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Review

A Review on Wearable Sensors for Sodium Detection in Human Sweat

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Abstract- Wearable Potentiometric Ion Sensors (WPISs) have emerged as a highly promising analytical tool that amalgamates advancements in chemistry, materials science, and electronics to provide essential physiological insights during various human activities. The remarkable capability of seamlessly integrating these analytical devices into everyday wearables, such as sweatbands, patches, and garments, without causing any discomfort to the wearer, has transformed WPISs into indispensable tools for both monitoring health parameters and enhancing athletic performance. Recent research has demonstrated a significant role for WPISs in tracking critical biomarkers, including sodium, potassium, calcium, magnesium, ammonium, and chloride, which are present in relatively high concentrations in sweat. The utilization of these innovative devices empowers us to continuously monitor patients' well-being and optimize athletes' performance. In this comprehensive review, we delve into a plethora of studies concerning wearable sensors designed for sodium detection and explore the latest materials utilized in the development of sodium-sensing wearables.

Keywords- Ion-selective electrodes (ISEs); Non-invasive monitoring; Potentiometric sensors; Wearable potentiometric ion sensors (WPISs)

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1. INTRODUCTION

The evaluation of human biomarkers via blood samples is a common practice; however, it can pose challenges because of the invasive nature of sample collection and the limited willingness of subjects to participate, particularly when blood collection is considered uncomfortable or problematic. Additionally, this method requires the presence of a skilled healthcare professional and access to costly centralized laboratory equipment [1–3]. Alternatives including sweat [4,5], saliva [6–8], tears [9], and urine [10] have been recognized as easily accessible bodily fluids that can provide critical healthcare information.

On the other hand, one of the challenges in healthcare, sport, and exercise, is the need for real-time and non-invasive monitoring of biomarkers for detecting disorganized human performance and health issues. Recent advances have been made in the development of sensors for noninvasive and least invasive real-time analyte monitoring. For instance, many efforts are currently underway to commercialize non-invasive biosensors, focusing on minimally invasive glucose sensors. Glucowise/MediWise (blood glucose, finger clip) and Noviosense (tear glucose, placed in the lower eyelid) can be mentioned among these devices [11].

What is commonly referred to as "wearable biosensors" is a portable electronic gadget that incorporates sensors either on the surface or inside the human body including tattoos, gloves, clothing, or implants. In conjunction with other electronic devices, these biosensors provide real-time monitoring, collect data, assist in data analysis, and interactive communication between medical professionals and patients, facilitating seamless exchange of information in both directions [12]. Innovative wearable technologies have been created to non-invasively assess athletes' performance thresholds in sports and challenging environments. Additionally, these devices serve the dual purpose of diagnosing and tracking conditions marked by metabolic imbalances in analytes, such as diabetes mellitus and cystic fibrosis [2].

While considerable effort has been put into developing such wearable sensors in recent years, as well as increasing attention being paid to various biomarkers that affect health [12], there is still a debate over whether the analytes and composition of readily accessible body fluids, such as sweat, will correlate with and reliably reflect plasma compositions as a gold standard [5,11–17]. Regardless, research in this field has grown exponentially in the past few years, and further research can provide a deeper understanding of future prospects and challenges. This review focuses on wearable devices that detect sodium in sweat.

2. A BRIEF HISTORY ON POTENTIOMETRIC SENSORS

Potentiometric sensors, developed from the integration of tests and methods for measuring key electrolytes such as Sodium (Na^+), chloride (Cl^-), potassium (K^+), total calcium ($_TCa$), total CO_2 ($_TCO_2$), and total magnesium ($_TMg$) in clinical laboratories [18], are credited to the research of James Ross and Martin Frant of Orion Research, known as the founding fathers of ISEs, who introduced calcium and fluoride ISEs in the mid-1960s [19].

More ion-selective electrodes (ISE) for various ions and microelectrodes for in vivo and clinical measurements were introduced during the 1970s and 1980s; however, shortly thereafter the technology was viewed as mature and no further significant developments seemed possible [18,20–23].

Early in the 1990s, the potentiometry research field appeared to have ceased, and a number of scientists involved shifted their focus to other areas instead. Nevertheless, a new phase of ISE research was established during the 1990s when ion fluxes were discovered across the polymer membrane of ISEs and the mechanism of sensory response was elucidated as a process of non-equilibrium ion exchange, resulting in the emergence and advancement of non-classical potentiometry, followed by significant accomplishments [24,25].

Schazmann et al. reported the first prototype of a wearable potentiometric sensor in 2010. It consisted of a Na^+ sensor belt containing a sodium ion selective electrode (ISE) to monitor real-time quantitative sodium in sweat during exercise at an interface to the human skin [26]. Wearable sensors have only been assessed in the diagnosis of cystic fibrosis as the only successful example of using these devices in clinical settings [27–30].

3. SWEAT SENSING

Sweat is a transparent, hypotonic liquid often characterized as an ultrafiltration of plasma. This bodily fluid is abundant in various electrolytes, biomolecules, metabolites, and can even contain foreign substances (xenobiotics). Sweating is a natural response triggered by factors such as heat, physical exertion, and emotional stress [3,31–33]. The rate of sweat secretion varies with individual differences, exercise, environmental conditions, and certain diseases. On the basis of location, structure, and function, sweat glands are classified as eccrine, apocrine, and apocrine [5]. The eccrine gland, abundant and widely spread, plays a key role in thermoregulation by continuously secreting serous fluid with various solutes over most of the body surface [34]. Since the eccrine sweat glands are densely distributed on the human body, and secrete significant amounts of sweat, epidermal wearable biosensors can be used to collect sweat data without invasive procedures [5]. It primarily consists of ions, notably sodium, potassium, calcium, magnesium, chloride, and lactate. Sweat is conveniently obtainable, and the average sweat rate in adult males typically registers at approximately 0.85 milligrams per square centimeter per minute when measured at the lower back [31].

Sweat serves as an excellent source for continuous and noninvasive monitoring of biomarkers, as well as various neuropeptides and cytokines. Extracting biomarkers from eccrine sweat glands offers several advantages over alternative sources like urine, blood, tears, and apocrine sweat glands. These advantages include their high abundance on the body (typically exceeding 100 glands per square centimeter), easy accessibility, efficient sampling and detection processes that minimize the risk of foreign contamination, and the ability to preserve the integrity of analytes.

However, there are some drawbacks associated with using eccrine sweat as well. These include the possibility of skin contamination, relatively low sampling rates, the potential presence of dried sweat on the glands, and the enrichment of analytes upon evaporation, which can lead to inaccuracies in concentration measurements and distort the results [5,35,36].

4. SWEAT SODIUM LEVELS

Sodium stands out as the most prevalent and extensively researched solute in sweat, exerting a significant impact on human fluid balance. The cells in eccrine gland ducts actively reabsorb ions like Na^+ (sodium) and Cl^- (chloride) through various transport mechanisms such as Na^+/K^+-ATPases and cystic fibrosis transmembrane conductance regulators (CFTRs). This reabsorption process leads to variations in sweat sodium, chloride, and potassium concentrations that can be influenced by factors like age and location on the body.

At the outset, within the sweat gland, sodium concentration closely mirrors that of plasma sodium and remains relatively isotonic, irrespective of sweat rate. However, as sweat travels through the duct towards the skin surface, sodium adsorption occurs, causing the sodium concentration to become hypotonic compared to plasma. The reabsorption of sodium in sweat is influenced by the limitations in both the rate and capacity of sweat ducts to reabsorb it. As a result, the concentration of sodium in sweat on the skin's surface increases as sweat rates rise, ranging from approximately 20 mM/L at low sweat rates to about 100 mM/L at maximum sweat rates.

In specific conditions, particularly during moderately hot weather, certain individuals may experience significant sodium loss through sweating, which can amount to 4–6 grams of sodium (equivalent to 12–15 grams of NaCl) per day.

Although there is ongoing discussion about the exact nature of the relationship between sweat sodium concentrations and sweat rate, it is widely acknowledged that linear relationships are present within particular ranges of sweat rates [14,16].

Sodium, is a marker for electrolyte imbalance and is important for monitoring athletic performance in hot environments, where sweat (and electrolyte) losses can impair physiological function [35]. Proper hydration is key to success as under drinking can lead to hypohydration and over-drinking can lead to hyponatremia (low-serum sodium concentration) [26]. In healthcare, a significant loss of sodium in patients with cystic fibrosis can also cause hyponatremia [35]. It is noteworthy that sodium levels vary considerably depending on the point of the body where they are measured. For example, the forehead range was previously found to be as high as 28.9- 56.7 mmol Na^+ whereas the lower back typically gives half these values [26].

5. WEARABLE SODIUM SENSORS

5.1. Specifications

Wearable electronics are specialized devices designed to be worn on or attached to the human skin. They offer the valuable capability of continuously and noninvasively monitoring an individual's physiological biomarkers by measuring biochemical markers in bodily fluids, all while ensuring the wearer's comfort.

Recent technological strides in this field have led to the development of fully integrated multiplexed sensing systems. These systems, along with innovations like iontophoresis for inducing sweat in sedentary situations, have significantly enhanced the practicality and versatility of electrochemical sweat sensors.

Additionally, the integration of microfluidic technology has further improved the overall functionality of these devices. It has led to advancements in data integrity, sweat collection techniques, and the accuracy and temporal resolution of analyte measurements, making electrochemical sweat sensors even more powerful tools for continuous health monitoring [17].

Diagnosing conditions like hypertension, cardiovascular diseases, cystic fibrosis, kidney disease, acute kidney injury, renal tubular acidosis, and adrenal gland problems often requires monitoring the concentrations of electrolytes, such as sodium and potassium. Traditional methods like flame photometry, ion chromatography, surface plasmon resonance, and inductively coupled plasma mass spectrometry are highly sensitive and selective but require expensive laboratory-based equipment for quantifying these electrolytes in complex biological samples.

Recognizing the potential for improved clinical outcomes through point-of-care (POC) monitoring of biomarkers, there is a growing demand for the development of electrolyte detection systems that can be used with miniaturized portable devices in biomedical diagnosis. In recent years, there has been significant progress in this field with the integration of electrolyte detection into wearable devices.

Incorporating the concept of potentiometric ion sensing into wearables offers several notable advantages (i) Portability; These miniaturized and non-invasive sensors are highly portable, allowing individuals to monitor their health on the go; (ii) Analytical and Mechanical Robustness; These sensors maintain their performance and durability even during physical activities. This robustness is partly achieved through the use of all-solid-state sensing technology; (iii) Decentralized Analysis; Wearable devices equipped with advanced technology for electronics and data transmission enable fully decentralized analysis, reducing the need for centralized laboratory testing; (iv) Affordability; The development of cost-effective devices, from fabrication to data interpretation, makes this technology more accessible to a wider range of individuals and healthcare settings. The integration of potentiometric ion-sensing technology into wearables holds great promise for improving the early diagnosis and management of various health conditions while offering the convenience of continuous monitoring and affordability [37].

Potentiometric-based biosensors advance the detection of several biomarkers and help in early diagnosis of various diseases. They belong to the portable analytical class of biosensors for monitoring biomarkers in the human body. Ion-sensitive membranes sensors can be used to determine potassium, sodium, and chloride ions activity while being used as a biomarker to gauge human health. The potentiometric based ion-sensitive membrane systems can be coupled with various techniques to create a sensitive tool for the fast and early detection of cancer biomarkers and other critical biological compounds.

Potentiometry based on Ion-Selective Electrodes (ISEs) represents an economical technique that can be easily adapted into portable kits. It offers fast response times, a wide dynamic range, straightforward operation, portability, ease of customization, and cost-effectiveness. Given these advantages and the ability of potentiometric membrane sensors to assess biomarkers and biological compounds, it becomes clear that potentiometric methods provide a practical and efficient approach for diagnosing and treating individuals with chronic diseases. These methods empower healthcare professionals to make informed decisions and tailor treatments to individual patient needs [38].

Using wearable sweat biomarker devices must meet specific criteria: (1) The sweat analyte should correlate with blood circulation (2) Sweat rate should be steady or account for dilution and sensor dependencies (3) Swiftly transport sweat to sensors to minimize interference is a must, and (4) It should display continuous raw data for both sweat and blood to address confounding factors [35].

5.2. Wearable potentiometric biosensors

Wearable potentiometric sensors (WPISs) offer a fresh perspective on the practical application of potentiometric sensors in both physiological and clinical contexts. These sensors have garnered considerable attention in research due to their unique ability to harness chemical, material, and electronic components to provide valuable insights into an individual's physiological status.

Despite ongoing efforts to advance wearable potentiometric sensors, there remains a significant gap in meeting all the requirements necessary to enhance these systems. Notably, more than a quarter of published papers related to the development of wearable electrochemical sensors focus on WPISs, underscoring the rapid evolution of electrochemical sensor technology in this direction.

WPISs have opened up new avenues for monitoring biomarkers and pH levels within the human body. pH monitoring, for instance, proves invaluable in the management of chronic wounds, while the measurement of critical cations and anions aids in understanding and controlling various diseases. These conditions encompass heart disorders, cystic fibrosis, hypokalemia, hyperkalemia, hyponatremia, and hypernatremia.

What makes WPISs particularly appealing is their versatility in design, ranging from sweatbands to patches, all without compromising wearer comfort. This adaptability has facilitated the integration of potentiometric ion sensors into numerous aspects of daily life. WPISs, at their core, are electrochemical systems that utilize ion-selective electrodes integrated with materials and electronics to enable on-body measurements. These systems serve as invaluable tools for detecting biomarkers and assessing the concentration and activity of essential ions in body fluids, thereby providing comprehensive insights into an individual's physiological activities.

Electrodes play a pivotal role in potentiometric sensors, and various materials are commonly employed. These include gold (Au), carbon-based compounds such as graphite, nanotubes, or glassy carbon mounted on polymeric substrates like PVC, poly (methyl methacrylate) (PMMA), and polyethylene terephthalate (PET). Additionally, conventional reference electrodes in WPISs typically consist of Ag/AgCl/KCl. In summary, wearable potentiometric sensors represent a dynamic and innovative approach to monitoring physiological parameters and biomarkers, with the potential to transform healthcare and personal health monitoring [39–42]. Conducting polymers (CPs) and carbon-based (nano) materials have long been pivotal in the development of indicator electrodes for WPIS. However, the explosive growth of nanomaterials and the recognition of their unique properties have led to a surge in research aimed at leveraging these materials to enhance the sensitivity of WPISs.

One notable example is the work by Parrilla et al., who introduced a biomarker detection tool using WPIS technology to sense ion concentrations in human sweat. In this context, WPISs have demonstrated the capability to detect ions such as Cl^-, K^+, and Na^+, as well as pH activity. This achievement is primarily attributed to the use of all-solid-state ion-selective electrodes, which come with several advantages. These advantages encompass low sample volume requirements, miniaturization, cost reduction, versatility, and simplicity in biomaterial sensing.

While WPISs are gaining traction as valuable tools for rapid analysis, they still face some challenges. These include potential issues like skin contamination, relatively low sampling rates, and the presence of dried sweat on the glands, which can skew analyte measurements. As a result, ongoing research efforts are directed toward addressing these challenges and further improving the utility of WPISs in real-world applications [38,43–45].

5.3. Types of wearable biosensors

A wide range of wearable designs are employed for potentiometric ion detection, and these designs can be categorized into various configurations for detecting ions in sweat and other biological fluids. These configurations include sweatbands, tattoo-like patches, epidermal patches, textile-based patches, electronic and/or microfluidic arrays, and garments. The primary distinction among these designs lies in how sweat comes into contact with the electrodes, either directly from the skin or through a sampling method. In this context, we classify wearables based on their sweat collection mechanisms, particularly focusing on the use of sweat-collecting tourniquets.

5.3.1. Sweatbands

Sweatbands are among the most commonly used platforms for wearable potentiometric ion sensors (WPIS) due to their practicality. Implementing electrodes and a sampling cell on the band is straightforward. Typically, the electrodes are first prepared on a separate flexible substrate and then attached to the sweatbands. This design allows for the disposable use of the electrodes while maintaining the same wearable band. Once the electrochemical cell demonstrates the required resilience and sensitivity, the calibration process is conducted outside the wearable platform. Following successful calibration, the sensor is integrated into the wearable configuration and ready for on-body testing. However, one limitation of using sweatbands is that individuals can only wear the WPIS on specific parts of the body where the bands can be securely fastened.

In some cases, incorporating nanoparticles into sweatbands proves highly beneficial because it maximizes the utilization of the collected sweat. This is made possible by the unique properties of nanoparticles, particularly their high surface area-to-volume ratio. Here, we present an example: Shuqi Wang et al. introduced an innovative all-solid-state Ion-Selective Electrode (ISE) based on a gold nano dendrites (AuNDs) array electrode as the solid contact, along with a polyvinyl acetate/inorganic salt (PVA/KCl) membrane coated all-solid-state reference electrode (RE). They utilized a simple, reliable, and controllable method to fabricate the gold nano dendrites array (AuNDs) on a chip with microwells. Furthermore, they designed a miniature chip with a polyvinyl acetate/KCl (PVA/KCl) membrane-coated all-solid-state RE. This setup was then integrated into a wearable sweatband platform, allowing for the continuous collection and analysis of sodium ion concentration ([Na^+]) in sweat. Incorporating such innovative designs and nanomaterials into sweatbands enhances the capabilities of WPIS, making them powerful tools for real-time monitoring of physiological parameters [46], (Figure 1A).

5.3.2. Microfluidics

Recent studies have developed thin, skin-compatible microfluidic systems for wearable sweat sensors to capture and analyze sweat from the skin surface. These systems allow for precise location-based analysis of sweat rate and chemistry, protecting sensors from biofouling and minimizing signal noise. Utilizing lab-on-a-chip concepts, these advanced microfluidic designs use complex valving and routing strategies to isolate and reduce sensing errors [47]. Microfluidics-based epidermal patches offer a highly flexible and conformable platform with exceptional adaptability when placed on the body. These wearables exhibit a great deal of versatility, and they hold the potential to reduce fabrication costs while introducing the concept of disposability for the entire patch.

However, the stringent requirements for durability in these epidermal patches are considerably higher compared to those for sweatbands. This is due to the fact that the material serving as the base must not only be flexible but also possess the ability to stretch and conform, replicating the physical characteristics of human skin accurately, especially during intense physical activities such as sports. The main hurdle in designing these patches revolves around the fabrication of sensors directly onto these resilient materials.

Moreover, there are practical considerations to take into account when employing these epidermal sensors. These include the necessity for efficient sweat renewal across the sensor area and the potential for contamination from other parts of the body, both of which can pose substantial challenges. These limitations must be carefully addressed to ensure the reliability and precision of the data gathered from these kinds of wearable epidermal sensors.

5.3.3. Paper-based microfluidics

These promising platforms have demonstrated remarkable potential in the advancement of point-of-care diagnostics. The concept of point-of-care diagnostics within microfluidic devices was initially introduced by the Whitesides group in 2007. Since that pivotal moment, numerous methods and techniques have been put forth to fabricate microchannels and enhance the capabilities of these diagnostic platforms [48].

Paper-based analytical devices have become the focus of attention in the diagnosis domain due to the aforementioned advantages along with the fact that paper can be easily printed and coated with biomolecules in order to develop a portable and ideal platform for the detection of clinically significant markers. PADs have been coupled with numerous optical, electrochemical, and spectroscopy read-out techniques for the detection of a wide range of clinically relevant analytes including tumor markers [49–52].

Salzitsa Anastasova et al. introduced a wearable multi-sensing Patch for continuous monitoring sodium in sweat. They made a novel thin flexible wearable patch that incorporates a paper microfluidic channel by using Whatman 4 and Whatman 113 papers with embedded flexible microneedle-based sensors connected with a wireless potential stat [31].

Qingpeng Cao and collaborators developed a smartwatch capable of monitoring sodium and potassium levels in sweat. They created a microfluidic patch using paper that featured a three-dimensional structure. The patterns for this paper-based microfluidic patch were designed using CorelDRAW software and then printed onto Whatman #4 filter paper using a wax printer (XEROX 8570) [53].

Possible advances in this direction will be electronic board attached sensors with capability of wireless connection to smartphones [54–56].

Anastasova and her team employed a paper-based microfluidic channel to address the challenges associated with sweat accumulation on the skin's surface. This innovative approach utilized capillary forces to draw sweat into the channel, propelling it along the paper's length. The sweat thus transported was gathered at the channel's end in reservoirs, where it underwent continuous evaporation. This fluid manipulation process allowed for the real-time monitoring of pH, sodium levels, and lactate concentration in sweat, all facilitated by a wireless system.

The microfluidic patch consisted of multiple layers, including polymer, paper microfluidics, and flexible sensors. A CO_2 laser fabrication system was employed to intricately cut structures into the various polymer layers, enabling the creation of this novel device [31], (Figure 1B).

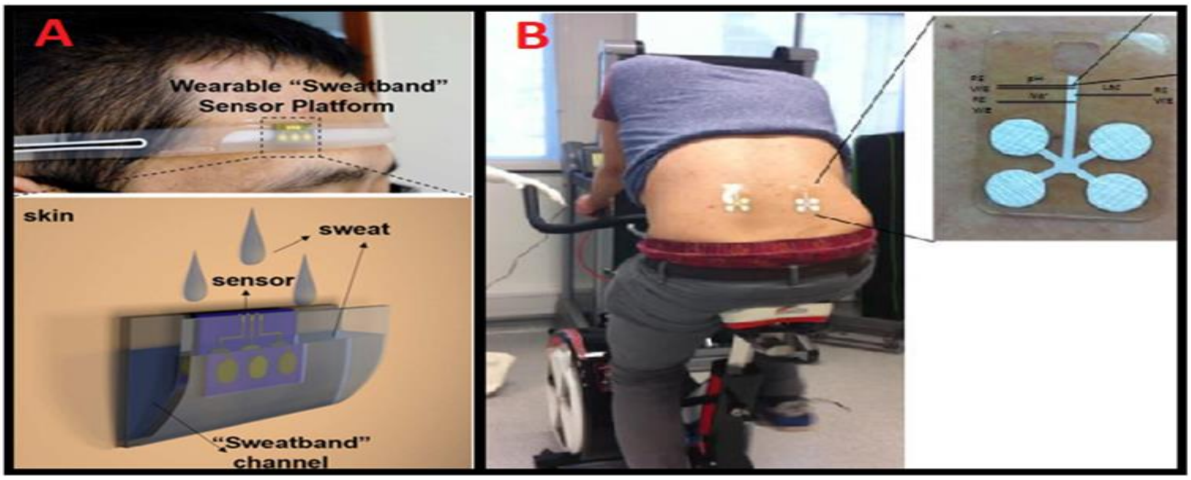

Figure 1. A) Photographs of sweatband-type wearable biosensor for real-time sodium monitoring via collecting sweat during indoor cycling by a channel made of silicone; reproduced with permission from ref. [46]; B) schematic illustration of real-time sodium concentration monitoring by a wearable patch with a paper microfluidic made of Whatman 113 and Whatman4 paper; reproduced with permission from ref. [31]

5.3.4. Paper-based metal electrodes

Sakata et al. introduced a wireless potentiometric measurement system for wearable biosensors using paper-based metal electrodes focusing on sodium ions and pH detection. The electrodes, coated with functional membranes, show stable and sensitive detection of pH and sodium ions, even when bent, making them suitable for flexible body patch biosensors, including real-time evaluation of sodium concentrations in sweat samples [57].

5.3.5. Epidermal microfluidics

Amay J. Bandodkar et al. fabricated a characterization and application of an epidermal temporary- transfer tattoo-based potentiometric sensor. Na-tattoo pattern was superimposed on a laser-printed color rendering of an artistic “Tiger Face”. The layer of the transparent insulator screen-printed on to the entire tattoo-base paper sheet. The contacts for interfacing the Na-tattoo sensor were fabricated via screen printing carbon ink on a flexible poly ethylene terephthalate (PET) substrate and the sodium selective membrane based on PVC layer. a fluidic channel and sink (stick-on fluidic channel) were fabricated atop the Na-tattoo [58], (Figure 2A).

Silvia Demuru et al. fabricated flexible microfluidics-integrated platform with an array of printed ion-selective Organic electrochemical PEDOT: PSS-based transistor (OECT) for detecting of sodium and potassium in sweat. ISMs are prepared on PVC matrices to achieve selectivity for K^+, Na^+, and H^+ ions. A PET foil was used for the flexible fluidics system. The foil was patterned by CO_2 laser etching to define the shape of the micro-fluidic channel, the reservoir, the inlet and the outlet [59], (Figure 2B).

Rajendran Vinoth et al. introduced a clean-room free fabrication of wearable microfluidic sensors soft silicon-rubber based microfluidic channels were prepared using a screen-printed carbon pattern as a master mold. The. This patch was integrated with a costume-made miniature printed circuit board [60], (Figure 2C).

Hnin Yin Yin Nyein et al. introduced a wearable sweat sensing patch for detecting sodium. Sweat was collected by an epidermal microfluidic patch that was made of PDSM [61], (Figure 2D).

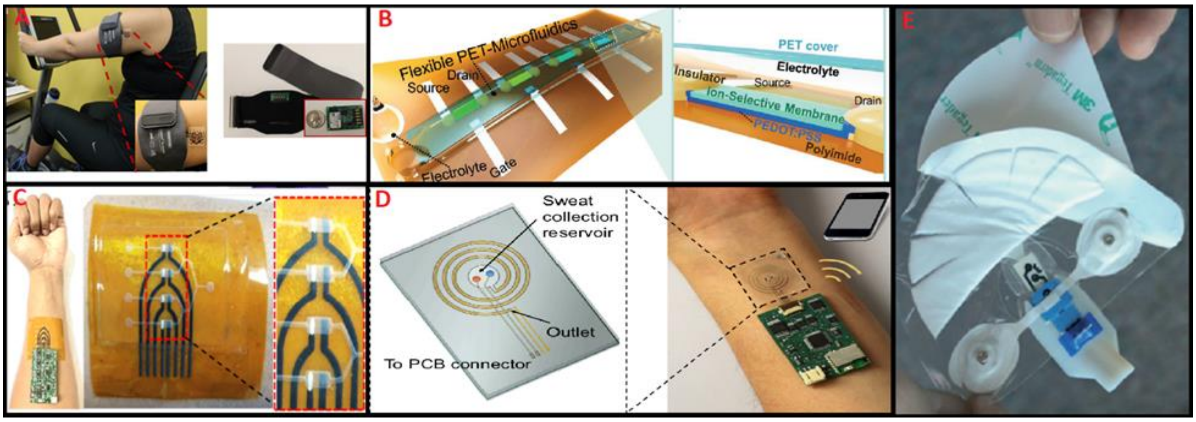

Figure 2. A) Schematic pictures of real-time sweat monitoring by Na-tattoo, collecting sweat via a fluidic channel, reproduced with permission from ref. [58]; B) images of the biosensor with a flexible PET-Microfluidic, reproduced with permission from ref. [59]; C) schematic of on-body test for collecting and monitoring sweat by wearable biosensor with silicon-rubber based microfluidic pattern-reproduced with permission from ref. [60]. D) wearable sweat sensing patch with an epidermal microfluidic patch that was made of PDSM, reproduced with permission from ref. [61]; E) picture of a patch with a fluidic system fan-shaped wick design that is made of a small Whatman Standard 17 "pre-wick" to transfer sweat from the fluidic channel to the reservoir-reproduced with permission from ref. [14]

Azar Alizadeh and colleagues have introduced a wearable patch designed to monitor electrolyte levels during physical activity. This patch incorporates a fluidics system optimized for efficient sweat collection from the skin, particularly effective at moderate to high perspiration rates. It also features a sophisticated electronics module housing, an overall device integration strategy, and signal processing algorithms that ensure minimal noise while providing a comfortable wearing experience. To facilitate the movement of fluid into the channels, they have employed laminated microfluidics created using one or more hydrophobically-treated plastic films with adhesive patterns. In this additive technique, a cutting plotter is utilized to pattern each layer, followed by lamination. This method allows for swift prototyping and the ability to implement changes to the channel geometry without the necessity of specialized tools like masks or stamps, as well as without the need for curing [14], (Figure 2E).

5.3.6. Sampling cell

Marc Parrilla and his team have been actively involved in the development of a wearable potentiometric ion patch for monitoring electrolyte levels in sweat. They have made significant progress by focusing on the reproducibility and double validation of on-body measurements facilitated by these new Wearable Potentiometric Ion Sensors (WPISs).

Their innovative electrode array is constructed using multi-walled carbon nanotubes (MWCNTs) as an ion-to-electron transducer, which is integrated onto a flexible polyurethane (PU) substrate. The electrode array comprises five circular patterns made with stretchable carbon ink, and these patterns are connected to a serpentine track created using stretchable silver ink.

To complete the system, they have designed a sampling cell that fulfills all the essential requirements for effective ion monitoring. This microfluidic cell is 3D-printed with the same flexible PU substrate, providing the necessary conformability to the device for comfortable attachment to the human body. This innovative approach holds great promise for continuous and non-invasive monitoring of electrolyte levels in sweat, which can have important applications in healthcare and sports performance monitoring [62], (Figure 3A).

5.3.7. Microfluidic chip based

The emergence of microfluidics technology has indeed sparked a significant revolution in the development of miniaturized devices capable of performing a wide range of functions. These functions include trapping and sorting particles or cells based on size, synthesizing nanomaterials, creating droplets, and even facilitating drug delivery. Among these microfluidic devices, soft microfluidic systems have been specifically designed for sweat collection, sampling, and analysis. They play a pivotal role in real-time measurements of chemical markers and the monitoring of electrolyte levels and compositions.

Furthermore, the integration of nanoparticles and threads has the potential to enhance the functionality of microfluidic chips, making them even more versatile. Here are a few noteworthy examples G. Matzeu and colleagues developed an SC-ISE for sodium on a dual screen-printed substrate. To aid fluid movement into the microfluidic chip, they utilized cotton threads extracted from medical bandages. Additionally, they employed PMMA (polymethyl methacrylate) for the construction of the microfluidic chip layers, ensuring its functionality. PMMA was also used to enclose the entire system.

These advancements demonstrate the innovative potential of combining microfluidics, nanoparticles, and threads to create sophisticated sensing platforms. Such developments have broad applications, from healthcare to environmental monitoring, and continue to push the boundaries of what can be achieved with miniaturized devices [63].

Margaret McCaul and her colleagues have made a SwEatch platform for detecting sodium in sweat that is made by cotton threads for which the electrode membranes could be formed, two separate holes 3 mm in diameter were laser cut in PMMA [64], (Figure 3B).

Furthermore, Tom Glennon et al. have demonstrated a passive (pomp-free) liquid flow SwEatech platform by using a PMMA based microfluidic chip and a solid-state ISE that was prepared on a conducting carbon ink insulated layer, these layers were screen printed on a thick PET sheet [65], (Figure 5C).

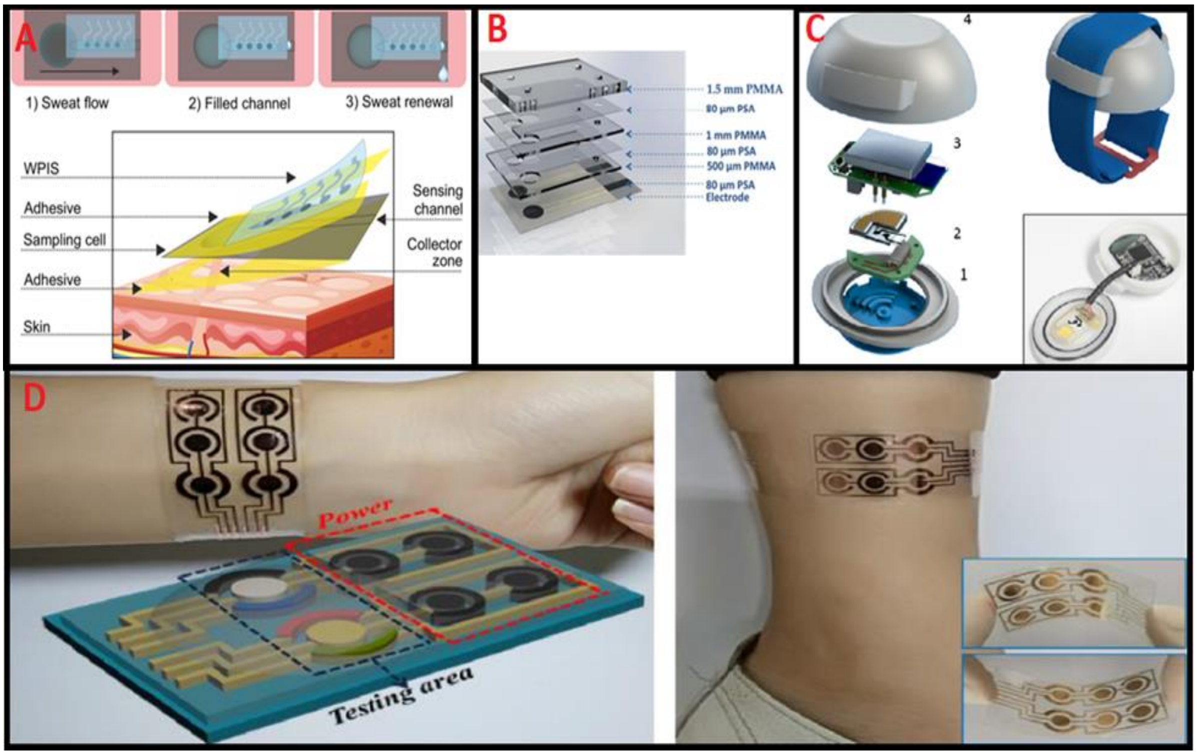

Figure 3. A) images of the sampling cell function and patch type biosensors layers, reproduced with permission from ref. [62] B) pictures of different layers to build up the microfluidic chip for collecting sweat, reproduced with permission from ref. [64]; C) SwEatech platform with a microfluidic chip made of PMMA, PSA layers and cotton thread, reproduced with permission from ref. [65]; D) Direct connection of wearable sweat monitoring sensor with skin, reproduced with permission from ref. [66]

5.3.8. Direct contact

In certain situations, there is no intermediate mechanism for gathering sweat, and sensors come into direct contact with the sweat emanating from the skin. Yao Lu and colleagues engineered a wearable self-powered sweat monitoring system featuring integrated micro-supercapacitors (MSCs). This system comprised a glucose sensor made from $NiCo_2O_4$/chitosan, ion-selective membrane-based sensors for sodium ([Na^+]) and potassium ([K^+]), and $NiCo_2O_4$-based micro-supercapacitors situated on a flexible PET substrate, serving as the power source for the sensor arrays [66], (Figure 3D).

5.3.9. Textiles

Textile-based wearable devices offer a wide array of possibilities in terms of materials and manufacturing techniques. These devices can be created using diverse materials, ranging from individual threads transformed into conductive surfaces and equipped with sensing membranes to clothing items directly enriched with electrodes. Consequently, various production methods like dip-coating, printing, and drop-casting can be utilized to craft these textile-based sensors.

One notable advantage of utilizing textiles is their compatibility with traditional manufacturing methods, making the production of textile-based sensors relatively straightforward compared to other wearable materials. Textiles are flexible and moldable, enabling sensors to be applied to almost any exposed skin surface for sweat monitoring.

Nevertheless, to enhance the stability and reduce potential contamination effects of these sensors, it is advantageous to incorporate an ion-to-electron transducer between the sensing membrane and the conductive pathway. This improvement helps ensure the precision and dependability of the measurements.

For instance, Xuecheng He and collaborators developed innovative Janus textile bands capable of self-pumping sweat collection and analysis. They achieved this by electrospinning hydrophobic polyurethane (PU) nanofiber arrays onto hydrophilic gauze, showcasing the potential of textile-based technology in this field. The Janus textile, in this case, serves as a unidirectional conduit, efficiently transporting sweat from the skin (hydrophobic side) to the embedded electrode surface (hydrophilic side). This self-pumping textile-based device effectively drains sweat from the wearer's epidermis side to the external electrode. Additionally, an insulator layer fabricated using PET (polyethylene terephthalate) prevents electrical contact between metal wires and perspiration.

Such innovations in textile-based wearable devices hold tremendous potential for non-invasive and continuous monitoring of human perspiration, offering insights into various aspects of health and performance [67].

Nicola Coppedè and colleagues introduced Textile Organic Electrochemical Transistors (txOECTs), a novel device designed for measuring electrolytes in sweat. The fabrication of this device involved a series of sequential functionalization steps applied to textile fibers. First, they coated the textile fiber with the conductive polymer poly(3,4-ethylenedioxythiophene): poly (styrene sulfonate) (PEDOT: PSS). This conductive layer enhances the electrical properties of the textile. Subsequently, an ion-selective membrane was applied to the textile fibers. This membrane is designed to selectively interact with specific ions, allowing for the measurement of electrolytes present in sweat.

Overall, the integration of these functionalized textile fibers into txOECTs provides a unique and promising platform for non-invasive and continuous monitoring of electrolyte levels in sweat, which has various applications in healthcare and sports performance monitoring [68], (Figure 4A).

Trupti Terse-Thakoor et al. designed a thread-based multiplex sensing patch for continuous stimulation in-skin monitoring of sweat. In their development of a sweat sensor platform, the researchers utilized flexible threads coated with conductive inks to serve as sensing electrodes. They employed various types of threads, including polyester (PE) and stainless steel (SS) threads, which were coated with conductive inks such as carbon ink and Ag/AgCl ink to enable selective potentiometric sensing of electrolytes.

To construct these sensing patches, the researchers assembled the sweat sensor platform in the form of a patch. They placed the coated threads directly onto the fabric gauze of a commercial bandage. This gauze material played a crucial role in facilitating the transport of sweat from the sensing area or the inner side of the patch to the backside of the patch, where it could evaporate.

To prevent sweat from evaporating from the sensing area and ensure accurate measurements, the edges of the gauze were meticulously sealed to both the patch and the wearer's skin. This sealing mechanism helped create a controlled environment within the sensing area, allowing for reliable and consistent sweat analysis.

Overall, this innovative approach using flexible threads and gauze-based patches enhances the functionality and practicality of sweat sensing platforms, offering a valuable tool for continuous monitoring of physiological parameters [69], (Figure 4B).

Wenya He and colleagues have introduced an innovative flexible sweat analysis patch that is based on a carbon textile derived from silk fabric. This wearable patch is designed for the simultaneous detection of six health-related biomarkers. The unique properties of the silk-derived carbon textile contribute to its effectiveness in sweat analysis.

The carbon textile is characterized by a porous structure, which provides several advantages, including excellent electrical conductivity, a high density of active sites, and good water wettability. These features promote efficient electron transmission and enhance the patch's performance as a sensor for monitoring biomarkers in real time. What sets this wearable sensor apart is its use of silk, a natural fiber with a rich history. The core material, known as SilkNCT, is derived from silk fabric and features intrinsic nitrogen (N) doping, resulting in a graphitic nanocarbon structure. SilkNCT boasts high electrical conductivity, thanks to this unique nanocarbon structure, and its woven, porous configuration further enhances its properties. SilkNCT is directly employed or combined with other compounds to serve as the working electrode in the flexible electrochemical sensors used in the patch. The circuitry for the patch is created using a conductive Ni-coated textile tape through a straightforward digital laser writing technique. The combination of a hierarchical porous structure and the graphitic nanocarbon structure in SilkNCT offers excellent flexibility, increased accessibility to reactants, and superior electrical conductivity. These attributes position SilkNCT as a promising material for use in the working electrodes of electrochemical sensors, making it a valuable component of this innovative sweat analysis patch [70].

Brock Brady et al introduced a colorimetric ion-selective optodes on sports fabrics such as a Nike Dri-FIT shirt made of polyester spandex. This device was based on a Chromoionophore III-based optodes on polyester–spandex, in fact Chromoionophore I with a lower pKa was more sensitive Na^+ and K^+ at physiological sweat concentrations [71].

Wei Gao et al. introduced a wearable flexible integrated sensing array (FISA) through a flexible printed circuit board (FPCB) for simultaneous and selective screening of a panel of biomarkers in sweat. They used a water absorbent thin rayon pad for collecting sweat on a flexible plastic substrate. They fabricated the sensors on a polyethylene terephthalate (PET) substrate and ion-selective electrodes (ISEs), coupled with a polyvinyl butyral (PVB)-coated and carbon nanotubes reference electrode to maintain a stable potential in solutions with different ionic strengths. poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT: PSS) was used as an ion-to-electron transducer in the ISEs [72].

Qingfeng Zhai et al. fabricated a tattoo-like device by using mushroom-like gold nanowires (v-AuNWs) as intrinsically stretchable ion-selective electrodes (ISEs). Their gold nanowire electronic tattoo selective membrane is based on PVC. Their device offered intrinsic stretchability without the need for extrinsic structural design yet achieved an ultrathin, tattoo-like layout, and the sensors could be conformally attached to the human skin and function under various deformations The on-body sweat analysis was performed on a subject’s wrist, and a piece of tissue paper was attached on the sensing area for sweat collection [73].

Benjamin Schazmann and his team have unveiled a wearable electrochemical sensor called the Sodium Sensor Belt (SSB), designed for tracking sodium concentration levels. This device comprises an impermeable plastic base that houses ISEs and a sweat-absorbing mechanism (pump), along with a potentiometer for measurements. The ISE electrodes were internally constructed using PVC tubing as their casings. The sweat collection system relies on specially designed fabrics (a blend of polyimide and lycra) with innate moisture-wicking capabilities facilitated by capillary action [26].

3.10. Macroduct and iontophoresis

The Macroduct Sweat Collector is a disposable plastic device designed to cover the skin area previously stimulated by pilocarpine iontophoresis. When firmly applied to the stimulated area, it causes the skin to protrude into its concavity, eliminating any air gaps. As a result of hydraulic pressure, sweat secreted by the sweat glands moves upward through the sweat duct and emerges from the skin. With over 5 million sweat tests conducted using the existing Macroduct® Sweat Collection System, the Macroduct® Advanced represents more than 40 years of continuous innovation aimed at standardizing pilocarpine iontophoresis and sweat collection. The Macroduct system, including the Webster Sweat Inducer and the Macroduct Sweat Collector, has had a significant impact on laboratory sweat tests for cystic fibrosis, bringing early intervention to numerous CF patients worldwide.

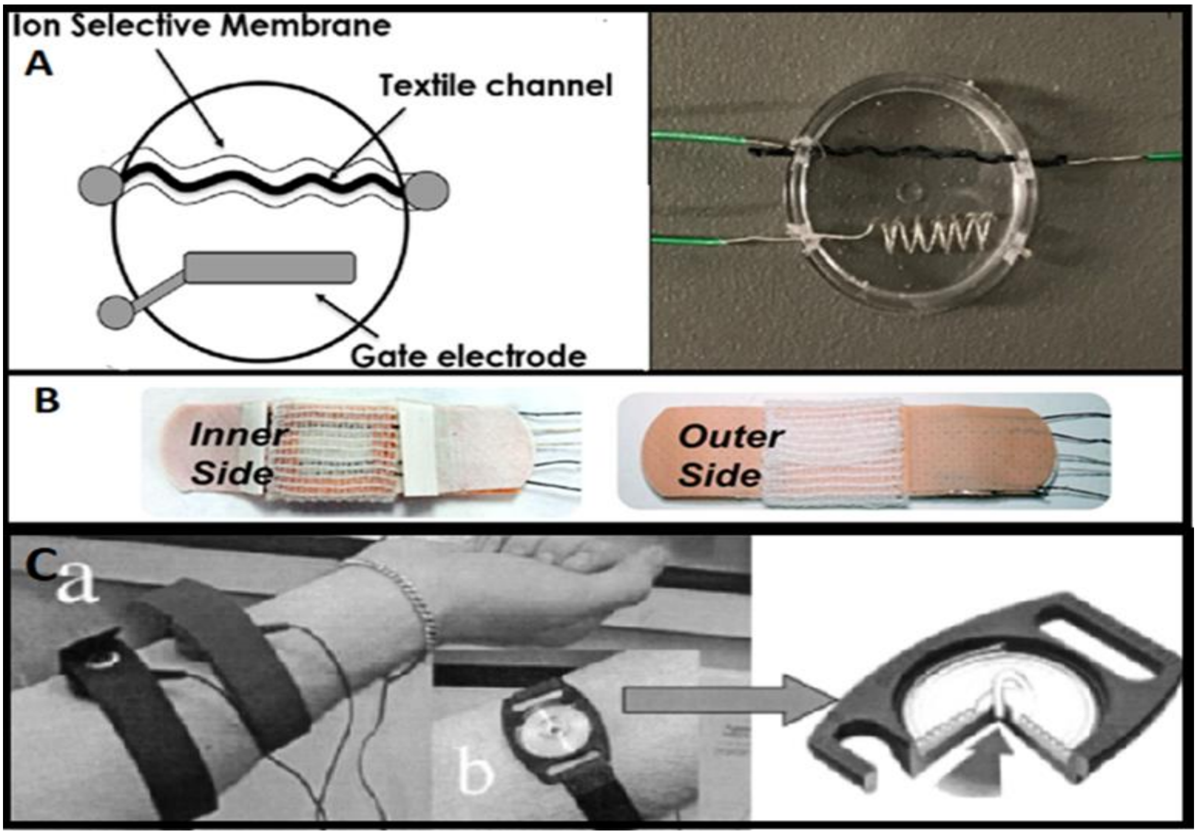

Figure 4. A) the schematic illustration and picture of the micro-sensor with a textile channel for soaking sweat from the skin, reproduced with permission from ref. [68]; B) thread-based multiplex sensing patch with a fabric gauze for soaking sweat, reproduced with permission from ref. [69]; C) iontophoresis with pilocarpine to stimulate sweating collecting it into a coiled tube section of a macro duct that is in the form of a wristwatch, reproduced with permission from ref. [76]

Paolo Pirovano and colleagues have developed a wearable sensor called SwEatch, which resembles a watch and is capable of detecting sodium and potassium levels in human sweat during exercise. This device utilizes PEDOT-based NA+ Ion Selective Electrodes (ISE). What sets this device apart from previous SwEatch platforms is its ability to monitor two channels for direct electrolyte measurement, resistance to movement artifacts, and the capacity to collect and transport sweat, all of which are integrated within the dual Macroduct system. [74].

Aogán Lynch et al. made a micro-sensor array for the detection of sodium, potassium and chloride in sweat by using iontophoresis with pilocarpine to stimulate sweating, the sweat is collected using the macroduct unit which is strapped over the stimulated region like a wristwatch [75].

Nanette V. et al used iontophoresis for extraction of sweat owing to examined the effect of spironolactone on sweat sodium concentration [76], (Figure 4C).

6.CONCLUSION

In conclusion, this comprehensive review highlights the significance and advancements of wearable sensors for sodium detection in human sweat. These innovative sensors have shown great potential in providing non-invasive and continuous monitoring of sodium levels, offering valuable insights into individual health and physiological conditions. The various types of wearable sensors and technologies discussed in this review demonstrate their versatility and applicability in diverse fields, including sports, healthcare, and medical diagnostics. As research in this area continues to progress, wearable sodium sensors are poised to revolutionize personalized health monitoring and contribute to the advancement of preventive and precision medicine.

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Declarations of interest

The authors declare no conflict of interest in this reported work.

REFERENCES

[1] R. Ghaffari, D.S. Yang, J. Kim, A. Mansour, J.A.J. Wright, J.B. Model, D.E. Wright, J.A. Rogers, and T.R. Ray, ACS Sens. 6 (2021) 2787.
[2] W. Gao, G.A. Brooks, and D.C. Klonoff, J. Appl. Physiol. 124 (2018) 548.
[3] J. Gilnezhad, A. Firoozbakhtian, M. Hosseini, S. Adel, G. Xu, and M.R. Ganjali, Anal. Chim. Acta 1250 (2023) 340981.
[4] M. Gamella, S. Campuzano, J. Manso, G.G. de Rivera, F. López-Colino, A.J. Reviejo, and J.M. Pingarrón, Anal. Chim. Acta 806 (2014) 1.
[5] X. Yuan, C. Li, X. Yin, Y. Yang, B. Ji, Y. Niu, and L. Ren, Biosensors 13 (2023) 313.
[6] M. Augusto-Oliveira, G. de Paula Arrifano, A. Lopes-Araújo, L. Santos-Sacramento, R.R. Lima, M.L. Lamers, J. Le Blond, and M.E. Crespo-Lopez, Environ. Res. 200 (2021) 111432.
[7] R.-E. Tiongco, A. Bituin, E. Arceo, N. Rivera, and E. Singian, J. Clin. Exp. Dent. 10

(2018) e902.
[8] L.F. Hofman, J. Nutr. 131 (2001) 1621S.
[9] R.C. Tseng, C.C. Chen, S.M. Hsu, and H.S. Chuang, Sensors 18 (2018) 2651.
[10] B. Sequeira-Antunes, and H.A. Ferreira, Biomedicines 11 (2023) 1051.
[11] J. Kim, A.S. Campbell, B.E.-F. de Ávila, and J. Wang, Nat. Biotechnol. 37 (2019) 389.
[12] A. Sharma, M. Badea, S. Tiwari, and J.L. Marty, Molecules 26 (2021) 748.
[13] M. Cuartero, M. Parrilla, and G.A. Crespo, Sensors 19 (2019) 363.
[14] A. Alizadeh, A. Burns, R. Lenigk, R. Gettings, J. Ashe, A. Porter, M. McCaul, R. Barrett, D. Diamond, P. White, P. Skeath, and M. Tomczak, Lab Chip. 18 (2018) 2632.
[15] L. Klous, C.J. de Ruiter, S. Scherrer, N. Gerrett, and H.A.M. Daanen, Eur. J. Appl. Physiol. 121 (2021) 803.
[16] J.N. Hussain, N. Mantri, and M.M. Cohen, Clin. Biochem. Rev. 38 (2017) 13.
[17] F. Gao, C. Liu, L. Zhang, T. Liu, Z. Wang, Z. Song, H. Cai, Z. Fang, J. Chen, J. Wang, M. Han, J. Wang, K. Lin, R. Wang, M. Li, Q. Mei, X. Ma, S. Liang, G. Gou, and N. Xue, Microsystems Nanoeng. 9 (2023) 1.
[18] C.C. Young, J. Chem. Educ. 74 (1997) 177.
[19] R.P. Buck, and E. Lindner, Anal. Chem.73 (2001) 88A.
[20] E. Bakker, and E. Pretsch, Anal. Chem. 74 (2002) 420A.
[21] M.R. Ganjali, M. Hosseini, M. Salavati-Niasari, T. Poursaberi, M. Shamsipur, M. Javanbakht, and O.R. Hashemi, Electroanalysis 14 (2002) 526.
[22] T. Poursaberi, M. Hosseini, M. Taghizadeh, H. Pirelahi, M. Shamsipur, and M.R. Ganjali, Microchem. J. 72 (2002) 77.
[23] F. Faridbod, M.R. Ganjali, L. Safaraliee, S. Riahi, M. Hosseini, and P. Norouzi, Int. J. Electrochem. Sci. 4 (2009) 1419.
[24] E. Bakker, and E. Pretsch, Angew. Chem. Int. Ed. Engl. 46 (2007) 5660.
[25] J. Ding, and W. Qin, TrAC Trends Anal. Chem. 124 (2020) 115803.
[26] B. Schazmann, D. Morris, C. Slater, S. Beirne, C. Fay, R. Reuveny, N. Moyna, and D. Diamond, Anal. Methods. 2 (2010) 342.
[27] S. Emaminejad, W. Gao, E. Wu, Z.A. Davies, H. Yin Yin Nyein, S. Challa, S.P. Ryan, H.M. Fahad, K. Chen, Z. Shahpar, S. Talebi, C. Milla, A. Javey, and R.W. Davis, Proc. Natl. Acad. Sci. U. S. A. 114 (2017) 4625.
[28] J. Gonzalo-Ruiz, R. Mas, C. de Haro, E. Cabruja, R. Camero, M.A. Alonso-Lomillo, and F.J. Muñoz, Biosens. Bioelectron. 24 (2009) 1788.
[29] D.H. Choi, Y. Li, G.R. Cutting, and P.C. Searson, Sensors Actuators B Chem. 250 (2017) 673.
[30] D.-H. Choi, A. Thaxton, I. cheol Jeong, K. Kim, P.R. Sosnay, G.R. Cutting, and P.C. Searson, J. Cyst. Fibros. 17 (2018) e35.
[31] S. Anastasova, B. Crewther, P. Bembnowicz, V. Curto, H.M. Ip, B. Rosa, and G.Z. Yang, Biosens. Bioelectron. 93 (2017) 139.
[32] S. Ganesan, K. Ramajayam, T. Kokulnathan, and A. Palaniappan, Molecules 28 (2023) 4617.
[33] M. Bariya, H.Y.Y. Nyein, and A. Javey, Nat. Electron. 1 (2018) 160.
[34] K. Sato, Rev. Physiol. Biochem. Pharmacol. 79 (1977) 51.
[35] D.R. Seshadri, R.T. Li, J.E. Voos, J.R. Rowbottom, C.M. Alfes, C.A. Zorman, and C.K. Drummond, NPJ Digit. Med. 2 (2019) 72.
[36] Z. Sonner, E. Wilder, J. Heikenfeld, G. Kasting, F. Beyette, D. Swaile, F. Sherman, J. Joyce, J. Hagen, N. Kelley-Loughnane, and R. Naik, Biomicrofluidics 9 (2015) 31301.
[37] M. Parrilla, M. Cuartero, and G.A. Crespo, TrAC Trends Anal. Chem. 110 (2019) 303.
[38] H. Karimi-Maleh, Y. Orooji, F. Karimi, M. Alizadeh, M. Baghayeri, J. Rouhi, S. Tajik, H. Beitollahi, S. Agarwal, and V.K. Gupta, Biosens. Bioelectron. 184 (2021) 113252.

[39] M.R. Ganjali, H.A. Zamani, P. Norouzi, M. Adib, and M. Rezapour, M. Aceedy, Bull. Korean Chem. Soc. 26 (2005) 579.
[40] M.R. Ganjali, T. Poursaberi, F. Basiripour, M. Salavati-Niassari, M. Yousefi, and M. Shamsipur, J. Anal. Chem. 370 (2001) 1091.
[41] H.A. Zamani, J. Abedini-Torghabeh, and M.R. Ganjali, Electroanalysis 18 (2006) 888.
[42] H.A. Zamani, M.R. Ganjali, P. Norouzi, and M. Adib, Mater. Sci. Eng. C. 28 (2008) 157.
[43] M. Shamsipur, S. Rouhani, H. Sharghi, M.R. Ganjali, and H. Eshghi, Anal. Chem. 71 (1999) 4938.
[44] H.A. Zamani, M.R. Ganjali, P. Norouzi, and M. Adib, Sens. Lett. 5 (2007) 522.
[45] M.R. Ganjali, R. Nemati, F. Faridbod, P. Norouzi, and F. Darviche, 3 (2008) 1288.
[46] S. Wang, Y. Wu, Y. Gu, T. Li, H. Luo, L.H. Li, Y. Bai, L. Li, L. Liu, Y. Cao, H. Ding, and T. Zhang, Anal. Chem. 89 (2017) 10224.
[47] A.J. Bandodkar, W.J. Jeang, R. Ghaffari, and J.A. Rogers, Annu. Rev. Anal. Chem. 12 (2019) 1.
[48] S. Liu, W. Su, and X. Ding, Sensors 16 (2016) 1.
[49] S. Abarghoei, N. Fakhri, Y.S. Borghei, M. Hosseini, and M.R. Ganjali, Spectrochim. Acta Part A Mol. Biomol. Spectrosc. 210 (2019) 251.
[50] N. Fakhri, S. Abarghoei, M. Dadmehr, M. Hosseini, H. Sabahi, and M.R. Ganjali, Spectrochim. Acta Part A Mol. Biomol. Spectrosc. 227 (2020) 117529.
[51] P. Jafari, S.M. Beigi, F. Yousefi, S. Aghabalazadeh, M. Mousavizadegan, M. Hosseini, S. Hosseinkhani, and M.R. Ganjali, Microchem. J. 163 (2021) 105909.
[52] N. Fakhri, M. Hosseini, and O. Tavakoli, Anal. Methods 10 (2018) 4438.
[53] Q. Cao, B. Liang, X. Mao, J. Wei, T. Tu, L. Fang, and X. Ye, Electroanalysis 33 (2021) 643.
[54] A. Firoozbakhtian, M. Hosseini, M.N. Sheikholeslami, F. Salehnia, G. Xu, H. Rabbani, and E. Sobhanie, Anal. Chem. 94 (2022) 16361.
[55] A. Firoozbakhtian, M. Hosseini, Y. Guan, and G. Xu, Anal. Chem. (2023) https://doi.org/10.1021/acs.analchem.3c03285.
[56] M. Mousavizadegan, A. Firoozbakhtian, M. Hosseini, and H. Ju, TrAC Trends Anal. Chem. 167 (2023) 117216.
[57] T. Sakata, M. Hagio, A. Saito, Y. Mori, M. Nakao, and K. Nishi, Adv. Mater. 21 (2020) 379.
[58] A.J. Bandodkar, D. Molinnus, O. Mirza, T. Guinovart, J.R. Windmiller, G. Valdés-Ramírez, F.J. Andrade, M.J. Schöning, and J. Wang, Biosens. Bioelectron. 54 (2014) 603.
[59] S. Demuru, B.P. Kunnel, and D. Briand, Adv. Mater. Technol. 5 (2020) 1.
[60] R. Vinoth, T. Nakagawa, J. Mathiyarasu, and A.M.V. Mohan, ACS Sensors 6 (2021) 1174.
[61] H.Y.Y. Nyein, L.C. Tai, Q.P. Ngo, M. Chao, G.B. Zhang, W. Gao, M. Bariya, J. Bullock, H. Kim, H.M. Fahad, and A. Javey, ACS Sensors 3 (2018) 944.
[62] M. Parrilla, I. Ortiz-Gómez, R. Cánovas, A. Salinas-Castillo, M. Cuartero, and G.A. Crespo, Anal. Chem. 91 (2019) 8644.
[63] G. Matzeu, C. O'Quigley, E. McNamara, C. Zuliani, C. Fay, T. Glennon, and D. Diamond, Anal. Methods 8 (2016) 64.
[64] M. McCaul, A. Porter, R. Barrett, P. White, F. Stroiescu, G. Wallace, and D. Diamond, ChemPhysChem. 19 (2018) 1531.
[65] T. Glennon, C. O'Quigley, M. McCaul, G. Matzeu, S. Beirne, G.G. Wallace, F. Stroiescu, N. O'Mahoney, P. White, and D. Diamond, Electroanalysis 28 (2016) 1283.
[66] Y. Lu, K. Jiang, D. Chen, and G. Shen, Nano Energy 58 (2019) 624.

[67] X. He, S. Yang, Q. Pei, Y. Song, C. Liu, T. Xu, and X. Zhang, ACS Sensors 5 (2020) 1548.
[68] N. Coppedè, M. Giannetto, M. Villani, V. Lucchini, E. Battista, M. Careri, and A. Zappettini, Org. Electron. 78 (2020) 105579.
[69] T. Terse-Thakoor, M. Punjiya, Z. Matharu, B. Lyu, M. Ahmad, G.E. Giles, R. Owyeung, F. Alaimo, M. Shojaei Baghini, T.T. Brunyé, and S. Sonkusale, Npj Flex. Electron. 4 (2020) 1.
[70] W. He, C. Wang, H. Wang, M. Jian, W. Lu, X. Liang, X. Zhang, F. Yang, and Y. Zhang, Sci. Adv. 5 (2019) 1.
[71] B. Brady, R. Wang, R. Cheong, X. and Wang, Analyst 146 (2021) 6119.
[72] W. Gao, S. Emaminejad, H.Y.Y. Nyein, S. Challa, K. Chen, A. Peck, H.M. Fahad, H. Ota, H. Shiraki, D. Kiriya, D.H. Lien, G.A. Brooks, R.W. Davis, and A. Javey, Nature 529 (2016) 509.
[73] Q. Zhai, L.W. Yap, R. Wang, S. Gong, Z. Guo, Y. Liu, Q. Lyu, J. Wang, G.P. Simon, and W. Cheng, Anal. Chem. 92 (2020) 4647.
[74] P. Pirovano, M. Dorrian, A. Shinde, A. Donohoe, A.J. Brady, N.M. Moyna, G. Wallace, D. Diamond, and M. McCaul, Talanta 219 (2020) 1.
[75] A. Lynch, D. Diamond, and M. Leader, Analyst 125 (2000) 2264.
[76] N.V.L. Lee, P.W. Miller, and M.J. Buono, Clin. Physiol. Funct. Imaging 30 (2010) 13.