Review of Recent Advances in Non-invasive, Flexible, Wearable Sweat Monitoring Sensors

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Abstract: Wearable health-monitoring devices are novel and integral developments based on smart-textiles. Conventional wearable technology consists of micro-controllers and a variety of electronic devices embedded on the skin, or incorporated into the apparels, where they act as signal receptors, analytical devices and transmitters of the signals generated from the human body. Invasive methods are currently more commonly practiced where biofluids are obtained by penetrating the body by incision or injection, while in non-invasive methods no such penetrations take place. A critical review of current non-invasive wearable technology, including colorimetric, enzymatic, pH based, electrochemical and conductivity sensors, is presented in this paper along with the challenges and limitations they pose. Additionally, novel techniques of analysis have been explored concluding that a textile-based medium offers higher compatibility for integration of such sensors in comparison to other existing substrates.

Key words: Smart-Textiles, Biosensors, Non-invasive Sampling, Wearable Electronics

1 Introduction

1.1 Autonomous Non-invasive Sampling Necessity

As in all analytical methods, for both continuous and non-continuous health-monitoring, access to a representative sample is vital [1]. Conventional, wearable health monitoring and tracking devices use invasive sampling methods and non-invasive sampling methods to collect and analyze bio fluids of the human body. Invasive methods include sampling of bio fluids such as blood, cerebrospinal fluid whereas non-invasive methods use biofluids such as sweat, tears, saliva and skin interstitial fluid that are naturally excreted from the human body [2]. However, limitations exist in invasive sampling, including infections resulting from frequent sampling, being more prone to defilement, limited storage period and difficulties in continuous monitoring [3]. In addition, the intrusive nature of these sensors poses a risk to the patient, especially with neonatal, and elderly patients suffering from hemophobia, thus consequently impeding the process of obtaining patient data that is desired for diverse biomedical applications [2].

Saliva, tear, sweat and skin interstitial fluid have been investigated through literature as alternative non-invasive sampling methods as opposed to invasive sampling methods including blood and urine [2]. “Sweat” or the action of “sweating” is a physiological process that provides evaporative cooling of the skin as necessary to regulate the body temperature [4]. While 99% of sweat constitutes water, it also consists of many different inorganic and organic bio chemical compounds including mineral salts, ammonia, urea, lactate, glucose, cortisol, uric and ascorbic acids, amino acids, lipids, proteins, peptides, metal ions, inhibitors, antibodies, and a variety of xenobiotics [5, 6]. Therefore, as a bio-fluid, sweat has the potential to offer a broad diagnostic value in clinical medicine, military medicine, and sports science as it can be locally and non-invasively induced [3]. Thus, the above limitations have been overcome with sweat, tears, and urine sampling, which are non-invasive sampling methods, as these bio fluids have been found to be excellent analyzing media and health indicators.

1.2 Bio-medical Validation of Non-invasive Sweat Sampling for Health-monitoring

Various experiments have been conducted in the previous decades involving athletes and non-athlete personnel to determine an existing correlation and draw parallels between components of sweat and their corresponding concentration levels in blood. These experiments involve heated conditions, sprinting, cycling, vigorous exercises and tennis matches [1], [7–12]. Certain components such as sweat ammonium and lactate levels have been established under these conditions, since sweat, unlike blood, has a very low protein content (0.20 to 0.77 g l-l), and is therefore a better component for continuous monitoring [8]. Moreover, on-body assessment of sweat Calcium ion concentration and pH has been performed with a 5 min ramp-up and a 20 min biking at a power of 150 W, followed by a 5 min cool-down session, where sweat pH was observed to increase gradually mainly due to a decrease of lactic acid concentration in sweat and then stabilizing [13]. In addition, co-relations between the concentrations of the components, including electrolytes, in blood and sweat have also been established through medical research [12]. Further, a statistically significant correlation between Sweat Glucose and Blood Glucose in a group of subjects with diabetes have been recognized through experimentations with obtaining data as the sweat rate varied over a ten-fold range [14].

Mostly, the stimulations of sweat sampling have been based on active perspiring individuals, such as athletes and workers, but studies have revealed that sensing of sweat analytes could be performed over one time sampling and beyond active perspiring individuals with continuous sweat access in individuals at rest [15]. On that ground, different sample preparation strategies have been demonstrated to maximize the metabolite detection of sweat using human excreted sweat collected after moderate exercising. The sweat collection had been performed by excluding use of deodorants, perfumes and cosmetics one day prior to sweat collection, where active sweat was sampled by different body areas (forehead, chest and back) after moderate exercise of 30minutes, whereas passive sweat has been collected using sweat analyzing system from individuals at rest, concluding that a sample preparation is required before analyzing low molecular weight compounds (direct analysis was a failure) and that Dichloromethane is recommended as the solvent to extract non-polar and polar compounds from sweat [16]. Moreover, human trials have been conducted to detect dehydration and it was able to detect in less than an hour of relatively heavy exercise when combined with fluid restriction [17]. Hence, through literature, sweat can be established as a satisfactory bio indicator.

Moreover, the mechanism of the nervous system that regulates the secretion of sweat is acutely sensitive and extremely precise [4], thus meeeting the above requirements of non-invasive sampling, researchers have identified and established sweat as a suitable non-invasive bio marker, since the sweat constituents have been testified as indicators of different physiological conditions through literature as demonstrated in Table 1.

Many researchers have prepared artificial sweat solutions according to the Standard ISO 3160-2 (20 g/L NaCl, 17.5 g/L NH4OH, 5 g/L acetic acid and 15 g/L lactic acid) to simulate the sweat response [26]. However, specific extraction of each of these components have been conducted using Ion Selective Electrodes (ISE) to capture ionic components [19, 27], and by using bio enzymes such as Lactate Oxidase [8, 28, 29] and Glucose Oxidase [29–32] to capture organic compounds present in sweat for analysis.

Table 1 Sweat Components and Their Corresponding Physiological Response

Component	Physiological Response
Alcohol	Increase triggers hypoglycemic glucose levels [18].
Ammonium Ions	Increase is related to an increase in anaerobic metabolism, which involves the glycolysis pathway and purine nucleotide cycle (PNC) [8].
Calcium Ions	Excessive accumulation in bio-fluids affects the function and structure of human body, causing myeloma, acid−base balance disorder, cirrhosis, renal failure, and normocalcaemic hyperparathyroidism [13].
Chloride Ions	Potential indicator of Cystic Fibrosis where presence of potential fibroids results in an above 60mM concentration level of Chloride ions in sweat [19].
Cortisol	Cortisol is released in response to stress and low blood-glucose concentration. Excess release increases blood sugar through gluconeogenesis, suppress the immune system, and aid in the metabolism of fat, protein, and carbohydrates while also decreasing bone formation. This can also be used to diagnose Cushing's syndrome and Addison's disease [20].
Glucose	Diabetes and accompanying complications including cardiovascular and kidney diseases, stroke, blindness, and nerve degeneration [21].
Lactate	Lactate concentration levels is an indicator of physical exhaustion levels pressure ischemia and formation of pressure ulcers. It is also important for diabetes control and sports medicine [8], [11], [22].
Immunoglobulin-A	Plays a major role in immune defense mechanisms [23].
Sodium Ions	Holds a key role in the ionic equilibrium of body fluids and has a strong co relation between heart rate, sub-lingual temperature, and sweat rate. Patients with Addison's disease admitted to the hospital with severe deoxycorticosterone acetate intoxication have demonstrated abnormally low concentrations of sweat sodium and chloride, which could in turn be used as a potential indicator of the disease [5, 12].
Urea, Uric Acid & Creatinine	Uric Acid has been found to be a risk factor for cardiovascular disease, type 2 diabetes2, renal disease, and gout [24].
Zinc Ions	Change in zinc concentration in bio fluids is related to muscular damage and immune damage due to physical stress [25].

1.3 Limitations and Challenges of Using Sweat as an Analytical Medium for Bio-sensors

Several challenges persist when using sweat as an analyzing medium. Challenges include irregular or low sweat generation rates during exercise, susceptibility of contamination with skin (bio) markers; cross contamination from old sweat, irreproducible sample transport over the detector surface, and lack of control of sample evaporation and volume [7]. Other challenges include prevention of cross contamination and enabling evaporation after the analysis, and avoiding potential microbial growth on the accumulating surface [3]. Furthermore, sample collecting may also present itself as a concern. Studies have shown that measurement of ionized calcium for clinical applications is not easily accessible due to its strict procedures and dependence on pH, therefore collection, measurement and analysis is required to be conducted under prescribed pH conditions [33]. Moreover, certain substantial variations may also present itself depending on the individual. Medical studies have concluded that the secretion of sweat chloride ions may vary from person to person, and the frequency of clinical diagnosis of Cystic Fibrosis may change especially within the intermediate range of 30-60mM [19]. On the other hand, literature presents instances where a correlation between the concentration of the constituent in blood and sweat cannot be established. [30] has stated that their research has concluded that an individual's blood glucose changes are not consistently matched by sweat glucose changes and that fasting sweat glucose levels do not strongly correlate with fasting blood glucose levels. [34] also follows this perception from a medical point of view, concluding that sweat uric acid concentration is minimal, and hence may be insignificant for comparison across individuals. However, it does not bar the possibility of more complex, individual-specific correlations [30].

1.4 Overcoming These Challenges through Application of Wearable Technology

An ongoing proliferation persists in the field of developing wearable biosensors for non-invasive monitoring of chemical/biological markers. Tech giants, including Apple and Google, are currently exploring avenues to access biochemical data, to move beyond the mature sensor technologies currently employed in exercise and sports, which are based on physical transducers or imaging technologies embedded within smart devices [1]. Wearable electronics itself has developed over the years and is at the brink of commercialization with products such as Lifeshirt®, Vivometrics®, Bodymedia® a body monitoring system, and the Nike Apple iPod Sports Kit that facilitates controlled individual feedback on performance during exercise [35]. With wellness devices being recognized as such, commercially, one basic challenge that needs to be addressed is the requirement of continuous, non-invasive monitoring of bio chemical markers to determine current physiological status as well as to detect underlying chronic health conditions [18].

2 Investigation of Wearable Bio-sensor Technology

2.1 Colorimetric Analysis

Earlier literature studies have demonstrated whole body wash down techniques after a rigorous physical activity [4, 8, 26]. However, this cannot guarantee high accuracy, and can also be regarded as an invasion of privacy. Other sampling methods include skin patches attached to adhesive membranes [36], textile based [37] with colorimetric analysis techniques. Colorimetric analysis determines the concentration of the compound using a color reagent. Nevertheless, these systems are not able to provide real-time data since there is a substantial delay between data collection and analysis [26]. Furthermore, risks involving cross contamination of the samples, during sample handling and analysis [26], issues such as inability to quantify sweat volume, inability to extract and store sweat for further analysis [3], exist in this method. On the other hand, colorimetric analysis is simple and cost effective [3]. Moreover, colorimetric analysis has also been incorporated into miniature cartridges that can be inserted into smartphones, together with a luminometer for analysis. To the contrary, background florescence and light scattering present in smart phones exist as key challenges that need to be addressed regarding this methodology [22].

2.2 Enzymatic and Electrochemical Analysis

One major requirement of a wearable electrochemical sensor is its ability to selectively discriminate and measure target components [13]. Literature presents instances where electrochemical analysis has been coupled together with or without enzymes, as presented in Table 2.

The use of portable electroanalytical techniques in sweat-based wearable technology includes amperometric, cyclic voltammetry, Chrono ampero-metric, and Electrochemical Impedance Spectroscopy (EIS) [20]. However, the use of enzymes has demonstrated issues in some instances. [15] states that a stimulation of sweat ethanol with enzymatic analyzing has been left with two unsolved disputes including where the rapid increase and gradual decay in sweat generation rate with time which had obstructed prolonged monitoring and unpredictable analyte dilution due to hydrogel reservoir where the enzymatic sensor is located.

2.3 pH-based Analysis

By way of an alternative, pH is an easier to

Table 2 Developments Associated with Enzymatic and Electrochemical Analysis

Development	Reference
Paper based microfluidic electrochemical glucose biosensor on RGO-TEPA/PB sensitive film	[38]
3D micro patterned stretchable substrate	[39]
Three-dimensional paper-based microfluidic electrochemical integrated devices (3D-PMED) for wearable electrochemical Glucose detection	[9]
Development of a wearable electrochemical sensor for voltammetric determination of Chloride ions	[40]
Epidermal microfluidic electrochemical metabolite detection	[7]
A stretchable and screen-printed electrochemical sensor for Glucose determination	[41]
Skin-attachable, stretchable electrochemical sweat sensor for Glucose and pH detection	[42]
Flexible and ultrasensitive electrochemical biosensor for sweat Glucose detection	[10]
A wearable electrochemical platform for noninvasive simultaneous monitoring of Ca^{2+} and pH	[13]
Dual signal amplification of Glucose Oxidase-functionalized nanocomposites as a trace label for ultrasensitive simultaneous multiplexed electrochemical detection of Tumor markers	[43]
A wearable electrochemical sensor for the real-time measurement of sweat sodium concentration	[44]
Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module	[21]
Ion sensor for the quantification of Sodium in sweat samples	[45]

measure physiological parameter in sweat [26]. The analysis of the acidic nature of human excreted sweat, which corresponds to the pH measurement, dates back over a century where in 1892 Heuss outlined the acidic nature of the skin. Preliminary analysis has concluded that Acute eczema with skin surface erosion, Seborrheic dermatitis, Atopic dermatitis and Xeroderma is caused due to fluctuations in pH levels of the surface of the skin due to excreted sweat [46], hence facilitating pH monitoring as both an indicator as well as an analysis technique. In addition to that, pH is not heavily influenced by ambient temperature and measuring reagents (if used), and interferes minimally with complex bodily fluids [13].

Moreover, literature studies have demonstrated successful incorporation of pH sensitive dyes unto textile substrates [26], barcode systems using ionic liquid polymer gels [35], ISFET (Ion Sensitive Field Effect Transistor) membranes [47], and other wide range of substrates to evaluate the change in pH conditions of body sweat. Therefore, pH analysis techniques can be considered as a suitable approach to monitor sweat components, however, certain limitations exist in this regard. The concentration change should be sufficient to trigger a response in the pH level and the components should be of acidic or basic nature. On the other hand, a pH sensitive reagent can be introduced to the substrate itself, without incorporating additional devices, with real-time analysis data accessible through the process itself [26, 47], which is an added advantage over colorimetric analysis techniques. Thus, the pH analysis technique can be considered congruous with real-time sweat monitoring of acidic and basic components. Hence, the requirement of a technique for monitoring neutral components, and components with a small variation in the pH values can be considered still prominent.

2.4 Conductivity Based Analysis

A real time sweat analyzing system for artificial and human sweat based on alternating current conductivity has been developed with an efficient sweat collecting and detection system for dehydration based on 3D printing. Further studies have provided theoretical and experimental factors on the electrical and chemical behavior of artificial sweat with various concentrations within a temperature range of 50C - 500C [17].

This research presents that, in this system, the impedance measurement of solutions has been obtained using parallel-plate copper electrodes using the principle that when an electrode is immersed into an electrolyte solution, a layer is formed on the electrode surface from the adsorbed ions defining the inner Helmholtz plane (IHP), with the diffusion of ions occurring at the outer Helmholtz plane as represented by Warburg Impedance. Conductivity values required for the analysis has been obtained by conductance measurements with cell constant calibration and the respective values of different solutions have been plotted relative to the lowest concentrations predefined for each component establishing the relationship between relative concentration and conductivity and the results of the research is presented below in Fig 1.

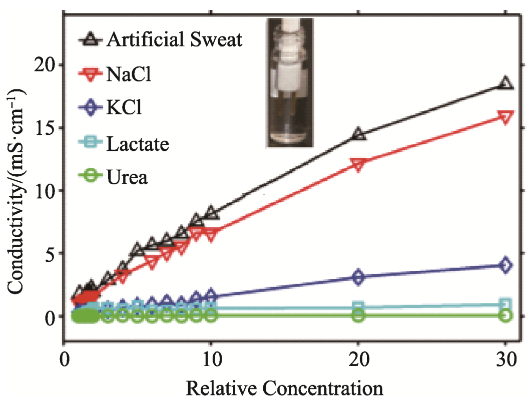

Fig.1 Relationship between Relative Concentration and Conductivity [17]

Furthermore, [17] has revealed that the conductivity of an ionic solution is partially dependent on the temperature which varies according to the surrounding weather conditions. As the mobility of ions increases while the viscosity decreases when temperature increases where both factors increase the conductivity.

Literature presents several methodologies of imparting conductivity directly to a textile including in-situ polymerization [48], coating using a conductive polymer [49] and electrospinning/spraying using a conductive polymer [50–55]. Screen printed sensors, graphene ink based printed sensors and coated textiles are susceptible to mechanical and chemical degradation over time [2]. Therefore, imparting conductivity to the textile is expected to be conducted through electro spinning where the surface areas of the bio sensors can also be improved by introducing Nano porous structures, [42] in addition to incorporating conductivity to the surface.

Micro controllers can be successfully used for such conductivity analysis, while replacing them with a specific controller; “Lilypad Arduino” has been specifically designed for wearable applications since it consists of pins that can be stitched to, using conductive threads [56].

Moreover, Internet of Things (IoT) platforms have emerged as a class of rapidly evolving embedded technologies that interconnects everyday objects in the environment with sensors using internet to create application specific solutions for remote, real-time monitoring as any contribution to IoT and rendering a service from IoT requires synergetic activities [57, 58]. IoT has primarily made its way into the bio-sensing applications market through continuous self- tracking of health indicators [59]. Therefore, the integrated data of a wearable devices have been aggregated on IoT platforms, to facilitate continuous monitoring [18].

3 Investigation of the Flexible Substrates Used in Incorporating Bio-sensor Technology

3.1 Application of Smart Textiles in Biosensors

Textiles have been recognized as a promising platform for the integration of wearable chemical sensors due to their inherent breathability, flexibility, softness and comfort [60]. This multifunctional interactivity, enabled by smart textiles, promotes a higher quality of life and progress in biomedicine, as well as in several health-focused disciplines, such as biomonitoring [61], telemedicine [62, 63], teleassistance [64-66], ergonomics [67], rehabilitation [65, 68] and sport medicine [69].

Consequently, textiles have been functionalized as smart textile sensors [70], as substrates for electro chemical devices [60], to incorporate Nano-spider technology as wound dressings and filter mediums [71], as potentiometric pH sensors [72], for textile based bio mechanics [73] and smart wound dressings [74], to be successfully utilized in the bio medical industry.

The advantages in application of smart textiles include the ability to impart desirable properties through selection and functionalizing of fibers, yarn spinning methods, fabric construction methods and fabric finishes. Such fiber functionalization has been presented in literature, including the development of Textile organic electrochemical transistors (txOECTs), where the selectivity of a textile biosensor has been improved by directly functionalizing the textile device with ion selective membranes through consecutive functionalization of the textile fiber [70], and the application of fiber-based implants (BTFIs) such as silk-based biomaterials (SBBs) for extracorporeal implants, soft tissue repair, and healthcare/hygiene products [75], as demonstrated below in Fig.2 (a), (b) and (c).

On the other hand, the fabric construction method, such as knitting and weaving technologies, have been used to develop textile-based wearable electrochemical devices that can be incorporated onto T-shirts and other apparels and to develop multiplex patch-based chemical sensors assembled into a textile, which exhibited excellent sensing performance by the hierarchical woven and porous structures [60].

Therefore, it is evident through literature that a textile possesses the capacity to be adapted and developed according to the requirements of a wearable sensing device, after adapting suitable techniques for incorporation onto the garments.

3.2 Adaptation of Smart Textile-based Substrates onto Wearable Devices

In terms of wearable substrates paper based analysis has become popular due to less sample consumption, rapidness, miniaturization, and low cost. However, paper based analysis is limited to colorimetric, electro-chem-luminescence, chem- luminescence and surface based Raman spectroscopy [38]. Therefore, real time in-situ analysis based on conductivity, which the current research is based on, cannot be proclaimed on a paper based approach. Nevertheless, fabrics can be considered as a suitable substrate due to excellent contact with the skin, which could be enhanced by developments of the textile. The large surface area also provides ample space for integrating supportive electronics [40].

Moreover, a textile substrate has many advantages including ease of manufacture, economical adaptability, compatibility with human skin and ease of incorporation into apparels [61]. Furthermore, Cotton, Wool and Nylon have proven to offer a wide variety of physical and chemical properties, favorable for bio chemical sensors [2]. Literature studies have presented several low cost textile-based electrochemical senses, that have utilized these favorable attributes. Besides, , textile substrates that have been used for developing wearable sensors consists of other inherent properties, in addition to those expected as a substrate material. These properties include a combination of moisture wicking properties and moisture absorbency [56].

Moreover, textile based structures can be utilized to create micro-fluid structures within the substrate [76, 77] as presented in Fig.3. The use of microfluidics enhanced the bio-fluid sampling process and achieved higher temporal resolution for wearable sensing by constantly supplying newly secreted bio-fluids to the sensor [24], therefore achieving this through the application of a textile substrate has been conducted in many researches.

Nonetheless, studies have revealed that the use of textiles in the field of wearable body-fluid monitoring devices is limited. This may be due the requirement of certain optimal properties of the substrate, including possessing inert properties, non-interference with the electrochemical behavior of the analyte [40], and the ability to generate a response based on colorimetric, amperometric or electric signals and triggers [7, 36, 40, 61]. Therefore, many textile-based devices have required external detection systems or external triggering systems to indicate a response upon receiving biometric data.

Moreover, fabrics are an excellent substrates to be developed as wearable sensors due to their durability, lightweight and its various physical and chemical properties, which could be utilized with electrochemical sensors [61, 78]. Most of the textile based electrochemical sensors are screen-printed onto various fabrics where the effect of various fabrics on the print quality and the analytical responses of the printed sensors have been examined under different conditions of mechanical stress and washing [78]. Researches have been conducted with healthcare monitoring electrochemical amperometric sensors printed directly on the elastic waist of undergarments and has detected positive responses and measurements [79]. In addition, textiles have proved to have excellent microfluidic capacities. Voids between fibers form capillary channels that facilitate liquid flow without the requirement of external pumping [77]. Researchers have used woven cotton cloth which have been considered to have wettability and hydrophilicity due to the porous

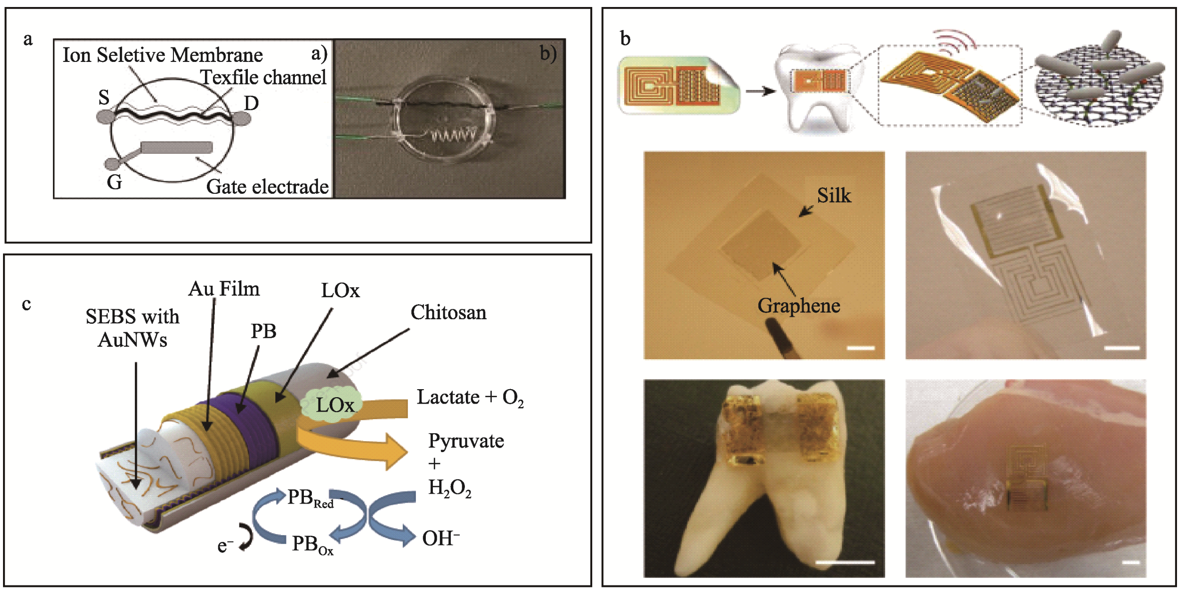

Fig.2 Textile Integrated Health Monitoring Devices (a) Textile organic electrochemical transistors [70], (b) Dry spun Gold fiber as a Lactate sensitive electrode [60], (c) A schematic and real image of a wireless tattoo-based resistive sensor for Staphylococcus aureus [2]

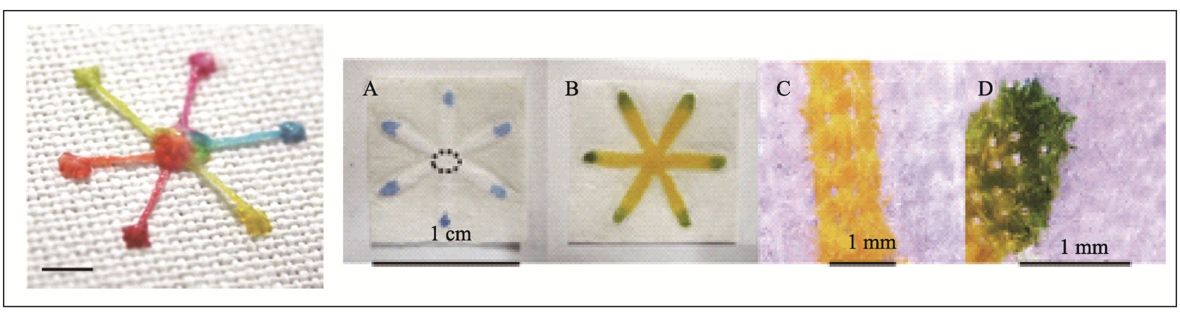

Fig.3 A Multi-inlet–single-outlet Design Fabricated Using Hydrophilic Cotton Yarn on a Superhydrophobic Textile [36]

structure of cloth formed by the gaps between the woven threads, demonstrating that this porous structure is sufficient for providing capillary force and rapid wetting and wicking [80], which is essential for collecting body fluids for health monitoring.

4 Investigation of Flexible and Wearable Device Technology

4.1 Classification of Recent Advances in Wearable Bio-sensor Technology

Different techniques and developments have been introduced to overcome several concerns that have been posed. Literature presents such research conducted on sweat analysis using a wide variety of different analyzing techniques that include calculating the sweat rate through a fabricated capacitive sweat sensor by measuring the capacitance vs voltage [81], measuring the volume and the chemical properties of sweat using dielectric detection, and also using colorimetric demonstrations, while using capacitive electrodes integrated with flexible and stretchable wireless sensors [82], using soft epidermal microfluidic devices for sweat monitoring have been developed to capture and store sweat for colorimetric analyzing [83], using fluorometric analysis integrating an imaging module which could be paired with a smartphone to measure the sweat content (chloride, sodium and zinc concentrations) [84], developing stretchable wireless sensor patches based on electrochemical analysis [31] and many other novel methods.

As of recent, the developed methods with the highest sensitivity per sweat component have been compared below in Table 3.

Furthermore, these devices possess unique technologies, such as water proofing techniques to facilitate use in aquatic and arid systems [12] as demonstrated micro fluidic channels with fluorescent probes to react separately with sweat components [86], and battery free wireless electronic sensing platform based on biofuel cells which integrates chronometric micro-fluid platforms to detect sweat rate, pH, lactate, glucose and chloride, where data transferred through NFC electronics, as shown in Fig.4.

4.2 Limitations and Challenges of Existing Wearable Devices Used for Non-invasive Sweat Monitoring

Literature has indicated several affairs that contribute negatively to the performance of existing sweat monitoring devices. According to the conducted literature survey, most wearable microfluidic platforms are based on silicone elastomers, which require complicated fabrication processes and expensive microfabrication facilities [11, 24, 86]. Moreover, sweat based Glucose sensing using Glucose Oxidase itself presents several challenges including activation of Glucose Oxidase due to Lactic acid secretion, surrounding temperature changes, mechanical friction causing the enzyme to delaminate and deformations of the skin [21]. Neverthless, studies on sweat Uric Acid, and their use for dynamic health monitoring and personalized intervention has not been investigated, since the task at hand has been considered challenging because of their low concentrations [24], and several researches have been conducted to find solutions for the elimination of the challenging factor of using sweat sensors in aquatic or arid environments. Researchers have discovered materials and designs for waterproof microfluidic systems for sweat patches to enable sweat collection, storage and analysis even in aquatic environments using laminated structures [87]

Other challenges include device resiliency, long term stability and bio compatibility, where additional issues are faced by textile based sensors of which washing exerts mechanical, heat and chemical degradation. Moreover, target analytes may require bio affinity protocols, which could be overcome through in vitro with s sensors being subjected to harsh conditions. Literature suggests further challenges including ability to detect low bio marker levels, powering the wearable device, where the latter has been addressed through wearable biofuel cells, piezoelectric energy harvesting, and thin film batteries [2].

Table 3 A Comparison of Developed Sweat Analyzing Devices

Sweat Component	Substrate	Method of Detection	Sensitivity
Alcohol	A gold Zinc Oxide (ZnO) thin film electrode stack has been fabricated on a flexible substrate	Immobilization has been achieved by incorporating enzyme complexes specific for alcohol detection on the Active ZnO region. The bio molecular interactions occurring at the electrode-surface interface have been detected by the changes in the impedance and capacitive currents, occurring as a result of charge modulation [18].	0.01mg/dl [18]
Calcium Ions	A flexible printed circuit board has been used.	Detection has been achieved through a disposable and flexible array of Ca^{2+} and pH sensors. An inductively coupled plasma-mass spectrometry technique and a commercial pH meter has been used for validation [13].	0.25Mm [13]
Chloride Ions	A flexible sweat patch has been used	Detection has been conducted through a reference electrode and an array of chloride selective electrodes. The chloride sensitive electrodes have been produced by screen printing AgCl paste on a polyethylene terephthalate (PET) substrate [85].	0.001M [85]
Cortisol	Uses MoS2 Nano-sheets and a Nano-porous flexible electrode system.	The MoS2 Nano-sheets have been surface functionalized with cortisol antibodies to develop a biosensor and sensing has been achieved by measuring impedance changes associated with cortisol binding along the MoS2 Nano-sheet interface using electrochemical impedance spectroscopy [20].	1ng/ml [20]
Glucose	Adapts a three-dimensional paper based micro fluidic device	Detection has been conducted through fabricating wax screen-printed layers of cellulose paper and a PET glucose sensing screen-printed integrated device. The corresponding glucose levels have been measured by an amperometric device[9].	0.1mM [9]
Lactate	An amperometric enzyme based highly flexible sensor	Consists of a highly flexible laminate with highly porous Polycarbonate membranes providing lateral support to the Lactate Oxidase enzyme, immobilizing through cross linking. Flexibility of the laminate has been achieved through using a Polyamide substrate [11].	1mM [11]
	Technology has been incorporated into a smart phone	Detection has been achieved with the technique of chemiluminescence.3D printing technology has been utilized to manufacture a disposable cartridge that can be inserted into the phone. An enzyme coupled reaction using Lactate Oxidase has been used for the luminometer to detect the presence of Lactate [22].	0.1mM/l (0.9mg/dl) [22]
Sodium Ions	A watch format in which platforms are designed to be securely attached to the skin using a Velcro strap.	Sweat enters into the device and passes over solid-state sodium-selective and reference electrodes and into high-capacity adsorbent material. The liquid movement is driven by capillary action, and the flow rate through the device can be mediated through variation of the width of a fluidic channel linking the electrodes to the sample storage area [1].	0.1mM [1]
	A microfluidic component that is embedded with ion-selective sensors on a flexible plastic substrate	Sampling is achieved by sweat flowing into the microfluidic device, governed by the pressure induced by the secreted sweat, electrochemical detection via a defined sweat collection chamber and a directed sweat route [86].	1µl/min [86]
Urea, Uric Acid & Creatinine	A laser-engraved sensor for simultaneous sweat sampling, chemical sensing, and vital-sign monitoring	A laser-engraved graphene-based chemical sensor (LEG-CS) has been used for monitoring low concentrations of Uric Acid with multiplexed LEG-based physical sensors (LEG-PS) for monitoring temperature and respiration rate and a laser-engraved multi-inlet microfluidic module for dynamic sweat sampling [24].	0.74µM [24]

Fig.4 A Battery Free Wireless Electronic Sensing Platform [67]

5 Conclusion

A variety of different sensor embedded technologies have been used to develop wearable non-invasive health monitoring devices, since invasive sampling consists of difficulties such as, infections from frequent sampling, being more prone to defilement, limited storage period, and difficulties in continuous monitoring which can be eliminated through non invasive sampling of human excreted saliva, tears and sweat.

Colorimetric, electro chemical, enzymatic, and conductive sensors have been developed with an array of different sensitivities to different components present in such excreted body fluids. These devices have been coupled together on different substrates including films, paper, and textiles. The devices that have been developed so far, consist of inherent capabilities as well as limitations, that are yet to be addressed through advancements of wearable technology.

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