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Real-time sweat analysis via alternating current conductivity of artificial and human sweat

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Dehydration is one of the most profound physiological challenges that significantly affects athletes and soldiers if not detected early. Recently, a few groups have focused on dehydration detection using sweat as the main biomarker. Although there are some proposed devices, the electrical and chemical characteristics of sweat have yet to be incorporated into the validations. In this work, we have developed a simple test setup to analyze artificial sweat that is comprised the main components of human sweat. We provide theoretical and experimental details on the electrical and chemical behavior of the artificial sweat for various concentration values within a temperature range of 5°C to 50°C. We have also developed an efficient sweat collecting and detection system based on 3D printing. Human studies were conducted and this particular protocol has shown that dehydration starts to take effect as early as 40 min into the physical activity if there is no fluid intake during the exercise. We believe that our device will lead to developing viable real-time sweat analysis systems. © 2015 AIP Publishing LLC. [http://dx.doi.org/10.1063/1.4916831]

Attempts for detecting cystic fibrosis1,2 in early stages paved the way for the research on sweat electrolytes as a biomarker.3,4 Although blood can provide more accurate and detailed information on the physiological condition of a human, analysis of sweat content would open the doors to a fast, easy to use, non-invasive, and real-time sensing of the hydration levels of performance athletes, in which hydration status significantly affects their performance.5–7 Since the electrolytes in sweat are mainly Na⁺ and K⁺, one potential method to measure concentration is to look at the electrical conductivity of the sweat. Several studies have investigated the impedance of NaCl and KCl solutions8,9 without considering the cross sensitivity of other main sweat components such as urea and lactate. Similarly, urea biosensors were developed as a kidney dysfunction biomarker by determining the enzymatic reactions and pH changes10–12 while lactate sensors focused on the lactate oxidase-based nanostructured electrodes and their impedometric analysis.13–15 In this work, artificial sweat contents such as NaCl, KCl, urea, and lactate were all mixed in one solution.

Recently, we have investigated the optical properties of an organic dye, lawson, under various concentrations of artificial and real sweat. We characterized salt-doped lawson thin films in terms of optical, chemical, and electrical properties.16 We then investigated the optical properties of artificial sweat on aqueous lawson solutions.17,18 In this work, we brought our research to the next level in which artificial sweat was directly used as a conductometric biomarker. We have characterized the artificial sweat for different concentrations in terms of its electrochemical impedance and postulated the equivalent circuits of the solution. Furthermore, we have conducted comprehensive temperature analysis of artificial sweat components. Our analytical experiment results were supported by the real-time human sweat test.

Artificial sweat was prepared using the EN1811:2012 standard9 by incorporating weight/volume ratios in deionized water: 0.5% of sodium chloride (VWR), 0.1% of potassium chloride (VWR), 0.1% of lactic acid (VWR), and 0.1% of urea (Fisher Scientific). The pH value for the artificial sweat was adjusted to 5.4 ± 0.3 by adding 0.001M ammonium hydroxide (Fisher Scientific) using an EcoTestr PH2 pH meter. Impedance analysis was performed using an Agilent 4294A precision impedance analyzer. Calibration of the conductivity from the conductance was carried out using a Horiba LaquaTwin conductivity measuring stick. Real-time sweat was collected using a 3d-printed sweat collector. A biocompatible plastic (FullCure 810 VeroClear) was used as the sweat collector that was 3d printed using a PolyJet based Stratasys Objet 30 Pro 3d printer. The collector design was created using CATIA.

The impedance measurement of solutions was obtained using parallel-plate copper electrodes. The Nyquist and Bode plots for a representative solution (65 mM artificial sweat) are shown in Fig. 1. The impedance spectrum was modeled with a modified Randle’s circuit (inset of Fig. 1). Several processes contribute to the double-layer circuit impedance. When an electrode is immersed into an electrolyte solution, adsorbed ions form a layer (~1 nm) on the electrode surface, defining the inner Helmholtz plane (IHP). At the wider (~10 nm) outer HP (OHP), diffusion of ions takes place.
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reveals the solution and charge transfer resistances. It must be noted here that each component was calculated and compared with the measurement results. Conductivity values of each component can be derived by Eq. (1), where $\Lambda_m$ is the molar conductivity, $\gamma_i$ is the activity coefficient, and $c$ is the concentration of the component. The activity coefficient $\gamma_i$ can be calculated as (2) by using Debye–Hückel limiting law, where $z_i$ is the charge number, $\epsilon_i$ is the elementary charge value, $\epsilon_0$ is the relative permittivity of the electrolyte, $\epsilon_0$ is the free-space permittivity, $k_B$ is the Boltzmann’s constant, $T$ is the temperature, and $N_A$ is Avogadro’s number.

$$\ln \gamma_i = -\frac{z_i^2 q^2 N_A^2}{4\pi\epsilon_0 k_B T} \sqrt{\frac{I}{2}},$$  

Here, $I$ defines the ionic strength which is given as $I = \frac{1}{2} \sum_i c_i z_i^2$, where index $i$ represents each ionic species in the solution. For strong electrolytes such as NaCl and KCl, $\Lambda_m$ is given by Kohlrausch’s law, where $\Lambda_m$ is the limiting

which is commonly represented by the Warburg impedance. Best fit results were achieved by assuming a finite length diffusion with reflective boundary, where $Z_w = W_{oc} / \sqrt{\omega(1-i)\coth(W_{oc}/\sqrt{\omega})}$. Further elements of the circuit are the capacitance $C_{dl}$ of the diffusion layer created by the IHP and OHP and the charge transfer resistance $R_{ct}$. At low frequencies, an additional impedance—possibly resulting from electrode passivation—is required to correctly model the experimental spectrum. This is represented by the parallel circuit of $C_{PE} = \frac{Q_{PE}}{i(\omega)}$ (a constant phase element) and $R_f$. Compared to $R_f$, the solution resistance $R_s$ is negligible (less than 1 $\Omega$) and was therefore not included in the fit. The fit parameters and their uncertainties are listed in the caption of Fig. 1.

The Nyquist plot of the data Fig. 1(a) at high frequencies reveals the solution and charge transfer resistances. It must be noted here that the artificial sweat solution consists of several ions: Na$^+$, K$^+$, Cl$^-$, urea$^-$, and lactate$^-$. Extrapolating the fit model to higher frequencies helps to complete the half circle in the Nyquist plot. The high frequency drop in $Z_{real}$ in the Bode plot Fig. 1(b) is associated with the charging/discharging behavior of the double layer capacitance ($C_{dl}$). While $Z_{real}$ stays relatively constant in the mid-frequency region, the imaginary part of the impedance ($Z_{imag}$) continues to decrease, making the overall impedance dominated by $Z_{imag}$. The conductance calculations were therefore obtained from the mid-frequency range (100 kHz) as shown in Fig. 1(b) to eliminate frequency dependent variations.

Conductivity values from the conductance measurements were calculated by cell constant calibration. The conductance values ($G$) were calculated at 100 kHz by taking the real part of the inverse of impedance ($G = \text{Re} \left\{ 1/(Z_{real} + iZ_{imag}) \right\}$), and conductivity ($\sigma$) was calculated from $\sigma = G/\kappa$ using the cell constant $\kappa = 0.43 \text{ cm}^{-1}$. Fig. 2 shows the conductivity values for various solutions including the artificial sweat. The values are given as relative to the lowest concentration that was selected for each component (lowest concentrations: Urea: 1.6 mM, lactate: 1.7 mM, KCl: 1.3 mM, NaCl: 8.5 mM, and artificial sweat: 13.1 mM). The theoretical conductivity values of each component were calculated and compared with the measurement results. Conductivity values of each component can be derived by Eq. (1), where $\Lambda_m$ is the molar conductivity, $\gamma_i$ is the activity coefficient, and $c$ is the concentration of the component. The activity coefficient $\gamma_i$ can be calculated as (2) by using Debye–Hückel limiting law, where $z_i$ is the charge number, $\epsilon_i$ is the elementary charge value, $\epsilon_0$ is the relative permittivity of the electrolyte, $\epsilon_0$ is the free-space permittivity, $k_B$ is the Boltzmann’s constant, $T$ is the temperature, and $N_A$ is Avogadro’s number.

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FIG. 1. Impedance analysis of the artificial sweat with a concentration of 65 mM, which is considered to be the average value for real human sweat. Dotted lines represent the fit obtained from the equivalent circuit. The fitted component values are $R_1 = (14.0 \pm 0.5) \Omega$, $x = (0.968 \pm 0.002) \Omega$, $R_{CT} = (76.14 \pm 0.05) \Omega$. $C_{dl} = (31.8 \pm 0.2) \text{ pF}$, $W_{oc} = (5.38 \pm 0.03) \Omega$ s$^{-1/2}$, and $W_{ac} = (0.107 \pm 0.006) \Omega$ s$^{-1/2}$. (a) The Nyquist plot suggests that the solution resistance is very small (~0.1 $\Omega$), whereas the charge transfer resistance ($R_{ct}$) is on the order of 80 $\Omega$. (b) The low-frequency region in the Bode plot is dominated by electrode passivation (represented by $R_1$ and $C_{PE}$), whereas the high-frequency response results from the diffusion and charge-transfer processes in the Helmholtz planes (represented by $C_{dl}$, $R_{ct}$, and $Z_w$).

FIG. 2. Conductivity of the solutions using the 2-electrode, parallel-plate sensing apparatus at a frequency of 100 kHz. Each marker point represents the measurement points. Solid lines are the theoretical calculations using Eqs. (1)-(4). Since lactate and urea are considered weak electrolytes and do not dissociate into their ions as much as strong electrolytes, conductivity values do not change significantly with increasing concentration. NaCl is the main contributor to the overall conductivity. It must be noted here that each concentration for individual solutions was given as relative concentration where lowest concentration value for each solution was taken as 1. This approach was followed in order to be able to show different solutions in one scale. Photo of the experiment setup is shown in the inset.
molar conductivity and $K$ is the Kohlrausch coefficient that is given by

$$\Lambda_m = \Lambda_m^0 - K \sqrt{c}.$$  \hspace{1cm} (3)

Weak electrolytes, on the other hand, such as urea and lactic acid behave differently from strong electrolytes due to the incomplete dissociation of ions. Molar conductivity becomes a function of the dissociation constant ($K_a$), $\Lambda_m = z \Lambda_m^0$, where $z$ is the degree of dissociation. $K_a$ is linearly dependent on the concentration and $x$, $K_a = c x^2/(1 - x)$, which can then be reorganized as

$$\frac{1}{\Lambda_m} = \frac{1}{\Lambda_m^0} + \frac{\Lambda_m c}{K_a (\Lambda_m^0)^2}.$$  \hspace{1cm} (4)

It can be calculated that only 9.6% of lactate will be dissociated into lactate ions (lactate$^-$) and 2.8% of urea will form urea$^-$.

Fig. 2 shows that the measured conductivity values for weak electrolytes contribute to the overall conductivity much less than strong electrolytes. It is important to note that the concentration of NaCl is much higher than other artificial sweat components as dictated by the standard.

Solid lines in Fig. 2 represent the theoretical conductivity values, which match quite well with the measurement data. The theoretical conductivity value for artificial sweat solutions were calculated by simply superposing the individual ion calculations from electrolytes under the assumption that the interactions between the ions are minimal. It is important to mention here that the artificial sweat pH value was adjusted to regular human sweat pH using ammonium hydroxide, hence the conductivity calculations deviate from the measurements.

The conductivity of an ionic solution is, in part, dependent on the temperature. As the temperature varies around the sensor due to the weather conditions, it is important to characterize the temperature behavior of the conductivity for all compounds in the artificial sweat. As the temperature increases, the mobility of the ions increases while the viscosity decreases. Both these effects increase the conductivity. Furthermore, the dissociation of the ions is enhanced with the increasing temperature (a significant effect on weak electrolytes such as urea and lactate), leading to a larger conductivity. This temperature dependence of conductivity is usually represented by the temperature coefficient, $\theta$, which is given as the percentage change in the conductivity for each degree of temperature change, i.e., $% \sigma/\Delta T$. Selected artificial sweat solutions were characterized for their temperature behavior. A hot plate was used to increase temperatures up to 45°C, whereas an ice-filled container was utilized to cool the temperature to 5°C. Fig. 3 illustrates that the conductivity is linearly dependent on the temperature. Linear fit lines agree with the measurement data. The temperature coefficients for each artificial sweat solution were calculated by averaging consecutive data point calculations ($\theta = ((\sigma_2 - \sigma_1)/\sigma_2)/(T_2 - T_1)$). Fig. 3 inset shows these calculated average $\theta$ values for selected artificial sweat concentrations. The average value was found to be $1.3 \pm 0.2\%/^\circ\mathrm{C}$.

![FIG. 3. The conductivity at 100 kHz is a linear function of the temperature. This is mainly due to the mobility of the ions in the solution. The temperature coefficient ($\% \sigma/\Delta T$) was calculated from the data. Average $\theta$ is $1.3 \pm 0.2\%/^\circ\mathrm{C}$.

Proof-of-concept real-time measurements were carried out using a flexible silicon tubing (2 mm inner diameter) with silver wires punched through it, as sketched in the inset of Fig. 4. This preliminary device was used to verify the instantaneous conductivity readings for different concentrations. Only 2 wires were used for the measurements at 100 kHz, since the experiments showed that the conductivity readings are essentially the same as 4 wires with the only advantage being the elimination of the polarization at low frequencies. Fig. 4 was obtained by injecting various artificial sweat solutions into the tubing one by one to see the conductivity change, i.e., different concentrations were pumped through the tubing over time. The measurements were also stable over the course of time. The conductivity values did not change over 2 h. Although the parallel plate copper electrodes were used for the characterization of the artificial sweat solutions in Figures 1–3, by using a different cell constant and calibration parameters, the effect of utilizing silver wires was calibrated.

Fig. 5 shows a representative real-time human test. Subject consent was obtained according to the approved Institutional Review Board protocol at Central Michigan University. The 3d printed sweat collector has a hole (2 mm in diameter) in the bottom where it touches the skin. The
collector was designed to have a curvature with a 1 mm sagitta to maximize the skin coverage. In this design, sweat glands act as hydraulic pumps where sweat is pumped through the collector’s opening that is attached to a flexible tubing. Silver wires were used for the conductivity probes. Powerflex tape was used to attach the sweat collector on the subject’s left forearm (close to the elbow region). A photograph of the subject’s forearm with the sweat collector during the test was shown in Fig. 5(a). CAD drawing and the actual photograph of the sweat collector were given as insets in Fig. 5(a). The subject cycled in a lab environment for 55 min at 80% of maximal aerobic work load (average heart rate of 144 bpm). Previous work has observed that subjects exercising at this rate of 144 bpm). Previous work has observed that subjects exercising when combined with fluid restriction. With the high demand on real-time physiology monitoring in mind, proposed device can offer researchers a qualitative and quantitative information about one’s hydration condition, which would be vital for performance athletes and soldiers.

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FIG. 5. Real-time human sweat tests were performed using a 3d-printed sweat collector on a healthy subject’s left forearm. (a) Actual photograph of the device during the sweat collection. Left inset shows the collector itself from the side, whereas right inset shows the computer aided design (CAD) drawing. (b) The real-time human sweat test reveals that the conductivity increases as dehydration gets more prominent after the sweat collector was flushed of skin residuals (at around 40 min).

19EN 1811:2011, “Reference test method for release of nickel from all post assemblies which are inserted into pierced parts of the human body and articles intended to come into direct and prolonged contact with the skin,” German version EN 1811:2011.