of AI and ML in the field of medicine.**



***Index Terms*— Artificial intelligence (AI), e-skin, graphene, health care, machine learning (ML), wearable technology.**

I. INTRODUCTION

BIOSENSING devices are critical diagnostic tools to analyze various biomolecules qualitatively and quantitatively with sensitivity, selectivity, and efficacy. They play a prominent role in monitoring environmental and industrial conditions, food safety, agriculture, and medicine. The role of biosensors in healthcare and medicine is indispensable. The interface of human skin is an active research platform to incorporate physical and biosensors for the detection of various stimuli like temperature, pressure, and tactile in addition to chemical analytes. In this regard, electronic skins (e-skins) made of 2-D material, as a class of biosensors, have attracted significant research attention to cater to the needs of healthcare [1], [2], [3]. E-skin is an artificial skin simulating the sensing and mechanical abilities of human skin. It is an electronic device with the capability to biconically mimic human skin and can be conveniently adhered to the human body [4]. It is a synthetic skin that exhibits stretchability, flexibility, and is capable of intelligent processing [5]. Structurally an e-skin is composed of multiple layers of different materials each performing a specific function.

In general, an E-skin consists of a protective layer, the sensor layer, the signal processing layer (SPC), and the substrate layer [7]. The protective layer encapsulates and safeguards the sensor array and transduces the physical stimuli to the sensor. The sensor is a sandwich-like structure consisting of

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TABLE I
ADVANTAGES AND DISADVANTAGES OF E-SKIN BASED BIOSENSORS

Advantages	**Disadvantages**	**Ref.**
Facilitate non-invasive qualitative analysis	Lack long term reproducibility.	[1]
Mass fabrication through printing makes their production economical.	Printing techniques employ chemicals and practices contrasting green fabrication procedures.	[1]
Highly efficient, sensitive and selective.	Need to be calibrated from time to time.	[160]
Flexible, stable and stretchable.	Poor air permeability and waterproofness.	[161]
Conveniently adherable to external body parts and or clothing.	Require signal amplification, expensive equipment and skilled personnel for operation.	[119]
Employ nanomaterials as active sensing materials enabling generation of rapid response to stimuli.	Biocompatibility and cytotoxicity of active nanomaterials is debatable.	[120]

the conductive electrode, active sensing material, and encapsulation layers on top and bottom. The sensor converts the acquired physical/chemical information into electrical signals and passes them on to the SPC which then transmits them to the substrate layer at the bottom [6], [7]. The structure of the e-skin is represented schematically in Fig. 1. Evolution of e-skins equipped with the abilities to self-heal and self-power by means of artificial intelligence (AI) integrated functionalities [8] is considered to be "smart skin". Many attempts associated with a variety of mechanisms/approaches and materials/structures have been developed to match the e-skins to the functions of specific applications. Currently, high sensitivity, mechanical and electrical flexibility, multifunctionality, and biocompatibility are common driving forces in the research area of e-skin and associated electronics. New materials, with a variety of structures and unique properties, offer plenty of freedom in designing and fabricating e-skins [9]. The advantages and disadvantages of e-skin-based biosensors are summarized in Table I.

The development of e-skin facilitates improved healthcare by restoring sensational ability in case of external skin damage [10]. In this context, several attempts have been made in the development of artificial skin since the 1970s. For example, Y. Zhou et al reported the development of an artificial prosthesis to provide sensational ability in amputees [6]. E-skins today also find applications in disease diagnosis through the detection of signals which are physiological in nature such as human pulse, electroencephalogram, and electrocardiogram (ECG) [11], [12].

AI has become a progressively prevalent research topic in medicine. AI is used for informing clinical decisions made through insights obtained from sensors, and prior data, thereby helping providers and recipients. It stands as a supporting pillar for doctors and supports under-resourced communities [13]. For instance, in tuberculosis-prevalent countries where radiological expertise in remote areas is limited, AI was used to correctly diagnose pulmonary tuberculosis with a sensitivity of 95% and specificity of 100% [14]. Applications of AI include the detection and differentiation of benign and malignant skin lesions, the detection of inflammatory skin diseases [15], allergen exposure, ulcers, etc. AI is also used in artificial skin, closely knit or attached to human skin, thus helping to monitor, detect and review a person's "electronic footprint". For example, Liao et al. [16] demonstrated the use of machine learning (ML) to predict ventilator-associated pneumonia (VAP) by developing an e-nose system. Here, the E-nose consisting of 28 metal oxide semiconductor gas sensors was developed for predicting the presence of infection after patients have been intubated in the intensive care unit. The ML model was developed with support vector machines (SVMs) and artificial neural network architectures and the effectiveness of VAP identification was verified using clinical data.

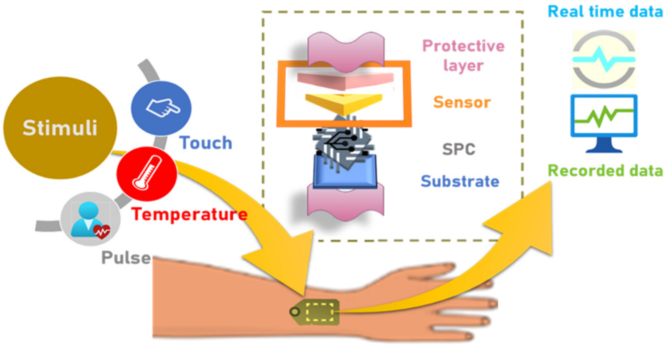

Fig. 1. Schematic of structure and working of e-skin.

Owing to the development of e-skin-based biosensing platforms for advanced diagnostics and care, this short perspective article intends to summarize the recent progress in e-skins coupled with AI for applications in medicine. Herein, we present and limit our discussion to graphene-based e-skins as graphene has emerged as a novel 2-D-carbon nanomaterial endowed with characteristic features suitable for fabricating e-skins. Further, the existing challenges and perspectives on future research direction are presented. This article is aimed at providing comprehensive insights and research focus to novices in wearable technology particularly e-skin-based biosensors, and the use of AI with respect to medicine and health care.

II. TRENDS IN GRAPHENE-BASED E-SKIN

One of the major challenges in the design and preparation of e-skin is the rigid planar electronics while the functionality of e-skin requires flexible electronics [7]. In regard to this various nanomaterials like 1-D [example: nanofibers (NF), nanowires (NW), and nanotubes (NT)] and 2-D (example: graphene) have been explored for the fabrication of e-skins [17], [18], [19]. Of the above, graphene is attractive compared to others. The structure as well as its inherent material properties make it an ideal material for e-skin. Graphene is a layered structure with strong π–π bonding and van der Waals interactions making it an outstanding material. In addition, its enhanced conductance, flexibility coupled with high Young's modulus [20], extreme lightweight, and superior mechanical and chemical properties play a vital role in constructing e-skins [21], [22], [23]. The limitation of the use of conventional materials is that they are prone to damage or breakage upon external pressure or stress as usually thin conducting films are used as active sensing material in e-skins. Graphene exhibits high stability under compression, stretching, or twisting that aid in optimizing the performance of the e-skin [8].

Moreover, graphene exhibits superior carrier mobility and thermal conductivity [24], [25]. These diverse properties of graphene make it an appreciated and most sought-after material for sensor applications. Its high specific surface area and thickness of an atom enable its carbon to be in direct contact with the stimuli or analyte rendering superior sensitivity as compared to silicon or other substrate materials. For instance, Qi et al. [26] reported the development of a pristine graphene-based dopamine sensor that could detect dopamine up to a limit of 2 μM in the presence of ascorbic acid and urea [27]. It allows for intimate contact of the e-skin with the epidermis of the human skin because of superior mechanical flexibility and ultrathin thickness allowing for capturing uninterrupted signals and motions. This particularly is useful in tracking heart rate and pulse [28], [29], [30]. For example, Wang et al. [31] reported the development of reduced graphene oxide (rGO) based piezoresistive sensor with a sensitivity of 15.6 per kPa for monitoring real-time pulse and muscle movements. Further, electrophysiological signals can be acquired with a high signal-to-noise ratio due to efficient signal transmission and high electrical conductivity. More discussions on the properties of graphene have been summarized in notable reviews [9], [32], [33].

Graphene can be fabricated by top-down [mechanical and chemical exfoliation (ME and CE)] and bottom-up [chemical vapor deposition (CVD) and molecular beam epitaxy] and laser-induced techniques. The ME graphene is a small-sized single-layer 2-D microstructure with excellent conductivity and few defects leading to reduced inherent noises [34], [35]. It has superior carrier transport properties and exhibits Hall effect at room temperature with ambipolar field effect features [36]. These properties entitle it to be an excellent gas sensor that enables the detection of analyte gases, at concentrations as low as 1 ppb, through variation in Hall resistance [37]. This wearable technology use of ME graphene could facilitate the detection of poisonous gases in the environment. CE on the other hand, results in oxidized multiple graphitic (GO) layers of medium size with lattice defects and poor conductivity. CE graphene is therefore reduced thermally to generate rGO with lowered oxygen-containing groups that can be altered covalently to bind with certain functional molecules, which further improves the sensitivity of sensors. rGO is electrochemically active and can detect biomolecules like glucose and chemicals like hydrogen peroxide when combined with polymer substrates that act as matrix-supporting active material [38], [39]. Fundamentally, rGO finds sensory application whereas CE only aids in the economic production of bulk GO [36], [40].

CVD results in large-sized single 2-D planar graphene layers with outstanding conductivity. CVD films of graphene can be grown on metal substrates with defective carbon lattice to facilitate the doping of heteroatoms which can significantly aid in improving the sensitivity of the sensor [36], [41]. In addition, the large-sized layers facilitate a large detection area and are therefore more suitable for organic thin film transistors (OTFTs). This large detection area has particularly been exploited in the detection of ammonia, hydrogen, and glucose [42], [43]. Another method, epitaxial growth of graphene on silicon carbide (SiC) produces large-sized single 2-D planar graphene layers with superior conductivity. The interaction of as-formed graphene layers with the SiC results in a bandgap of 0.25 eV which is desirable for sensors working on induced field effects such as pH sensors [44], [45]. Laser-induced graphene (LIG) has a 3-D porous network with 2-D sheets of high surface area that provide abundant adsorption and active sites for various stimuli as well as analytes. Such sheets serve as active material in e-skins for sensing a range of biomolecules, gases as well as tactiles [46], [47], [48]. Thus, different fabrication methods lead to obvious differences in the properties of graphene so obtained. Therefore, with respect to the above discussion, a combination of graphene with diverse functional materials is a common approach for fabricating sensors of high performance. Graphene also serves as a good platform for the functionalization of metals and conductive polymers that allow for delocalized transport of charge carriers at the interface between graphene active material an analyte/stimulus for greater sensory response [49], [50], [51].

E-skins detect the stimulus by converting the external mechanical signals into electrical signals by piezoresistive capacitive, piezoelectric, and triboelectric mechanisms. Therefore, it is necessary that the substrate used responds to the stimulus according to the conduction mechanism used in the fabrication of E-skin. For example, piezoresistive type sensors are best suited for detecting pressure variation by corresponding changes in their resistance. Similarly, capacitive sensors are flexible strain sensors that detect the force applied (and strain thereby) by corresponding changes in capacitance. Polymers, in fact, possess high mechanical hysteresis leading to long response and recovery times thereby decreasing sensor performance. Graphene, on the other hand, provides a channel for electron penetration and transport and retains conductivity even under applied pressure enabling the detection of external mechanical signals like stress, force, or pressure. Thus, when blended with polymer matrix, the polymer matrix yields to compression under external stress while graphene facilitates charge transport and allows for sensing of stress [6], [52]. Yao et al. [53] reported the development of a 3-D conductive sponge made of polyurethane (PU) nano-fibers wrapped in rGO nanosheets. When this sponge was compressed, the PU NF would contact each other leading to a surge in the contact area of fibers. When the sponge was released the fiber network would lose contact and recover the deformation, as shown in Fig. 2, leading to a decrease in contact area causing a change in resistance, thereby allowing for the detection of compressive stress [53]. Gao et al. [54] developed another fiber-inspired tactile wearable sensor capable of sensing multiple mechanical deformations such as tensile strain, twist, and bending motions. As seen in Fig. 3(a), the authors reported of a compression spring and coated rGO around the PU fiber.

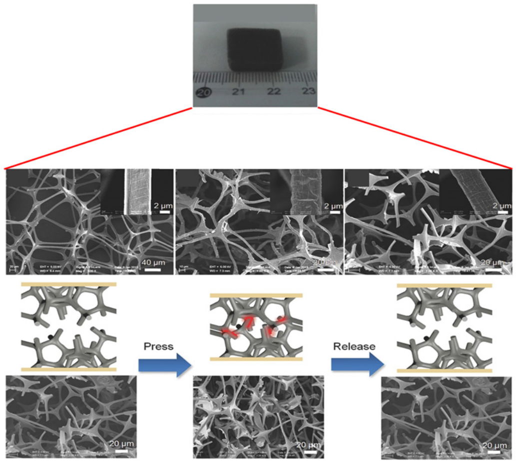

Fig. 2. Mechanistic illustration of rGO/PU conducting sponge [53].

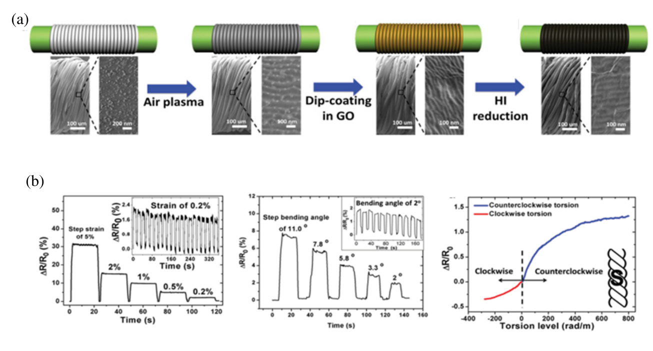

Fig. 3. (a) Fabrication of graphene-based PU fiber tactile sensor and (b) performance of tactile sensor in terms of change in resistance to applied tensile strain, bend, and twist [54].

The as-developed sensor had remarkable sensitivity to tensile strain and excellent bending and torsion sensitivity [Fig. 3(b)]. Such sensors based on other carbonaceous materials (carbon black and active carbon) and conducting polymers are known to be unable to attain such simultaneous high sensitivity and stretchability. The performance of graphene-based tactile sensors makes it possible to detect a wide range of human activities from pulse monitoring to complex motions [54], [55]. In addition to the above tactile sensors, graphene, and its composite with PU, polymethyl methacrylate (PMMA), and polydimethylsiloxane (PDMS) have been reported to be used as electrode and dielectric materials in capacitance-based tactile sensors. For instance, Su et al. fabricated a CVD-graphene/PMMA composite film sensor for pressure analysis that had a sensitivity (15.2 fF kPa^{-1}) of more than eight times that of silicon-based sensors [56].

Graphene is endowed with superior thermal conductivity of about 5300 W $\text{m}^{-1}\text{K}^{-1}$, thermal emissivity, and sensitivity to changes in temperature making it widely used in temperature sensors. Further, such sensors have a negative thermal expansion coefficient (NTEC) as opposed to those from other traditional materials and conducting composites [57], [58]. In addition, thermoelectric material-based sensors such as those made of conductive polymers like polyaniline, poly-3-hexyl thiophene, and semiconducting metal oxide NW and thin films exhibit a delayed response (longer response time) and poor durability [59], [60]. For instance, Ko et al. reported the fabrication of a ferroelectric composite consisting of a polyvinyl difluoride (PVDF) matrix and rGO sheets (Fig. 4) that not only exhibited NTEC behavior but also was capable of generating temporal responses to continuous variations in temperature [61].

Fig. 4. Schematic of rGO/PVDF temperature sensor showing temperature distribution on human palm [61].

E-skins that are equipped with multifunctionality are an effective way of realizing the inspiration for their development, i.e., to mimic human skin. The coupling of flexible electronics with sensors catering to multiple functions has been extensively studied which represents a concerted effort in this direction. Potential applications of currently developed e-skin range from health care to human–machine interfaces through robotics. Several reports on graphene-based e-skin that combine tangible and temperature sensing in a single device are articulated [62], [63], [64] However, for the simultaneous perception and distinction of different stimulations like temperature, surface texture, humidity, and static and dynamic tactile, integration of multiple functional graphene-based e-skins is required. This motivated Ko et al. to develop ferroelectric films (PVDF/rGO) based e-skin capable of monitoring static and dynamic tactile as well as temperature [61].

In addition to multifunctionality, although not significant but directed efforts have been devoted toward the development of e-skin that can sense light and atmosphere [7]. The state-of-the-art e-skins not only are capable of mimicking human skin but also have surpassed human skin. The present-day e-skin is endowed with abilities like monitoring human pulse rate, rate of respiration, and blood pressure. The detection of these significant physiological signals aid in detecting health abnormalities thus broadening the scope of human health and diagnostics [65], [66], [67]. For example, Zhu et al. have reported a chemical vapor deposited (CVD)-graphene-based sensor for noninvasive and real-time monitoring of cardiovascular parameters [68] as shown in Fig. 5. It was demonstrated that this sensor when knit close to human skin could accurately detect and differentiate pulses among different age groups pre- and post-physical activities.

Moreover, e-skin can adhere to the knee and knuckle on the human body to monitor finger and limb movements [69], [70]. The ability to mimic human skin coupled with biocompatibility enables e-skin to be applied in bionics and robotics, a representative of human–machine interaction. This translates into advanced prosthetics and robotics with sensory functions and steerable abilities like that of humans. Several graphene-based devices such as data gloves have been reported [71], [72].

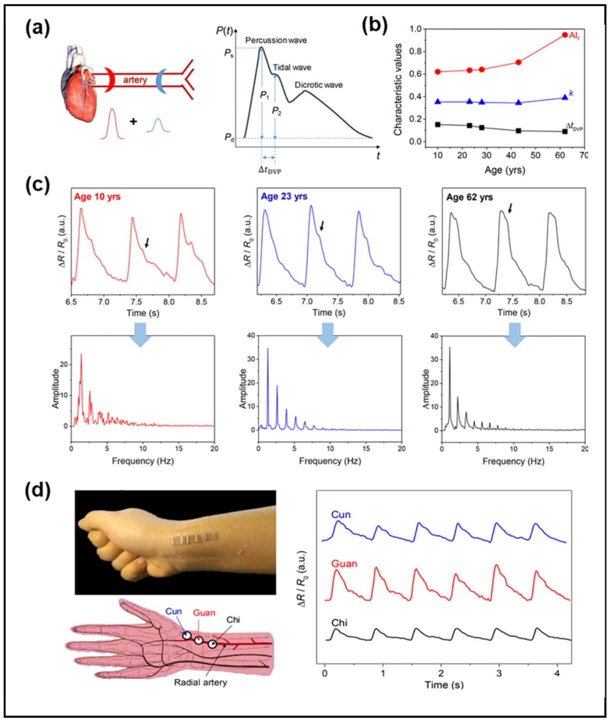

Fig. 5. Epidermal pulse monitoring with CVD-graphene-based tactile sensor. (a) Illustration of pulse generation and its waveform shape features. (b) Three health-related parameters for subjects of different ages. (c) Original pulse and its frequency spectra distribution for male volunteers of age 10, 23, and 62 years, the black arrows indicate the peak position of a tidal wave. (d) Multiposition pulse reading and location of the inch opening with pulse signals of the sensors located at the Cun (distal), Guan (middle), and Chi (proximal) positions [68].

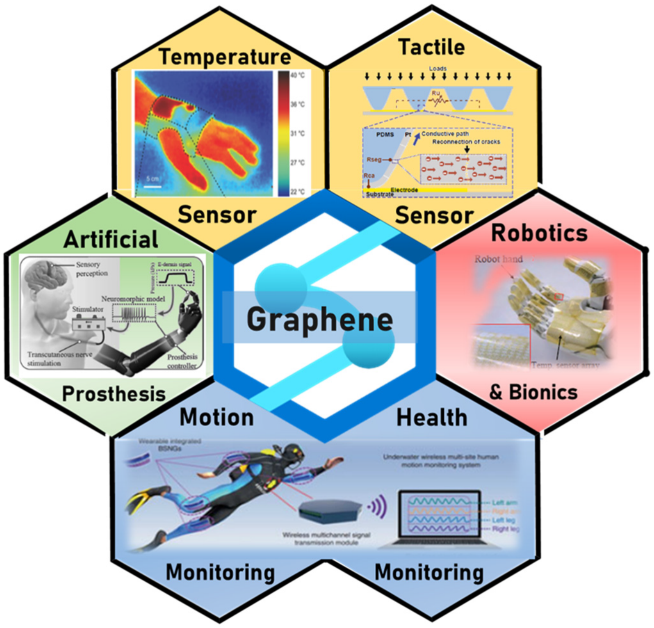

Fig. 6. Widespread applications of graphene-based e-skin (Temperature: [95], Tactile: [96], Robotics, bionics, and Artificial prosthesis: [97], Motion and health monitoring: [98]).

The wide applications of graphene-based e-skin are summarized in Fig. 6. To effectively mimic human skin, e-skins need to be multifunctional, and therefore, research in this direction has gained significant impetus. It is of vital importance that the artificial skin effectively and accurately identifies physical stimuli as well as human physiological signals. Since they detect and convert physical tactile into electronic data, e-skin is also known as tactile sensors. The activity of these tactile sensors is largely influenced by the material used and the mechanism of sensing. The sensing material is the active material possessing enhanced electrical, mechanical, and optical properties. This usually is exhibited by semiconductors such as NW of precious metals and NW of transition metal oxides, especially those of Si and Zn, carbon NT and graphene. Since it is not possible to find all the desired properties in a single material, the active material is often coupled with substrates that impart structural integrity to these sensors. Some commonly used substrates include poly vinyl alcohol (PVA), poly-ethylene terephthalate (PET), and PDMS [73], [74], [75].

Graphene with its enhanced surface composition and geometry is studied to fabricate flexible resistors as either 1-D fibers, 2-D films, or 3-D piezoelectric type. These can achieve the above-mentioned properties and also combine the advantages of wearable comfort, monitoring, and recording human body movements without interference, stability, and durability [76], [77], [78]. For example, Hu et al. have reported the development of a conductive graphene fiber core with a PVA sheath that exhibited superior stretchability (tensile strength of 590 MPa), strain-detecting ability with high sensitivity, and cyclic stability [79]. Pang et al. [21] have designed miniature graphene films that are extremely lightweight with a wide operation window of pressure or stress (0–200 kPa) and remarkable durability. Generally, graphene 3-D networks are classified as hydrogel, aerogel, sponges, and foams that are widely investigated as they offer cumulative advantages of high conductivity and compressibility due to 3-D network structure [80], [81], [82].

Human skin can detect and differentiate different information such as temperature, surface roughness or smoothness, touch, and vibration. Superior tactile sensitivity coupled with flexibility and rapid response can enable robots to mimic the human body's somatosensory system. There are several examples of extensive research carried out in this direction [83]. Wang et al. [84] have reported the fabrication of a self-powered multifunctional e-skin based on a triboelectric mechanism that not only can monitor temperature and pressure but also allows for the recognition of materials simultaneously. Further, they also synthesized successfully an e-skin made of graphene/PDMS composite that resembled a sponge and showed superior sensitivity to variations in pressure and temperature [84]. Park et al. [61] report the development of rGO/PVDF composite films that are ferroelectric in nature and micro-structured. These micro-structured films showed enhanced capabilities of simultaneous detection of temperature, pressure, and sound waves and were also able to identify different surfaces accurately. Ren et al. have used LIG on polyimide (PI) substrate to fabricate a wearable artificial throat capable of detecting and emitting sounds at the same time (Fig. 7). The throat takes advantage of high thermal conductivity and low heat capacity of LIG to emit sounds

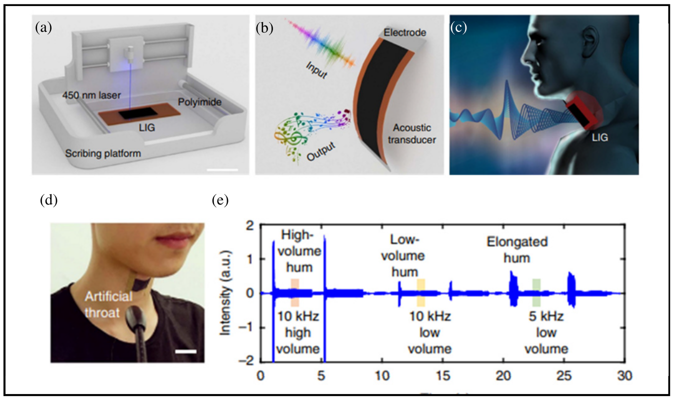

Fig. 7. LIG-based artificial throat. (a) One-step LIG fabrication process. (b) Ability to emit and detect sound waves in a single device. (c) Artificial throat. (d) Artificial throat tested on a user (scale bar: 1 cm). (e) High and low-volume and elongated humming sounds detected by LIG throat and converted into high-volume 10 kHz, low-volume 10 kHz, and low-volume 5 kHz sound, respectively [85].

in a wide range of 100 Hz to 40 kHz and porous structure of LIG allows for detection of even feeble sounds with high sensitivity [85].

OTFTs facilitate flexible electronics with multiple functions over large areas at a reduced cost with ease of assembly on polymer or plastic substrates at ambient temperature through solution processes [86], [87]. In addition, they also offer diverse applications, particularly e-skins. The research focus is on enhancing the career mobility and environmental stability of OTFTs so that OTFTs can compete with inorganic transistors [88]. However, OTFTs come with plenty of advantages for e-skin-based applications. They offer a large signal-to-noise ratio relative to piezoresistive and capacitive sensors [89]. They provide for seamless integration of sensors and transistors for simultaneous signal transduction and processing conferring smart functions to e-skins [90]. The inexpensive nature, large area processes, and flexibility of organic materials enable them to be coupled with monitoring devices adhered to human skin with ease. Hence, OTFT-based pressure sensors present promising systems in e-skin applications. But a current challenge for practical realization is the opposing trends of sensitivity and low operation voltage required for OTFT-derived sensors which necessitate a compromise between the two [91], [92], [93], [94].

From the ongoing discussion, the targeted application of e-skin-based sensors is dependent on the different properties of graphene that originate from its different formation methods. Graphene obtained from these methods however has potential limitations. For example, it is difficult to control the thickness of graphene under CE and ME and these techniques have limited substrate options further limiting the fabrication and application of graphene produced by them. CVD on the other hand is a high-cost and low-throughput graphene-yielding technique that obstructs the widespread electronic applications of grapheme [36], [99], [100]. SiC substrates are vulnerable to breakdown during etching and hence the quality of epitaxially grown graphene for sensors is often debated [36]. LIG, although has good conductivity, requires improvement in material quality in comparison to that of the CVD process.

An important characteristic of human skin is its ability to stretch and flex with bodily movements without incurring damage. Evenly matched mechanical properties anywhere on the body and the imperceptibility of electronics are two essential characteristics for future e-skin devices. While arrays of flexible electronics have been developed by using plastic substrates [101], stretchable devices have been more difficult to achieve, and new processes and materials are often required [102]. In general, stretchable devices can be fabricated by developing devices comprised of intrinsically stretchable materials or by the appropriate geometrical arrangement of conventional materials. Intrinsically stretchable may have an advantage in applications where full area coverage and coplanar devices are desired. Furthermore, intrinsically stretchable devices could realize a cost advantage by direct printing onto elastomeric substrates. Recent progress in stretchable materials development has enabled several intrinsically stretchable devices. Lee et al. [103] demonstrated a transistor with graphene electrodes and an active layer that showed reliable operation while stretching up to 5% for 1000 cycles. A detailed description of issues relevant to stretchable graphene-based transistors is available by Ahn et al. [104]. One challenge facing intrinsically stretchable devices is the difficulty of finding hermetic, stretchable encapsulants.

Electronic devices have historically been developed using brittle high-modulus materials such as inorganic semiconductors and metals. The development of intrinsically brittle materials with large-scale stretchability has been feasible by appropriate geometrical patterning and device design. While continuous plastic deformation can be promoted by adhesion to a compliant substrate [105], large-scale reversible elasticity is achieved using discontinuous structures that can distort while retaining electrical conductivity. The discontinuous structures can be patterned at different length scales but rely on similar mechanisms. At the microscopic level, discontinuous films on elastomeric substrates can be created by cracking a thin film while maintaining a percolating pathway [106]. Wagner et al. [105] investigated Au films on elastic substrates [107] and found that they could be stretched up to 100% with reproducible cycling.

The stretchability of conductors can be further improved by roughening the surface of the substrate [108] to inhibit the propagation of cracks through the conductive layer and preserve the conductive pathways. While cracking of a continuous film can create a randomly patterned conductor, similar results can be achieved by depositing a network of 1-D conductors [109]. To fabricate stretchable conductors on elastic substrates, convoluted pathways such as serpentine or horseshoe-shaped structures are effective, and the strain reduction in the structures is strongly dependent on the patterned geometry and materials properties [110]. In addition, patterning a flexible substrate into a discontinuous film is an attractive method of imparting stretchability level because it requires minimal changes to established fabrication methods. With this technique, strain is accommodated by twisting out of the plane of the distortion. High-performance stretchable systems can be realized by connecting conventional rigid device islands with interconnects that have been made stretchable using patterning or buckling.

The research group of John Rogers has pioneered many of the techniques to make buckled devices from traditional high-performance inorganic semiconductors and conductors. Many of their devices use inorganic NW, nanoplatelets, and nanomembranes obtained by etching thin layers of material from multilayer [111] or bulk wafers [112]. They have adhered inorganic nanostructures to stretchable substrates using transfer processing. Such transfer methods can achieve cost-effective large-area coverage by distributing active elements fabricated in a dense array over a larger area through successive transfer steps [113] by automated systems [113], and can be used to make 3-D circuits by adding multiple layers. The group has formed semiconductor devices into buckles [114], pop-up structures [115], and serpentine mesh layouts [116] to demonstrate a range of functionalities.

In another article [117], a novel fabrication method to introduce the kirigami approach to pattern a highly conductive and transparent electrode into diverse shapes of stretchable electronics with multivariable configurability for e-skin applications was proposed. These kirigami-engineered patterns impart tunable elasticity to the electrodes, which can be designed to intentionally limit strain or grant ultra stretchability depending on applications over the range of 0 to over 400% tensile strain with strain-invariant electrical property and show excellent strain reversibility even after 10 000 cycles stretching while exhibiting high optical transparency (>80%).

The above-mentioned studies indicate minimal to no change in the device performance upon varying mechanical deformations such as bending, twisting, and stretching due to intentional materials, device, or structural engineering. Further, a noteworthy remark from the ongoing examples and studies on device performance and mechanical deformations is that the role of AI algorithms in enhancing device performance subjected to mechanical deformities has not been clear, attracting the dearth of literature and the attention of the AI community.

Although e-skin-based biosensors are advanced, handy, and multifunctional, they still suffer from drawbacks that are both mechanism and application based. The intactness of the e-skin and its performance after repeated use is still questionable. For example, such sensors are prone to mechanical bending after multiple uses. Bending, in addition to restraining design freedom, also complicates the retention of connectivity and conductivity of active material [118]. Skin compatibility is a serious backdrop that interferes with the comfort of the users causing irritation and discomfort. Thus, e-skin performance is limited by its long-term reproducibility [119], [120]. In addition, the elasticity of human skin changes with age leading to noncompliance of e-skin with human skin. Further, there are limited options for the incorporation of e-skin with body parts with complex contours and deformations during natural body motions causing stress at interfaces. The possibility of a potential mismatch between inherently stretchable and nonstretchable skin mechanics also is a point of concern in the application of e-skin-based sensors [121], [122]. As e-skins become multifunctional, their size increases with an increase in functionality, causing inconvenience for the wearer of such devices. Also, such sensors should be self-calibrated so that they are readily operated by the wearer. In addition, such sensors should be producible in bulk economically for their practical realization.

III. IMPACT OF AI ON WEARABLE DEVICES

AI and ML have made a breakthrough in many fields including medicine and wearable technology thereby aiding in a wide range of applications from disease diagnosis to drug development. Wearable devices are used in applications such as sports, healthcare, industrial manufacturing, and human–robot interaction [123], [124], [125]. Following the extraction of relevant features, different categories of AI methods—i.e., supervised learning, unsupervised learning, reinforced learning, and semi-supervised learning—are used for specific applications.

The wearable devices are used in improving the player's skills in their respective sports, injury prevention and minimization, or in the form of e-skins may serve to be a mobile health-care monitoring device [123]. For instance, Chen et al. [126] developed a fuzzy logic inference system that receives data such as temperature, humidity, etc. from wearable devices and determines the wearer's heat stroke possibility. Their approach can detect the possibility of suffering from heat stroke and the wearer can be alerted in time.

Various ML have been used in the field of wearables. Saadatnejad et al. [127] suggested a novel ECG classification algorithm. On wearable devices, this method was used for continuous monitoring of cardiac disease. The advantage of this method was its low power consumption. Their method used multiple long short-term memory (LSTM) recurrent neural networks (RNNs) and wavelet transform and achieved high ECG classification performance. Hssayeni et al. [128] used an LSTM RNN to detect early signs of Parkinson's disease (PD) using accelerometers and gyroscope data. In another study, waist-worn accelerators and SVM were used to detect the freezing of gate (FoG) experienced by PD patients [129]. A comprehensive review of the applications of AI in wearables and the comparison of different ML algorithms can be found in earlier research [123]. There are several instances where wearables such as e-skin benefit from AI and non-AI techniques. One such example is denoising. For denoising, researchers have used different methods such as higher-order bandpass IR filters, deep convolutional networks, wavelet filters, statistical models, variable frequency demodulation algorithm, and adaptive mean filtering. Some of the filtering techniques have shown superiority over AI techniques indicating that AI is not always the solution for existing challenges in wearable devices.

Wearable devices that have the potential to serve as health care devices such as smartwatches, eyewear, and smart bands have been developed to derive data from monitoring heart rate, blood pressure, body temperature, physical activities, and posture. For example, wearable devices have been used to monitor patients with diabetes and connect them to their care teams for effective diabetes management [130], [131], [132]. Another typical application of e-skin-based devices is related to mental health. Choi et al. [133] detected stress patterns in children by collecting heart rate and audio signals from children and predicted the results using SVM, a supervised ML algorithm.

AI algorithms work by leveraging training data that helps the algorithm to learn. The way the data is acquired and labeled differentiates various types of AI algorithms. Fundamentally, an AI algorithm takes in training data that may be labeled or unlabeled and uses that information to learn and grow. Then, it completes its tasks, using the training data as a basis. AI algorithms can be taught to learn on their own while others need the intervention of a human. There are three major categories of AI algorithms: supervised learning, unsupervised learning, and reinforcement learning. The key differences stem from how they are trained, and how they function. Under the three categories, there are numerous different algorithms.

In supervised learning, labeled data is used to train the algorithm. It uses labeled data to predict outcomes for other data. Supervised learning algorithms can either be used for classification or regression, or both. On the other hand, unsupervised learning algorithms are given data that is not labeled to create models and evaluate the relationships between different data points to give more insight into the data. Many unsupervised learning algorithms perform the function of clustering, which means they sort the unlabeled data points into predefined groups. The objective is to have each data point belong to only one cluster, with no overlap. In reinforcement learning, a method of rewarding desired behaviors and punishing negative behaviors is utilized. This method assigns positive values to the desired actions to encourage the system and negative values to undesired behaviors. This programs the system to seek long-term and maximum overall rewards to achieve an optimal solution.

Human–robot interaction (HRI) is about establishing efficient, safe, and comfortable interactions between humans and robots [123] usually via an analog sensor medium. Although wearable devices have considerable potential applications in various domains, there are some risks/shortcomings that follow them. One such risk is data privacy. Wearable devices may have to connect to cloud services to process and store data collected by them, and thus, enforcing the privacy of patients' medical data is critical and necessary. As the trend to integrate AI and the number of devices grows, the amount of data generated also grows, thereby increasing the criticality of the privacy of patient data.

IV. AI IN MEDICINE

ML represents a category of algorithms and construction of classifiers. The algorithm automatically learns through the input data and builds a model based on the input data to accurately predict new data [134]. AI in medicine involves the utilization of ML models to search, explore, and gain insights from medically relevant data in order to help improve health outcomes and patient experiences. The utilization of ML techniques has demonstrated the potential to improve health outcomes, cut healthcare costs, and advance clinical research [135]. Owing to recent advances, AI is rapidly becoming an integral part of modern healthcare as illustrated in Fig. 8 [136]. The diagnosis of diseases is decisive for planning proper treatment and ensuring the well-being of patients. Human error hinders accurate diagnostics, as interpreting medical information is a complex and cognitively challenging task. The application of AI can improve the level of diagnostic accuracy and efficiency [137].

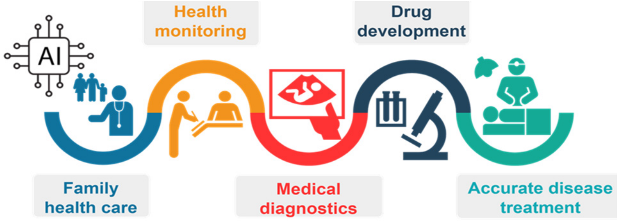

Fig. 8. Illustration of various applications of AI in medicine.

For instance, ML algorithms are able to ascertain lung cancer through CT scans, determine the possibility of cardiac attacks through cardiac MRIs, or detect skin lesions through skin images [136], including psychological symptoms such as depression through the ample amount of data, thus making these algorithms' decision prudent and effective. In fact, deep learning, which is a subset of ML, also plays an important role, especially in detection or recognition. For instance, a study conducted in 2017 [138] showed that convolutional neural networks (CNNs) were able to identify breast lesions more accurately when compared to computer-aided detection.

Another major application of AI is in the "effective" development of drugs. The development of drugs is believed to be accelerated through the utilization of AI and ML models. AI is used for the identification of target proteins through the availability of past data providing its compatibility and properties. Additionally, they are also used to predict the sustainability of the molecules based on certain parameters.

ML has the capability to augment the work of clinicians by processing the billions of patient data points that are stored in electronic health records (EHRs) [135] and it has been successfully applied in many clinical applications such as diagnosing respiratory conditions from chest X-rays and detecting early signs of lung cancer [139].

AI has been used to predict the risk of cardiovascular diseases such as acute coronary syndrome [140] and heart failure [141] better than conventional scales. Wearable technology coupled with AI has also been extensively used in the detection of neurological problems such as epilepsy wherein intelligent seizure detection devices can detect generalized epilepsy seizures and report to a mobile application, thereby alerting close relatives and trusted physicians with complementary information about patient localization [142]. Another area where AI-based systems are expected to have an impact is in robotic surgery where the surgeons are assisted by the AI system in treating the patients with precision and less pain in addition to reducing surgeon variations that could affect patient recovery. Other applications of AI are in nephrology, endocrinology, gastroenterology, pathology, and also in medical imaging [143].

AI has the potential to impact many domains and one such domain is the field of medicine [144]. It is poised to play an increasingly prominent role in medicine and healthcare because of advances in computing power, learning algorithms, and the availability of large datasets (big data) sourced from medical records and wearable health monitors. AI far exceeds human capacity and can assist the physician in surgery or diagnosis. AI and ML can make sense of massive amounts of clinical, genomic, and imaging data, thus helping to improve physician efficiency, increase diagnostic accuracy, and personalize treatment [145]. AI has also been consistently used for improving patient safety [146], improving quality of care [147], [148], and reducing healthcare costs [149], thereby making a positive impact on society.

V. CIRCUITRY SYSTEM FOR WEARABLE DEVICES

In wearable devices including e-skin, the electronic circuitry is achieved by heterogeneous integration of rigid chip components, soft thermoset polymers, and liquid (eutectic LM) materials through advanced mechanical design. In most wearable devices, off-the-shelf chip components provide high-performance sensing and monitoring of the human body, including physical motion tracking, temperature monitoring, and sensing of acoustic and ECG signals to name a few [150]. They are interconnected by intrinsically stretchable and robust liquid metal circuitry and encapsulated by a dynamic covalent thermoset polymer matrix. Enabled by the bond exchange reactions in the polymer network and fluid behavior of the liquid metal circuitry, wearable electronics can self-heal from damage and can be reconfigured into distinct configurations for different applications.

Conventional wireless e-skins rely on rigid integrated circuit chips that sometimes compromise the overall flexibility and consume considerable power. With the advancement in semiconductor processing, there exist reports of chipless e-skin. In a recent report [151], authors account for a chipless wireless e-skin based on surface acoustic wave sensors made of freestanding ultrathin single crystalline piezoelectric gallium nitride membranes. Surface acoustic wave-based e-skin seems to offer highly sensitive, low-power, and long-term sensing of strain, ultraviolet light, and ion concentrations in sweat. Integration is crucial for e-skin. On the one hand, e-skin devices only have primary signal acquisition capabilities, and external techniques involving big data, ML, and deep learning are required for complex processing and analysis processes. The development and use of miniaturized intelligent modules with stronger computing power in sensors will eliminate the dependence on rigid external devices and maximize the use of data to broaden the scope of health monitoring.

As e-skin increases in resolution, their signals could be processed to detect higher-order deformation modes and higher-level notions about the environment. However, obtaining this information requires algorithms that can extract useful information from large quantities of data. To handle the vast amount of data that e-skins can provide, ML is emerging as a versatile tool for making sense of large quantities of data [152]. For example, Piacenza et al. [153] obtained high-resolution data from a robotic fingertip and used ridge regression to process this data to estimate the locations of indentations. Similarly, Larson et al. [154] used CNNs to learn deformations on a sensor array that can interpret human touch in soft interfaces. In addition, researchers have also focused on recurrent neural networks, which have been shown to be advantageous for learning patterns in time series data [155], [156].

VI. CONCLUSION AND FUTURE SCOPE

In summary, e-skin is an artificial skin fabricated using different materials and structural designs. For practical applications, e-skins must be flexible, stretchable, multifunctional, mechanically stable, and could be prepared in large areas at a low cost. Graphene-based materials are most suitable for meeting these requirements. Among the different methods to produce graphene, graphene-based on LIG [157], owing to its porosity and 3-D structure, is a desirable material for wearable sensors. However, the laser induction method is challenged by several issues that require potential research attention.

1) The formation of a uniform honeycomb-like carbon arrangement is inhibited by the accompanying inevitable generation of unconverted amorphous carbon. A purification method is additionally required as substrate impurities in LIG influence its performance. The development of a comprehensive understanding of the conditions of laser induction and the structure of graphene is key to avoiding the formation of amorphous carbon and meeting sensing requirements.
2) Sensitivity and repeatability are key performance indicators of e-skin-based biosensors. Usually, LIG in strain sensors serves as a framework when combined with polymers, and for chemical sensors, LIG acts as a supportive base. Larger LIG sheets in such sensors are preferred for good repeatability of e-skin and therefore conductive, porous, and 3-D nature of LIG should be exploited to make high-performance sensors.
3) For monitoring physiological parameters and tracking motion (fingers, hands, knees, and legs), the e-skin attached to the body parts often undergo bending and deformation. LIG layer and most reported substrates like PI are known to have poor adhesion and LIG can easily be worn off from the substrate by even slight scratching, hence, LIG is not preferable for e-skin tracking motion [158]. One way of overcoming this issue is substrate transfer which coupled with appropriate device conformation can yield e-skins for tracking movements.

E-skins equipped with tactile sensors have already shown surpassed capabilities over biological skins in terms of heart pulse monitoring and ECG recording. Fabrication of e-skin has inherent challenges as follows.

1) First, the sensors used are conventional and have a narrow responsive range. Hence, e-skin equipped with highly sensitive sensors is a niche in wearable technology research.
2) Second, the integration of different sensors that are either piezoelectric, capacitive, or triboelectric is necessary to achieve multifunctional e-skins. Therefore, e-skins with a common platform that could accommodate the different sensing mechanisms are highly desirable for effectively mimicking human skin.

3) Third, flexible electronics are an inherent requirement of e-skins and to realize their full potential the existing rigid, planar electronics must be made flexible. The use of nanomaterials is a potential solution in this area [7].
4) The lifetime of e-skin-based wearable devices is dependent on chemical stability and mechanical durability. Tremendous improvement in the sensing performance with appreciable durability is the need of the hour.
5) To achieve economic fabrication of e-skins, the printing of non-planar sensors is a potential pathway yet to be explored fully.
6) From the medical perspective, the biocompatibility of wearable devices is imperative; however, this arena still lacks significant research attention.
7) Self-powered e-skin is a novel strategy to achieve sustainability targets by minimizing energy usage. The large area low-cost assembly of e-skin requires immediate attention, and this coupled with flexible and integrated electronics can revolutionize medicine and health care and enhance human–machine interface.

On the whole, future research should be directed at fabricating flexible, stretchable, self-powered, and self-healing e-skins to couple sensitivity with device lifetime. In addition to these, the focus of future research on enhancing skin compatibility, resistance to bending, and the development of miniaturized multisensing platform-based e-skin can bring biosensing under the limelight.

AI is changing the way we view conventional methods of treatment along with its varied operations, thereby helping to improve everything from routine tasks to data management and drug creation. The field of medicine has always chosen every opportunity for improvement and evolution and is currently opting for ML and AI to be utilized in most of its tasks such as diagnosis, drug creation, clinical trial efficacy, detection, patient care, risk management, etc. Although AI is rapidly expanding, it has some limitations/disadvantages. One of the major inherent limitations is the data, specifically "data bias" [159]. Training of ML models require data on a large scale, especially those applications that concern with detection and diagnosis. If, for instance, the data so acquired reflects only a certain specific population of people, then it may not be suitable for a general population, thereby yielding inaccurate results. Another scenario where data bias can occur is when the AI model is provided with incomplete or insufficient data, in which case, specific clusters may not be addressed appropriately.

Developing ML models requires well-structured training data about a phenomenon that remains relatively stable over time. A departure from this results in "over-fitting", where AI gives undue importance to spurious correlations within past data. In 2008, Google tried to predict the seasonal prevalence of influenza using only the search terms entered by its search engine. Because people's searching habits change dramatically with every passing year, the model was so poorly predictive of the future that it was quickly discontinued. Additionally, data that are anonymized and digitized at source are preferable, as this aids in research and development [13].

Another concern is the replacement of doctors by AI. Smart medical technologies mostly exist to assist the physician in attending to the patient, thereby improving patient management and not replacing him entirely. Physicians are still needed for traditional physical exams, especially in areas such as neurology, which require high-level patient-physician interaction and critical thinking [162]. Even though there have been recent studies indicating that solutions provided by AI and physicians differ in perspective [163], the possibility of replacement is not entirely true or possible in the present day.

Overall, future potential lies in the fabrication of low-cost large-area smart skin, and graphene owing to its structural features is a proven material for fabricating multifunctional e-skin-based wearable devices that have tremendous potential in biomimetics. Aided with AI and ML e-skins can advance the existing medicine and healthcare to an extent beyond human capabilities and reach.

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