Wearable Sweat Biosensors

Wei Gao, Hnin Y. Y. Nyein, Ziba Shahpar, Li-Chia Tai, Eric Wu, Mallika Bariya, Hiroki Ota, Hossain M. Fahad, Kevin Chen and Ali Javey*
Department of Electrical Engineering and Computer Sciences, University of California, Berkeley, California 94720, USA.
*Email: ajavey@berkeley.edu

***Abstract*—**Wearable perspiration biosensors enable real-time analysis of the sweat composition and can provide insightful information about health conditions. In this review, we discuss the recent developments in wearable sweat sensing platforms and detection techniques. Specifically, on-body monitoring of a wide spectrum of sweat biomarkers are illustrated. Opportunities and challenges in the field are discussed. Although still in an early research stage, wearable sweat biosensors may enable a wide range of personalized diagnostic and physiological monitoring applications.

I. Introduction

Wearable biosensors are expected to play a significant role in future healthcare as they allow real-time and non-invasive (or minimally invasive) monitoring of an individual's health state [1-4]. Currently commercialized wearable sensors are only capable of tracking an individual's physical activities and vital signs but fail to provide insightful physiological information at the molecular level. Human sweat, an important body fluid that can be retrieved conveniently and non-invasively, contains rich information about our health and fitness conditions. Therefore, sweat can be an ideal candidate for developing wearable chemical biosensors (Figure 1) [3-21] which may provide insightful physiological information. In the past decade, tremendous progress has been made on developing such sweat biosensors as illustrated in Table 1. These wearable biosensors have been used to measure the detailed sweat profiles of a wide spectrum of analytes including metabolites, electrolytes and heavy metals during various indoor and outdoor physical activities.

II. System design of wearable sweat biosensors

A. Platform of sweat biosensors

Wearable sweat biosensors are usually prepared on a flexible substrate that forms conformal contact with the skin, while minimizing the required sweat volume to perform proper sweat collection and analysis. Different sensing platforms have been developed in the past decade which include the epidermal tattoos, flexible patches/bands and textiles (Figure 2).

B. Target of analytes

A variety of sweat biomarkers are closely related to human health conditions, and they can serve as excellent targeting analytes for wearable sweat biosensors. For example, sweat chloride test is the gold standard for diagnosis of cystic fibrosis; excessive loss of Na^+ and K^+ in sweat could result in hyponatremia, hypokalemia, muscle cramps or dehydration; sweat ethanol and glucose are reported to be metabolically related to blood ethanol and glucose; sweat lactate can potentially serve as a sensitive marker of pressure ischemia. Monitoring these important biomarkers using wearable sweat biosensors can offer us insightful physiological and clinical information.

C. Detection techniques

Based on detection strategies, current wearable sweat biosensors include optical sensors for sweat rate and sweat pH analysis [13], impedance-based sensors for sweat conductivity and sweat rate monitoring [20], ion selective electrodes for electrolyte sensing (such as Na^+, K^+, H^+, NH_4^+, Ca^{2+}, Cl^-) [4, 6-9, 14-19], enzymatic amperometric sensors for metabolite sensing (such as glucose, lactate, uric acid, ethanol) [4, 10, 11], and stripping based sensors for heavy metal analysis (such as Cu, Zn, Pb, Cd, Hg) [5, 12] (Figure 3).

D. System integration

Since sweat secretion is complex, to extract more useful information, simultaneous detection of multiple sweat biomarkers through system integration is critical. A fully integrated multiplexed sweat sensing system has been developed by merging plastic-based sensors that interface with the skin and silicon integrated circuits consolidated on a flexible circuit board for complex signal processing. Figure 4a shows a schematic of the sweat sensor array consisting of 2 metabolite sensors (glucose and lactate), 2 electrolyte sensors (Na^+ and K^+) and a skin temperature sensor [4]. Figure 4b illustrates the system-level overview of the signal transduction, processing, and wireless transmission paths to facilitate multiplexed on-body measurements. Eventually the data from the system is wirelessly transmitted to a cellphone and displayed in a custom-developed application.

E. System level characterizations and compensation

It has been shown that each sensor can maintain excellent selectivity upon varying concentrations of each analyte during system-level multiplexed measurements (Figure 5a) [4]. However, temperature and pH have shown great influence on the performance of amperometric enzymatic based sensors (Figure 5b and 5c) [4, 14]. Utilization of such fully integrated wearable device can facilitate measurement accuracy through real-time calibration and signal compensation.

III. Real time on body sweat analysis for health monitoring

The sweat biosensors can be worn on body for real-time perspiration analysis during a variety of physical activities, allowing non-invasive health monitoring. Recently, the on-body evaluation of sweat biosensors has opened the door for a wide range of physiological and clinical investigations.

A. Real time analysis of major sweat metabolites (glucose and lactate) and major electrolytes (Na^+ and K^+)

Physiological monitoring of sweat lactate and sodium using wearable sweat sensors has been demonstrated on different platforms [7, 9, 16, 17]. Simultaneous measurements of multiple sweat analytes using a fully-integrated sensing system was also reported during a cycling exercise [4]. Figure 6 shows that, as perspiration begins, both lactate and glucose levels in sweat decrease gradually. The decreased sweat lactate and glucose levels is owing to the dilution effect caused by an increase in sweat rate, which is visually observed as exercise continues. Sweat [Na^+] increases and [K^+] decreases in the beginning of perspiration, in line with the previous *ex-situ* studies from the collected sweat samples [4]. Both [Na^+] and [K^+] stabilize as cycling continues.

B. Real time sweat Ca^{2+} and pH monitoring

Calcium is an essential component for human metabolism, and pH is crucial for potential disease diagnosis. Sweat pH sensors have been measured optically and electrochemically [7, 21]. A fully integrated wearable sensing device (Figure 7a) has also been demonstrated for simultaneous evaluation of pH and Ca^{2+} in human perspiration which is particularly important considering that free Ca^{2+} level in biofluids is dependent on pH [6]. Figure 7b displays the sweat profiles of a subject during a constant load cycling exercise: sweat pH increases gradually for 5 min and then stabilizes in the remaining cycling exercise while the Ca^{2+} sensor shows an opposite trend. The responses of these sensors were validated with a commercial pH meter and inductively coupled plasma-mass spectrometry (Figure 7b).

C. Sweat heavy metal monitoring

Besides metabolites and electrolytes, a variety of heavy metals can be found in human sweat and are closely related to human health conditions. Printed tattoo based sweat sensors have been used for sweat Zn monitoring [12]. Recently, a microsensor array containing biocompatible gold and bismuth electrodes has been developed to simultaneously measure multiple heavy metals in sweat including Zn, Cd, Pb, Cu, and Hg through stripping voltammetry (Figure 8a-c) [5]. Sweat Cu and Zn were monitored on-body during a cycling exercise (Figure 8d). These trace metals sensors can monitor heavy metal exposure and aid in related clinical investigations.

D. Ethanol monitoring

High blood alcohol levels can cause severe traffic accidents and increased risks for cancers while sweat ethanol is reported to be the same as blood alcohol concentration (BAC). Wearable sweat ethanol sensors which integrate an iontophoresis based sweat extraction system along with a flexible wireless circuit board have been developed [11]. These sensors demonstrate clear differences in the current response before and after alcohol consumption, reflecting the increase of blood ethanol levels (Figure 9).

E. Glucose correlation study

The wearable sweat biosensors can potentially be used for diabetes monitoring and control. A graphene-based electrochemical device has recently been developed to measure real-time sweat glucose through pH calibration [14]. With the aid of this device, a correlation between sweat glucose data from the wearable diabetes patch and those from a commercial glucose assay as well as blood glucose data from a commercial glucose meter was observed (Figure 10).

F. Dehydration monitoring

Monitoring hydration status is of the utmost importance to athletes because fluid deficit impairs endurance performance. The sweat biosensors can be potentially used for effective and non-invasive monitoring of the electrolyte loss (Figure 11a) [4]. Figure 11b shows that sweat [Na^+] measured from an integrated sensor array was stable throughout running in euhydration trials (with regular water intake). On the other hand, a substantial increase in sweat [Na^+] was observed in dehydration trials (without water intake) after 80 min when subjects had lost a large amount of water (Figure 11c). The results show that through sweat composition analysis, insightful information may be provided for athletic performance applications.

IV. Conclusion & Outlook

Wearable sweat biosensors deliver a practical wearable sensor technology that can facilitate personalized and real-time physiological and clinical investigations. Although significant progress has been made by different groups, several major challenges remain for sweat sensing: on-body stability and reliability of the chemical sensors are the key analytical challenges; there is a strong need to develop wearable power sources or minimize power consumption of the current wearable sweat sensors; on demand controllable extraction of sweat biomarkers; the correlation between the levels of sweat biomarkers with certain physiological or clinical conditions. We envision that these challenges could be addressed through innovative, collaborative and interdisciplinary research. The large data sets that could be collected through population based studies would greatly aid the investigations on the physiological status and clinical needs of individuals and society.

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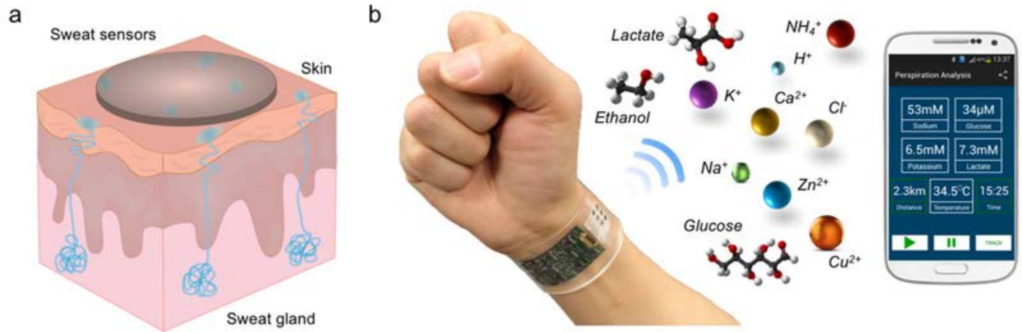

Fig. 1. Wearable sweat biosensors which continuously measure a variety of sweat compositions for health monitoring.

Platform	Analytes	Refs.
Temporary tattoo	Lactate, pH, NH_4^+, Na^+, Zn^{2+}, ethanol	7-12
	pH	13
Patch	Glucose, lactate, Na^+, K^+, pH, Ca^{2+}, Zn^{2+}, Cu^{2+}	4-6
	Glucose, pH	14
	Na^+	15-17
	Cl^-	18, 19
	pH	20, 21

Table 1. Summary of the wearable sweat biosensors.

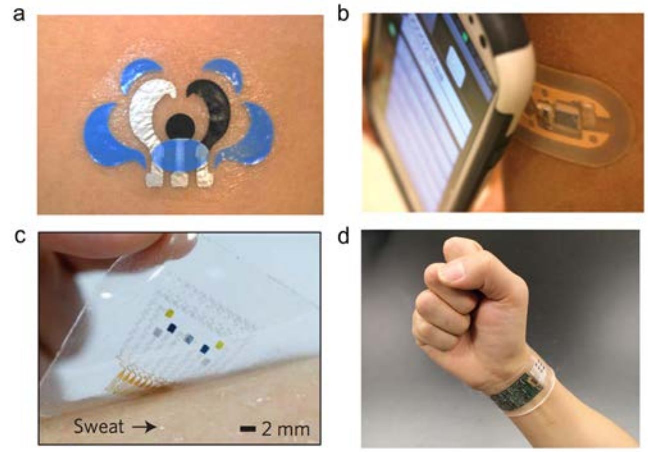

Fig. 2. The representative sweat biosensing platforms: a) epidermal temporary tattoo [8]; b) adhesive RFID sensor patch [15]; c) flexible and stretchable sensor patch [14]; d) fully integrated flexible sensor band [4].

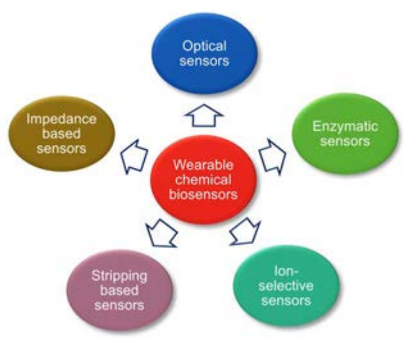

Fig. 3. The categories of wearable chemical sensors.

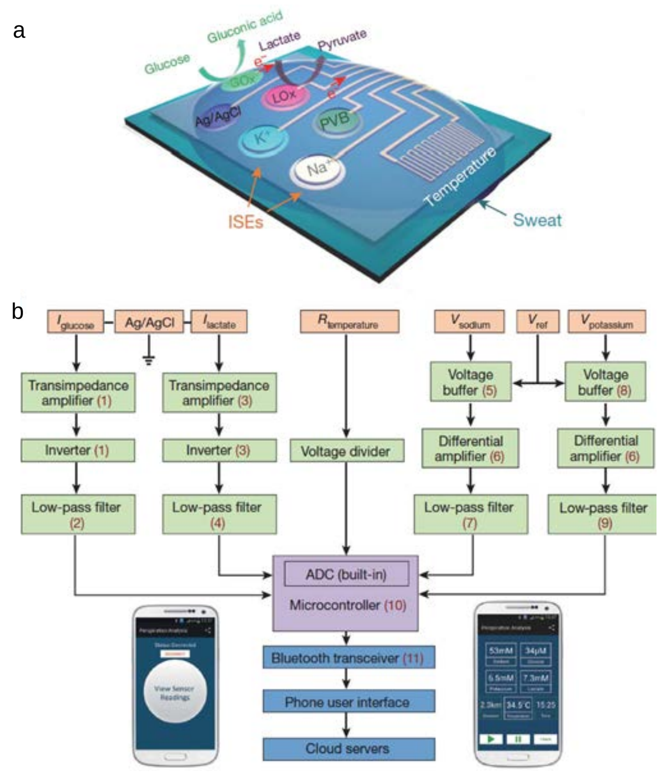

Fig. 4. Fully integrated sensor arrays (FISA) for multiplexed perspiration analysis [4]. a) Schematic of the sensor array (including glucose, lactate, sodium, potassium and temperature sensors). b) System-level block diagram of the FISA.

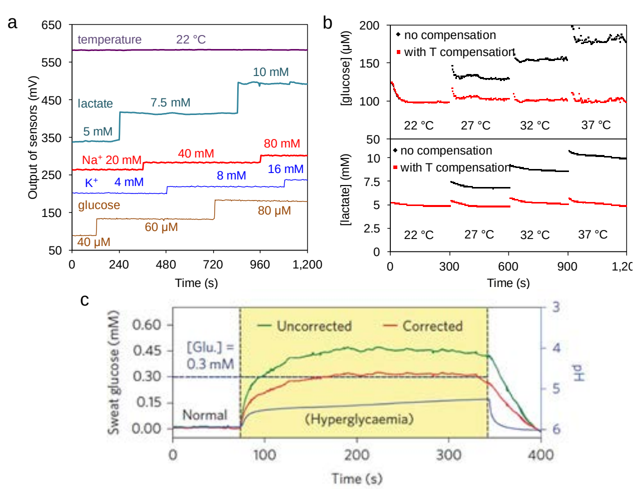

Fig. 5. a) System-level multiplexed measurements and interference studies [4]. b, c) System-level real-time temperature (b) [4] and pH (c) [14] compensation for enzymatic sensors.

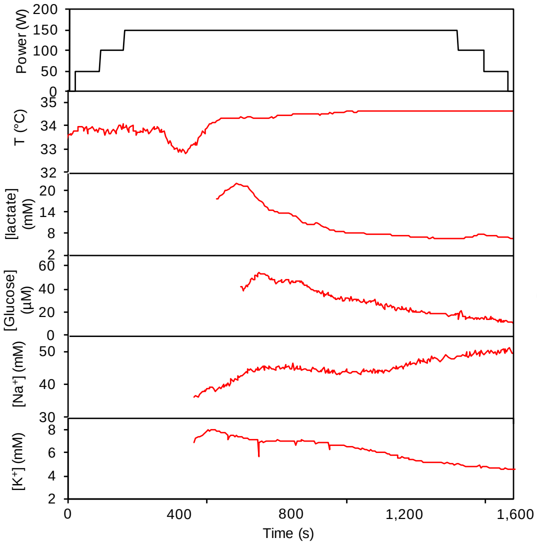

Fig. 6. On-body real-time multiplexed monitoring of sweat glucose, lactate, sodium, potassium as well as the skin temperature using a FISA worn on a subject's forehead during a constant-load cycling exercise [4].

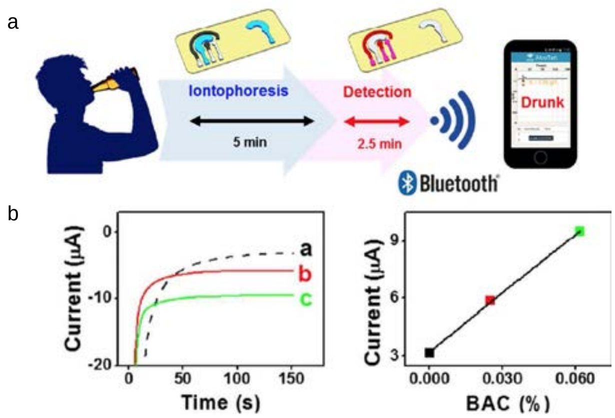

Fig. 9. Tattoo-based transdermal alcohol sensor [11]. a) Schematic diagram of the wireless operation of the iontophoretic-sensing tattoo device for transdermal alcohol sensing. b) experiments to demonstrate correlation between BAC level and current response from the tattoo biosensor measured.

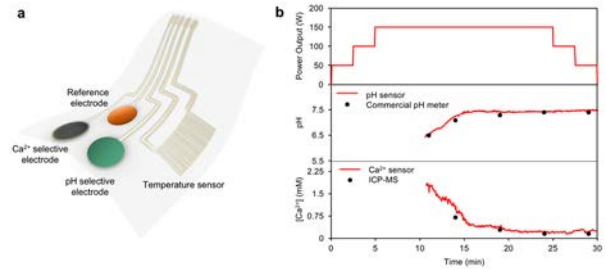

Fig. 7. Wearable sensors for Ca^{2+} and pH monitoring of body fluids [6]. a) A schematic of a flexible sensor array. b) On-body Ca^{2+} and pH analysis during a constant-load cycling exercise.

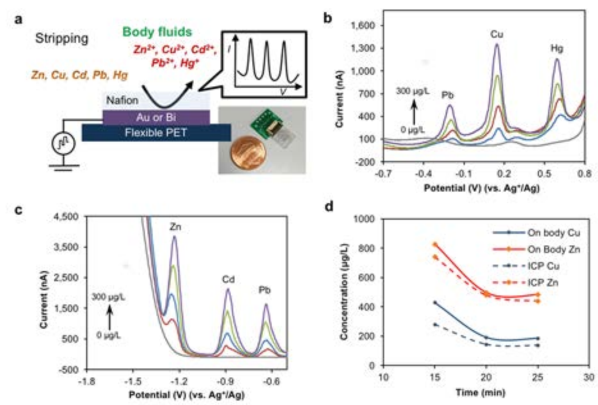

Fig. 8. Flexible microsensor arrays for multiplexed heavy metals analysis [5]. a) Schematic of microelectrodes. b, c) Characterization of Au and Bi microelectrodes for trace metal detection. d) On body trace metal detection during a constant-load cycling exercise.

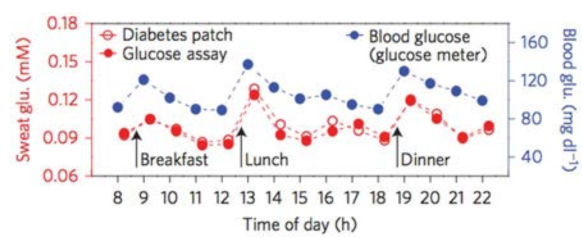

Fig. 10. One-day monitoring of sweat glucose concentrations using wearable diabetes patch and blood glucose levels using commercial blood glucose meter [14].

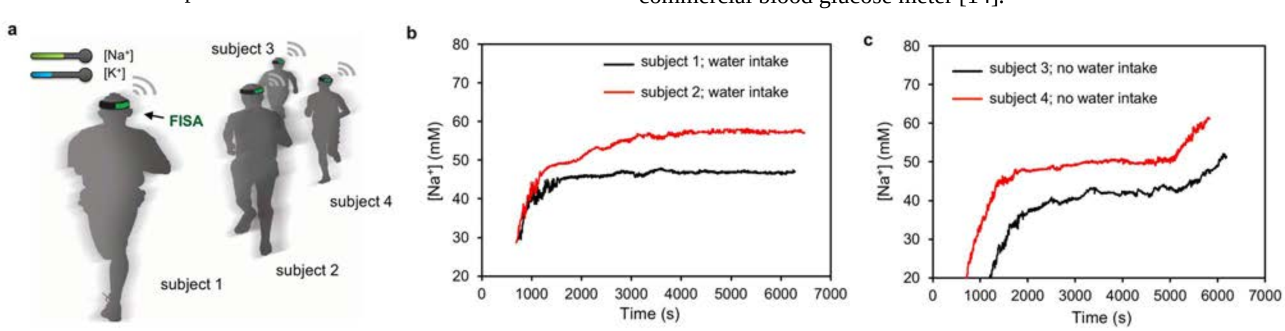

Fig. 11. Hydration status analysis during group outdoor running using the wearable sensors [4]. a) Schematic illustration showing the group outdoor running trial based on wearable FISAs (packaged as 'smart headbands'). The data are real-time transmitted to the user's cell phone and uploaded to cloud servers. b) Representative real-time sweat sodium levels during an endurance run with water intake (b) and an endurance run without water intake (c).