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Research Article

DESIGN OF SOFT, BIOCOMPATIBLE SWEAT-BASED BIOSENSOR SYSTEM FOR WEARABLE HEALTH-CARE TECHNOLOGY

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Abstract

In recent years, the development of wearable health-care technology has gained significant attention, driven by the need for continuous health monitoring and the integration of advanced materials. This paper presents the design and implementation of a soft, biocompatible biosensor system aimed at enhancing the wearable health-care devices. The proposed biosensor system incorporates flexible, skin-conforming materials to ensure comfort and long-term wear ability. By utilizing biocompatible polymers and innovative fabrication techniques, the system can accurately check the health status by monitoring of sweat composition, and biomarkers such as electrolytes, metabolites, and pH levels. The core component of the system is a flexible substrate embedded with microelectronic sensors and wireless communication modules, enabling real-time data acquisition and transmission to external devices for further analysis. Preliminary concept of the sweat-based biosensor system demonstrates high accuracy and reliability under various environmental conditions, making it suitable for diverse applications in personal health monitoring, medical diagnostics, and remote patient care. The integration of this soft, biocompatible sweat-based biosensor system into wearable health-care technology has the potential to revolutionize health data collection and utilization, promoting proactive health management and enhancing overall patient outcomes.

Keywords: Design, Health-care.

INTRODUCTION

The evolution of wearable technology has transformed the landscape of personal health monitoring, enabling continuous, non-invasive tracking of physiological parameters. Among the various innovations in this field, soft sweat-based biosensors have emerged as a promising solution for real-time health monitoring with high fidelity. These sensors offer unique features of flexibility, biocompatibility, and the ability to analyze sweat a rich source of biomarkers making them ideal for integration into wearable medical devices. Sweat contains a wealth of information about an individual's physiological state, including electrolytes, metabolites, hormones, and other biomarkers (1,2). Conventional biosensor includes invasive process for capturing blood or other bodily fluids from patient body. Unlike blood-based analysis, sweat collection is non-invasive, painless, and can be performed continuously without the need for specialized skills. This makes sweat-based biosensors particularly attractive for continuous health monitoring, especially in wearable technology applications. Human body has irregular, curve-linear surfaces, which diminishes accuracy of biosensor system integrated in form of watch and glasses owing to gap between skin and rigid nature of sensors. Soft, biocompatible materials play a critical role in the development of these biosensors, as they must conform to the skin, ensure user comfort, and avoid irritation during extended wear. Advances in materials science and micro fabrication techniques have enabled the creation of sensors that are not only flexible and stretchable but also capable of accurate and reliable measurement of sweat biomarkers (3,4). This review article aims to provide a comprehensive overview of the current state of soft sweat-based biosensors for wearable technology.

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It will cover the fundamental principles of sweat analysis, design of soft materials used in soft sensor development, and the integration of these sensors into wearable devices. Additionally, the article will discuss the potential applications of sweat-based biosensors in health monitoring, the challenges faced in their development, and future directions for research in this exciting field. Based on the latest advancements and ongoing research, this review seeks to highlight the potential of soft sweat-based biosensors to revolutionize wearable health-care technology, offering new avenues for proactive health management and improved patient outcomes.

Sweat as bio-fluid for health-care monitoring

Sweat includes important bio–molecules. Which can be clue for health-status. Comparing to conventional invasive methods, sweat-based biosensor enables continuous and noninvasive monitor those biomolecules. As sweat glands are widely distributed across the human body, this platform is anideal platform for safe and noninvasive biosensing. Response of eccrine sweat gland can be measured simply because sweat is directly secreted to the skin surface. Unusual health conditions and disease could be monitored by changes in concentration of sweat or emergence of new sweat. For example, concentration of alcohol in sweat is highly correlated with those in blood. The increase of ureaconcentration in sweat is related to kidney failure. Moreover, analysis of chlorine in sweat hasbeen a widely used method for diagnosis of cystic Fibrosis Trust (CF) because CF patients have high chlorine concentration. Among the measurement process, bio-marker partitioning in human sweat is important to study because most biomarkers come from blood. Therefore, correlating sweat biomarkers with blood can help us to infer about the health of a person. In some cases, like CF patients, independent concentrations in sweat can have significant value. Eccrine glands are the first place where sweat is produced and the sweat transport to the skin surface through dermal ducts. During this process, analytes travel into human sweat. Since sodium and chloride ions have the highest concentration in sweat and can stimulate hydration, they maintain electrolyte balance in the human body. K+ concentration can be used to predict muscle activity. Concentration of lactate can indicate physical exertion and exercise intensity. Sweat also contains larger molecules such as glucose or hormones, and the sebio-marks carry valuable information about the human body. For example, monitoring the concentration of glucose in sweat can provide continuous glycemic. These biomarkers can be used for multi-purpose biomonitoring. Although it is a viable option to test sensors by sweat from exercise, under such circumstances, alternative methods are needed to achieve continuous monitoring system. Iontophoresis is the most advanced method toinduce sweat at a selected location. By applying a potential drop across the two sides of the testarea, pilocarpine will be driven by a small current under the skin surface and trigger glands to secrete sweat for sensors to collect abundant samples. We will discuss about technical process in next section.

Biosensor with sweat-secretion device

A biosensor's layout is crucial in determining its efficiency, sensitivity, and overall performance. The design involves the strategic arrangement of various components, such as the bioreceptor, transducer, and signal processor, to ensure optimal interaction with the target analyte and accurate signal detection (Figure 1). Purpose of wearable biosensor is continuous monitoring on skin for a long-term usability. Beyond from basic functions of biosensors, the continuous input from the skin will be required to monitor the glucose level continuously. Compared to blood and urine analysis, sweat analysis offers several advantages. However, it also faces challenges. Monitoring health and diagnosing conditions through sweat can be difficult due to contamination, evaporation, and the absence of real-time sweat sampling and sensing equipment. Advances in sensors for continuous sweat monitoring and the development of multiple sensor arrays for real-time analyte detection are making sweat sensing a promising non-invasive technology for continuous analyte monitoring, drawing increased interest from researchers in this field. Sweat extraction could be realized with two methods: passive sweat extraction and active sweat extraction. Passive sweat extraction is a commonly used non-pharmacological method for capturing sweat. Currently, most wearable sweat sensors rely on this technique. However, they are effective mainly under specific conditions, such as during strong level of exercise. Typically, these biosensors are made from paper or flexible silicone and are applied to the skin on the arm or forehead using transparent medical tape or double-sided tape since these areas tend to perspire more quickly (5,6). They can also be integrated into an arm guard, wristband, or headband. To generate enough sweat, individuals usually need to engage in vigorous exercise (running, cycling, or arm movement) for a period ranging from several minutes to over an hour, as sweat rates vary from person to person. The sweat biomarkers detected are often closely related to exercise functions, including glucose, lactate, cortisol, Na+, Cl-, K+, and others. While previous studies have demonstrated the feasibility of detecting biomarkers in sweat during intensive exercise, the varying sweat secretion rates affect the accuracy and reliability of the results. Detection becomes difficult when the sweat secretion rate is low, such as during prolonged sitting or at low temperatures. Additionally, the exercise-induced method is unsuitable for certain populations, like infants and the elderly, and for detecting chronic disease markers.

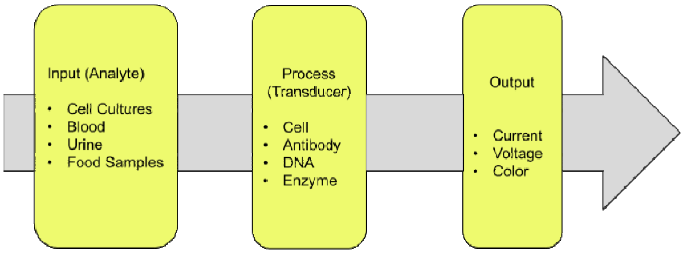

Figure 1. Representative components of biosensor and examples of each stage

To continuously collect sweat, active extraction methods such as iontophoresis and local thermal stimulation are necessary (Figure 2). Iontophoresis, also known as ion electrophoresis, employs a continuous direct current to drive ions or charged chemical drugs into the body using the principle of homoelectric repulsion. This method, developed by Gibson and Cooke in 1959, used the cationic drug pilocarpine to induce sweating. Short-term electrical stimulation can deliver secretory agonist molecules that stimulate sweat glands to produce sweat for several hours. Iontophoresis enables real-time active sweat extraction, addressing the challenge of monitoring sweat in natural conditions and is widely used in clinical research. Current studies primarily use iontophoresis to extract and monitor sweat with laboratory equipment. Recent study advanced this concept by integrating it with a wearable sensing unit, creating an electrochemically enhanced iontophoresis interface (7). This innovation allows for sufficient sweat extraction for stable analysis without causing discomfort to patients. The system can be programmed to periodically induce sweat secretion with different characteristics, providing new insights into sweat gland physiology and forming an autonomous platform for monitoring sweat analytes like glucose, Na+, and Cl-. This research enhances sweat health monitoring and contributes to disease diagnosis. The effects of different drugs and doses on sweat production time and rate were also studied to better control sweat extraction. Additionally, local thermal stimulation can efficiently and controllably induce sweat production (8). Compared to passive methods, active sweat extraction methods like iontophoresis and local thermal stimulation offer several advantages: they control sweat secretion, enabling in situ and real-time detection with improved reliability, eliminate the need for strenuous exercise, which is crucial for patients, the elderly, and infants, and expand the range of detectable sweat biomarkers. These methods have applications in diagnosing and managing conditions like cystic fibrosis, monitoring nutritional status non-invasively, and continuous point-of-care drug monitoring.

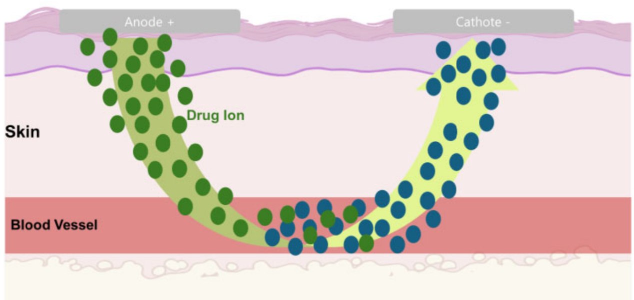

Figure 2. Schematic showing the mechanism of reverse iontophoresis

Despite these advancements, active sweat extraction research is still in its early stages, and further studies are needed to understand the core mechanisms and ensure long-term stability of these methods.

Design of soft materials for wearable biosensor

Conventional active materials are typically rigid and damage our soft human body or organs under dynamic movements. An ideal integrated wearable device should maintain their functions under many circumstances. In an engineering aspects, a soft wearable device will have interconnections, skin-contact electrodes, and device electrodes. For the interconnections, the conductive materials need to absorb mechanical stress originates from extreme mechanical deformations without deteriorating much conductivity. To meet this requirement, material design has been widely explored based on mechanical characterization by using stress-strain curve which is critically important method to determine the modulus (Figure 3). Stretchable nanowire materials, ionic conductors, and conductive polymers meet those requirements. For the skin-contact electrodes, conductive materials need to be highly conductive, biocompatible, stretchable, and durable. As for the device electrodes, the interface between soft sensors and wireless circuitry is a challenge. To solve this, conductive glue and liquid metals are often used. Some of nano or micro structural designs are not compatible with the modern printed circuit board industry because they largely depend on the control of the interface between rigid materials and soft elastomeric materials. The serpentine bridge-island design is an alternative strategy to combine the rigid printed circuit board based electronics ("island") and the soft interconnects ("bridge"). Serpentine design connects conventional rigid stretchable healthcare devices with stretchable serpentine conductive electrodes, which consists of photolithography patterned polymer thin film with metal evaporation. Therefore, it can be easily deformed to stretch and ensure the functionality of the overall structure. Single sinusoidal-like serpentine can give unidirectional stretch ability. This can be extended to fractal design that can stretch in both directions by introducing other fractal constructs to yield space-filling structures of electronic materials. Most extrinsic structural design involves templates or masks the stretchable patterns. Because it's indirect and time consuming, they create kirigami designs which directly modify the file-based electrodes through laser ablation patterning. Kirigami pattern, inspired by the ancient art of paper cutting, formed buckling deformation to offer extended stretch ability to extrinsic materials.

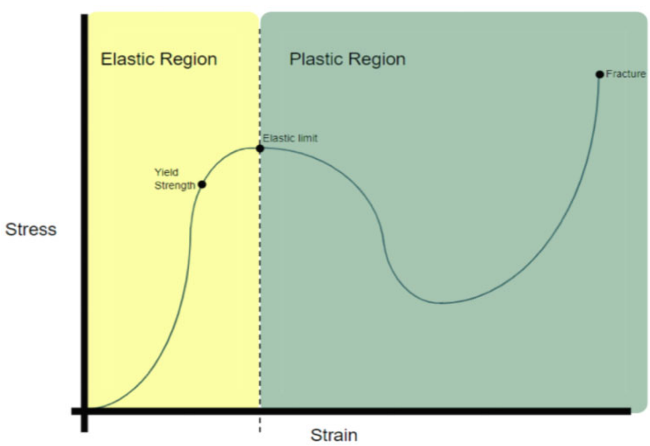

Figure 3. Strain-stress curve of typical elastic materials

For example, a uniaxial kirigami pattern of silver nanowire thin film was long to 200% of its original length before rupture. Applied stress is also well-distributed throughout the kirigami pattern. In addition, it can be programmed to enable uniaxial, biaxial and omnidirectional stretch ability. Unlike extrinsic stretchable structural design, novel nanomaterials can be stretched without sophisticated processing technology, which doesn't heavily rely on patterning and provides an alternative strategy to fabricate stretchable healthcare devices. Metallic nanomaterials have been broadly applied for the construction of soft wearable healthcare devices because its intrinsic conductivity is 2 orders higher than their carbon-based counterparts. Au and Ag have shown great potential for stretchable bioelectronic devices because use of active metal can limit their application for on-skin and implantable healthcare devices due to their oxidation process. AgNWs performed high conductivity and flexibility. The nanocomposites showed high conductivity of 41 850 S cm^{-1}, which yields an intrinsic stretch ability of up to 840% (9). The high stretch ability leads to the formation of electrically highly conductive Ag and Au. Liquid metal (LM) is gallium based alloys that exhibit both metallic and fluidic properties. Gallium Indium eutectic uses liquid metal and maintains a high electrical conductivity. However, it is required for on-skin and implantable healthcare applications. LM may be injected into the micro channels to fabricate a highly stretchable conductor. It can stretch to the stretching limit of the hosting elastomer without electrical failure. In addition, due to the property of LM, conductive traces can be cut and reconnected. The electronic properties of the composite are highly dependent on the amount of the incorporated LM. Conductive polymers have been used as soft wearable materials for hydrogel electronics. Printed conductive polymer thin film is rigid with a low fracture strain. Due to this, many strategies like modification of the polymer elastomer interface and addition of conductivity-enhancing do pants are applied to enhance stretch ability and conductivity of biosensor.

Non-invasive glucose monitoring from bodily fluids

Glucose can easily pass through blood vessel membranes due to its small size as an organic molecule. There are many controversial findings about the correlation between capillary blood glucose (CBG) and salivary glucose (SG) concentrations in the literature. In healthy individuals, there is no established connection between CBG and SG concentrations. However, in diabetic patients, studies have shown conflicting results, with some finding a positive correlation and others finding no correlation at all. This inconsistency makes using SG concentration as a reliable indicator for diabetes mellitus inconclusive. Gingival crevicular fluid (GCF) is an extracellular fluid secreted from the epithelia of the gingival crevice, a V shaped crevice surrounding all teeth. Researchers investigated the possibility of using gingival crevicular blood to measure glycaemia among diabetics. The results showed that there is a correlation between GCB glucose and CBG concentrations. Techniques using GCB can be used to diagnose diabetes or to monitor CBG level in known diabetics in an inexpensive, safe, and easy way to perform without the use of additional tools. In conclusion, GCB concentration fits for noninvasive CBG assessment among diabetics. The first glucose biosensor consisted of electrodes that monitored the consumption of oxygen catalyzed by glucose oxidase enzymes. Yamaguchi et al. developed a system that combined flow injection analysis and an O_2 electrode to determine SG concentration (10). The system allowed monitoring the real-time changes of SG level. It improved later by replacing the O_2 electrode with a hydrogen peroxide. In this improved sensor, an increase of hydrogen peroxide is observed as an increase in the output current. The use of hydrogen peroxide electrode type glucose sensor was more desirable than O_2 electrode type sensor because it reduced the influence of dissolved O_2. Another method is the cross linking method. The sensor eliminates O_2 levels dependence and it only took a few seconds to detect glucose measurement. Saliva samples were collected using a conventional sampling method and subsequently analyzed using the previously discussed SG sensors. Research was carried out towards the development of diagnostic devices to collect GCF glucose level. The GCF noninvasive monitoring system contained a disposable GCF-collecting device, glucose testing tape, and portable optical analyser. In the presence of glucose hydrogen peroxide was generated and this in turn oxidized the tetramethylbenzidine. This reaction catalyzed by peroxidase enzyme resulting in color change on the glucose testing tape from white to blueish green: The color intensity was then measured and the final output was displayed on the GCF glucose monitor. The device was later modified to reduce the sample volume size. The new GCF collecting device only collects the GCF sample alone while old models collect enzymes and chromogen also. Because the new GCF device increased accuracy, repeatability, sensitivity, and specificity it has potential to be used as a screening method for noninvasive CBG measurement among diabetics. In conclusion, the correlation between CBG and SG concentrations still raises controversy, new biosensing technologies that focus on the measurement of GCF glucose concentration are needed.

Conclusion

In this paper, we reviewed about state-of-art wearable biosensor technology, especially based on sweat-detection system. The design of a soft, biocompatible sweat-based biosensor system represents a significant advancement in wearable health-care technology. This innovative approach offers non-invasive, continuous monitoring of physiological parameters, providing real-time insights into an individual's health status. The integration of biocompatible materials ensures minimal irritation and maximizes user comfort, making it suitable for long-term wear. The capability of system to analyze sweat biomarkers with high sensitivity and specificity holds great promise for early disease detection, personalized health monitoring, and preventive care. Future work will focus on optimizing sensor accuracy, expanding the range of detectable biomarkers, and enhancing data processing algorithms to improve the overall functionality and usability of the biosensor system. As wearable health-care technology continues to evolve, the development of such biosensors will play a crucial role in the shift towards more personalized and proactive health management.

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