

Real-time Analysis of Electrolytes in Sweat Through a Wearable Sensing Platform [†]

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Abstract: The field of biochemical sensing is evolving from the use of bulky apparatuses to the development of miniaturized systems allowing personal sensing and point of care analysis. We report a wearable platform capable of measuring the concentration of multiple electrolytes in sweat (Na^+ , K^+ , Cl^-). The platform accesses sweat emerging through the skin, drawing it across solid-state ion-selective electrodes by capillary action. The electrolyte composition is monitored in real time by potentiometry. The sensor data is digitised and transmitted via Bluetooth to a mobile phone or laptop. The platform has been employed in on-body trials during controlled exercise.

Keywords: wearable sensors; ion-sensitive electrodes; sweat electrolytes; personal sensing; solid-state electrodes; fluidics

1. Introduction

Wearable sensors represent a growing field of research and a significant industrial sector. Within biomedical diagnostics, there is a drive towards the development of miniaturised systems, which would allow real time monitoring of the status of a patient and aid personalised medicine interventions [1]. A significant issue with biochemical sensors is the invasiveness associated with accessing biological fluids such as blood and intracellular fluid, coupled with the short lifetime of the sensors. In contrast, sweat represents a readily accessible biological fluid, and contains several analytes which can be indicative of the health status of the individual. Electrolytes such as sodium and potassium ions are, for example, important in determining the hydration status in athletes, and people who work in harsh conditions. Their concentration may also be altered in the sweat of people suffering from certain clinical conditions, such as cystic fibrosis [2]. It has even been proposed that, thorough the application of multivariate analysis algorithms, reliable information on the concentration of glucose in blood can be extracted from knowledge of the concentration of metabolites in sweat [3]. The research on wearable sweat sensors has been recently reviewed [4]. Our group has developed the so-called ‘SwEatch’ platform [5,6], a device which is capable of drawing sweat from the skin of the wearer, and continuously measuring the concentration of Na^+ ions through potentiometric sensors. Herein, we report an improved version of the platform which opens the road to the simultaneous real-time detection and measurement of the concentration of multiple analytes, demonstrated with Na^+ , K^+ and Cl^- sensors.

2. Materials and Methods

2.1. Materials

Sodium chloride, tetrahydrofuran (THF), 3,4-ethylenedioxythiophene (97%, EDOT), 4-tert-butyl-calix[4]arene-tetraacetic acid tetraethyl ester (sodium Ionophore X), valinomycin (potassium ionophore I), tridodecylmethylammonium chloride (TDMACl), potassium tetrakis(4-chlorophenyl)-borate (KTCPB), high molecular weight poly(vinyl chloride) (PVC), bis(2-ethylhexyl) sebacate (DOS), poly(methyl methacrylate-co-butyl methacrylate) (PMMA-co-BMA), bis(2-ethylhexyl) phthalate (DEHP) were all purchased from Sigma-Aldrich, Ireland and were all of selectophore grade. 1-Hexyl-3-methylimidazolium tris-(pentafluoroethyl)trifluorophosphate (HMIM FAP) was purchased from Merck. 1-Ethyl-3-methylimidazolium bis(trifluoromethane)sulfonimide (EMIM NTf₂, 99.5%) was purchased from Iolitec, Germany. All chemicals were employed without further purification. Carbon ink (C2030519P4) and dielectric ink (D50706D4) were purchased from Gwent Group, UK and used without purification. The device battery and electronics board were provided by Shimmer, DCU Alpha, Glasnevin, Dublin, Ireland. Platforms parts including the enclosure and reservoir fabricated using an Object260 Connex1 Polyjet 3D Printer (Stratasys, Rheinmünster, Germany). The materials were VEROBLACKPLUS RGD875, a rigid acrylic based resin, and TANGOBLOCK PLUS FLX980, a rubber-like acrylic resin. The support material was OBJET Support SUP706.

2.2. Instrumentation

A DEK 248 semi-automatic screen printer was used for the deposition of conductive and dielectric layers in the electrodes. PMMA parts were cut with an Epilog Zing Laser Cutter. Electrodeposition of PEDOT was carried out using a CH Instruments CHI630B electrochemical analyser. Potentiometric measurements were recorded with a multichannel Lawson Labs MCV potentiometer, and a double junction Ag⁺/AgCl electrode (Sigma-Aldrich Ireland Ltd., Arklow, Wicklow, Ireland).

2.3. Electrodes Fabrication

The electrodes were prepared according to a modification of the previously reported procedure [5–7]. The electronically conductive layer (carbon ink) and dielectric layer were screen printed on PET sheets. PEDOT (~0.8 mg per electrode) was deposited on the exposed surfaces of the electrodes by constant-potential electropolymerisation from 0.05 M solution of EDOT (97%) in EMIM NTf₂ (99.5%), using a three-electrode setup consisting of the carbon ink working electrode, a Pt wire counter electrode and a bare Ag wire as pseudo-reference electrode. A PMMA gasket of 500 µm thickness was affixed on the electrodes, in which wells were cut to host the polymeric membranes. Polymeric membranes were formed in the wells by drop-casting of THF-based cocktails. The cocktails for the Na⁺ ion-selective electrode (ISE) and reference electrode (RE) were prepared as previously reported [5,6,8]. The K⁺ selective ISE cocktail was composed of valinomycin (10% by weight), KTCPB (1:2 mol ratio vs ionophore), and 1:2 mass ratio of PVC and plasticiser (DOS). The Cl[−] ISE cocktail was composed of TDMACl (8% by mass), and 1:2 mass ratio of PVC to plasticiser (DOS). All electrodes were subject to conditioning in either deionised water or a solution of their primary ion (10^{−2} to 10^{−1} mol L^{−1}).

3. Results and Discussion

3.1. Electrodes Fabrication and Response

Combined electrodes were fabricated according to the above procedure, in either a two-electrode format, containing an ISE and an RE on the same substrate, or a four-electrode format, with Na⁺, K⁺, Cl[−] ISEs and an RE, as shown in Figure 1a. The employed fabrication procedure is inherently scalable, and potentially easily automated. The performance of the Na⁺ ISE and RE has been previously reported [5–7]. The K⁺ ISE is based on valinomycin, which is considered the optimum ionophore for

these ions. The Cl^- ISE is based on a simple anion exchanger, TDMACl. This electrode is known to have limited selectivity towards anions whose free energy of hydration is higher than that of chloride [9]. This issue is only of minor relevance for our system, as concentrations of the competitive anions in biological fluids is not significant (*i.e.* $C_{\text{Cl}^-} \gg C_{\text{Br}^-}, C_{\text{NO}_3^-}, C_{\text{ClO}_4^-}$)

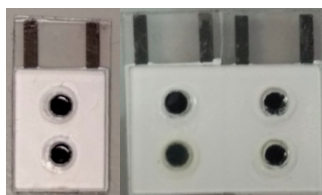


Figure 1. Combined electrodes. Left: ISE/RE setup, right: Na^+ , K^+ , Cl^- ISEs/RE setup.

All ISEs displayed linear, slightly sub-Nernstian response to their analyte in a range of $\log(\text{activity})$ from -4 to -0.5 . Figure 2 shows a calibration experiment in which the response of the three ISEs to alternating additions of NaCl and KCl were recorded. Importantly, no cross-sensitivity was detected: residuals from the linear regression of E_{Na^+} vs a_{Na^+} showed no correlation with a_{K^+} (slope of 0 ± 0.2 mV/decade). Furthermore, the electrode responses were stable, for at least 6 hours, to the exposure to a mixed solution of NaCl and KCl at concentrations typically found in thermogenic sweat ($4 \cdot 10^{-2} \text{ mol L}^{-1} \text{ Na}^+$, $5 \cdot 10^{-3} \text{ mol L}^{-1} \text{ K}^+$) [10], as confirmed by repeated calibration.

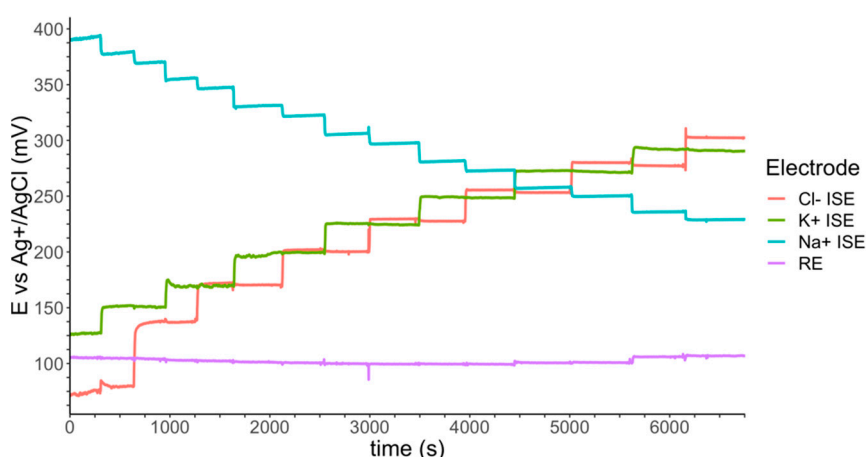


Figure 2. Potential response of ISEs and RE to increasing concentrations of NaCl and KCl. Activities determined by Debye-Hückel model, ranging from $\log(a_i) = -4.5$ to -0.5 ($i = \text{Na}^+$, K^+ , Cl^-).

3.2. Multiple Analyte Platform

The previously reported Sweatch platform allows for the measurement of a single analyte concentration; specifically, real-time monitoring of Na^+ concentration data was demonstrated [5–7]. However, other analytes can be measured using the SwEatch platform, with no further complications, by easily exchanging the Na^+ ISE/RE integrated electrode with either a K^+ or Cl^- selective electrode. Simultaneous monitoring of multiple electrolytes can be achieved by the use of more than one ISE, as in the 4-electrode format. However, electronics capable of multi-channel data acquisition and a reformulation of the fluidics setup are necessary for simultaneous multianalyte monitoring. Development of this system is currently in progress.

As an intermediate step to this goal, we have developed a platform which contains two independent ISE/RE electronic boards, each with its own fluidic system, drawing sweat from the same area of skin. The transport of sweat to the electrodes is enhanced by thread microfluidics. A single cotton thread, protruding from the base of the device, contacts with the emerging sweat and transports it by capillary action across the electrode membranes to a storage reservoir consisting of a cellulose-based absorbent material. Because of the symmetry of the two independent parts, the fluidic

behaviour is identical and analogous to those of the previously reported device (flow rate typically ~ 1 µL/min).

4. Conclusions

The SwEatch platform, which has been previously employed for real-time monitoring of sodium in sweat, has been further developed to enable simultaneous monitoring of multiple analytes. Currently, ISEs for Na⁺, K⁺ and Cl⁻ are being employed, but the approach can be further expanded to include other analytes accessible via known solid-state electrode technology. Such multi-channel detection presents new issues such as the need for an integrated fluidics and electronics design within a compact format, and consistency of the sweat sampling and passage over the various electrodes. The solutions presented here, while still limited, successfully meet these challenges, and will be further improved for testing in on-body trials.

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