Biosensors and Bioelectronics 93 (2017) 139–145

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

A wearable multisensing patch for continuous sweat monitoring

Salzitsa Anastasova[a,*], Blair Crewther[a,b], Pawel Bembnowicz[a], Vincenzo Curto[a], Henry MD Ip[a], Bruno Rosa[a], Guang-Zhong Yang[a]

[a] The Hamlyn Centre, Department of Computing, Imperial College, London, UK
[b] Institute of Sport – National Research Institute, Warsaw, Poland

ARTICLE INFO

Keywords:
Flexible patch
Microfluidic
Sensors
Exercise
Saliva

ABSTRACT

In sport, exercise and healthcare settings, there is a need for continuous, non-invasive monitoring of biomarkers to assess human performance, health and wellbeing. Here we report the development of a flexible microfluidic platform with fully integrated sensing for on-body testing of human sweat. The system can simultaneously and selectively measure metabolite (e.g. lactate) and electrolytes (e.g. pH, sodium) together with temperature sensing for internal calibration. The construction of the platform is designed such that continuous flow of sweat can pass through an array of flexible microneedle type of sensors (50 µm diameter) incorporated in a microfluidic channel. Potentiometric sodium ion sensors were developed using a polyvinyl chloride (PVC) functional membrane deposited on an electrochemically deposited internal layer of Poly(3,4-ethylenedioxythiophene) (PEDOT) polymer. The pH sensing layer is based on a highly sensitive membrane of iridium oxide (IrOx). The amperometric-based lactate sensor consists of doped enzymes deposited on top of a semipermeable copolymer membrane and outer polyurethane layers. Real-time data were collected from human subjects during cycle ergometry and treadmill running. A detailed comparison of sodium, lactate and cortisol from saliva is reported, demonstrating the potential of the multi-sensing platform for tracking these outcomes. In summary, a fully integrated sensor for continuous, simultaneous and selective measurement of sweat metabolites, electrolytes and temperature was achieved using a flexible microfluidic platform. This system can also transmit information wirelessly for ease of collection and storage, with the potential for real-time data analytics.

1. Introduction

One of the unique challenges in sport, exercise science and healthcare, is the need for continuous, non-invasive monitoring of biomarkers for assessing human performance, health and wellbeing Lo et al. (2011). For example, the monitoring of hydration status and other vital signs during sporting activities can provide a wealth of information regarding one's physiological capacity and efficiency under stress. Alternatively, it may assist in personalising programmes for optimal training gins and recovery. Biochemical markers, while being important for physiological and pathological characterisations, are typically measured with blood assays; however, these can be problematic due to the invasive nature of sample collection and associated risks, along with poor compliance rates among subjects where blood collection is undesirable and difficult.

Sweat has been recognised as an easily accessible bodily fluid that can provide important diagnostic information (Mena-Bravo and de Castro, 2014; Raiszadeh et al., 2012). For example, certain genetic disorders (e.g. cystic fibrosis) can be diagnosed in infants from their sweat composition (Rock et al., 2014). Sweat also contains other proteins and metabolites linked to disease and infection (Mena-Bravo and de Castro, 2014; Raiszadeh et al., 2012). Humans have two types of sweat glands; eccrine glands cover the entire body and produce sweat to regulate body temperature, whereas apocrine glands are mainly found in the armpits and have a limited role in body cooling. Sweat is a clear, hypotonic and odourless fluid often described as an ultrafiltrate of plasma. It contains mainly ions such as sodium, potassium, calcium, magnesium, chloride and lactate. Sweat is easily accessible, with a typical sweat rate of human males measuring 0.85 mg cm^{-2} min^{-1} at the lower back (Patterson et al., 2000).

Several key biomarkers relevant to human health and performance can be assessed in human sweat. Sodium, for instance, is a marker for electrolyte imbalance and important for monitoring athletic performance in hot and humid environments, where sweat (and electrolyte) losses can impair physiological function (Bandodkar et al. 2014). In healthcare, a significant loss of sodium in patients with cystic fibrosis (Mena-Bravo and de Castro, 2014) can also cause hyponatremia. Sweat pH is another indicator of health and wellness. Lactate concentration in

* Corresponding author.
E-mail address: s.anastasova-ivanova@imperial.ac.uk (S. Anastasova).

http://dx.doi.org/10.1016/j.bios.2016.09.038
Received 17 June 2016; Received in revised form 4 September 2016; Accepted 10 September 2016
Available online 21 September 2016

sweat can also indicate the energy pathways contributing to physical activity or general metabolic efficiency. A recent study reported a correlation between lactate levels in blood and sweat during exercise (Sakharov et al., 2010). This biomarker has additional potential for examining oxygen supply to tissue in diseased states, as a fall in oxygen delivery will produce a concomitant rise in anaerobic metabolism and thus, sweat lactate concentration. One such example is the testing of oxidative metabolism under pressure-induced ischemia (Arena and Sietsema, 2011).

Electrochemical sensors present a promising technique for continuous monitoring of localised biological changes in sweat, due to inherent advantages of miniaturisation and non-invasive sample collection (Gao et al., 2016; Kim et al., 2015; Lisak et al., 2015; Matzeu et al., 2015). One difficulty faced when developing wearable biosensors is the need for physical contact and continuous analyte sampling. Unlike spot measurements, where large quantities of sweat are collected in a time-lapse manner, continuous monitoring requires the management of continuous sweat flow. In addition, this must be achieved under those dynamic environments (e.g. exercise, training) that active a sweat response. Previous biosensors have some limitations, as they can only monitor a single analyte and do not have on-site signal processing circuitry and sensor calibration mechanisms (Bandodkar and Wang, 2014; Jia et al., 2013; Rose et al., 2015). Recently, Gao et al. (2016) reported a fully integrated system that could simultaneously and selectively measure different analytes, as well as skin temperature for real-time sensor calibration. We hoped to extend this work by achieving simultaneous and selective measurements using several integrated sensors, plus temperature control for internal calibration, along with additional capabilities to allow a constant sweat flow for analysis and wireless data transmission to make the platform robust, wearable and easy to use.

In this paper, we present the development of a wearable electronic sensor, complete with microfluidic sampling and wireless readout electronics, which simultaneously measures the concentrations of hydrogen and sodium ions, as well as lactate in human sweat. Additional temperature and humidity sensors were used for internal calibration. The proposed platform is tailored for sweat monitoring during exercise of extended periods by incorporating paper microfluidic channels and reservoirs (Thuo et al., 2014). Sweat enters the paper channel via a small window (10×10 mm) through capillary attraction. The small window size ensures that even a small amount of sweat is sufficient for detecting the parameters of interest. The natural liquid wicking properties of paper facilitates sweat sampling, circumventing the problem of sweat accumulation, which often leads to inaccurate acquisition during longer experimental periods (Gao et al., 2016). Sweat is continuously absorbed at the entry window of the smart microfluidic system while sweat collected at the exit ports (reservoirs) are evaporated. This provides a continuous flow through the sensor surface and avoids sweat accumulation.

2. Materials and methods

This study was conducted as a two-step process. First, a microfluidic platform was designed to create a constant flow of sweat within a robust and flexible embodiment for the chemical transducers. Low power wireless electronics were also developed and successfully integrated. The miniature electrochemical sensors were calibrated in the laboratory and checked against standard equipment. Second, the sensors were validated on human volunteers during running and cycling activities of increasing intensities. Saliva samples were also collected across exercise for tracking and comparing sodium, lactate and cortisol in this fluid, with an expected trend towards elevated biomarker levels with exercise intensity.

2.1. Microfluidic patch design

Several in vitro experiments were conducted with a novel thin flexible wearable patch that incorporates a paper microfluidic channel, with embedded flexible microneedle-based sensors connected with a wireless potentiostat. The advantage of using a microfluidic system is the possibility of using micro volumes of sweat for analyte testing. The fluid system is simple and the size can be modified and tuned depending on the attachment site on the body. An integrated sensing system inside the microfluidic channel also gives the advantage of minimum delay in sampling and subsequent analysis of the sample fluid.

The microfluidic patch consists of layers of polymer, paper microfluidics, and flexible sensors. A CO_2 laser fabrication system (Model VLS 6.6, Universal Laser System) was used to cut out structures on the various polymer layers, which includes a 80 µm thick layer of pressure sensitive adhesive (PSA) (layer 2 from the bottom, Fig. 1) that was laminated onto a layer of 50 µm thick Poly (methyl methacrylate) (PMMA) (layer 1 and 4 from the bottom, Fig. 1). The sensors were placed inside the microfluidic channel (Fig. 1) which draws a constant flow of fresh sweat passing through them. The continuous delivery of fresh sweat towards the biosensing area is essential for the correct operation of the biosensors during prolonged periods of exercise. However, the use of conventional or miniaturised pumping system

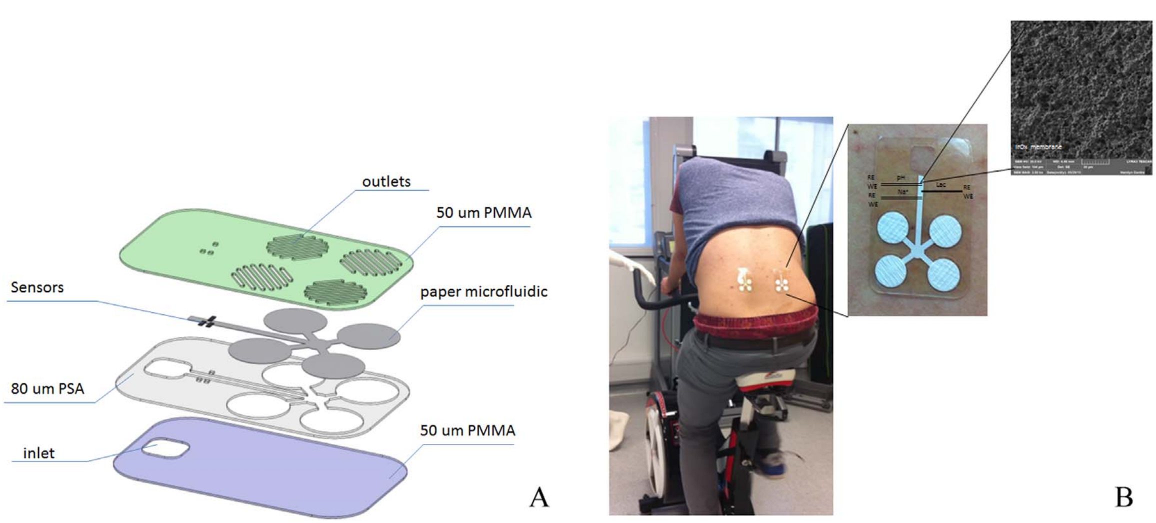

Fig. 1. (A) Schematic representation of the fabrication steps of the micro-fluidic chip; (B) photo of the platform attached to the body and scanning electron microscopy (SEM) image (magnification 2.00 k×) photo of IrOx pH sensor membrane on top of a 50 µm Pt wire.