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Proceeding Paper

A New Approach for Monitoring Sweat Ammonia Levels Using a Ventilated Capsule †

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Abstract: Ammonium levels in sweat can potentially be used to measure muscle fatigue and to diagnose particular metabolic myopathies. To research the potential use of ammonia in sweat as a biomarker, a new real-time monitoring system is developed. This system consists of a capsule that is placed at the skin and ventilated with dry air. A metal oxide gas sensor in the capsule detects the ammonia that is evaporated from sweat. The sensor system was built, and calibration experiments were performed. The sensors show good sensitivity from 27 mV/ppm to 1.1 mV/ppm in the desired measurement range of 1 to 30 ppm respectively. A temperature and humidity sensor are integrated to compensate for temperature and humidity effects on the NH_3 sensor.

Keywords: sweat sensor; NH_3; metal oxide gas sensor; ventilated capsule

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1. Introduction

Wearable sweat sensors offer new opportunities for continuously monitoring an athlete's condition unobtrusively. Sweat rate and sweat Na^+ and Cl^- concentrations may provide information about an athlete's hydration status and their core temperature [1]. Measuring muscle fatigue would be another interesting aspect of monitoring an athlete's health status and monitoring efficiency of training programs. To find a relationship between muscle fatigue and sweat constituents, more physiological research is required. Although lactate levels in blood are a well-known indicator of muscle fatigue [2], it is known that lactate is a by-product of sweat gland metabolism as well [3], and no significant relationship between lactate levels in blood and lactate levels in sweat have been found in literature [4]. As an alternative, several researchers highlighted the possibility using NH_4^+ in sweat as a potential biomarker for muscle fatigue [5,6]. NH_4^+ concentrations in sweat are relatively high (between 0.5 and 25 mM [7]). During very intense exercise, adenosine triphosphate (ATP) levels get very low, and inosine monophosphate (IMP) and NH_4^+ are produced from adenosine monophosphate (AMP). This is part of the purine nucleotide pathway [8], and results in the accumulation of ammonia in blood, which possibly results in an increase in NH_4^+ concentrations in sweat during exercise as well. To research if NH_4^+ levels in sweat are related to blood levels, and if sweat $[NH_4^+]$ can be used as a biomarker for muscle fatigue, reliable real-time NH_4^+ monitoring systems are required.

Moreover, monitoring of sweat $[NH_4^+]$ may have interesting clinical applications. Subjects with particular metabolic myopathies show abnormal concentrations of NH_3 during intense exercise. For example, subjects with myoadenylate deaminase (MAD) deficiency show very low ammonia variations in blood during ischemic exercise [9,10].

In this paper, we present a new way of monitoring NH_4^+ levels in sweat to research the potential of the abovementioned applications. Previous research focused on ionic content measurement using potentiometry [6,11]. Since NH_3(aq) is evaporating quickly, we propose to measure the NH_3 levels evaporated from sweat in a sensing capsule that is placed at the skin. A controlled air flow through the system is necessary to calculate the concentration in sweat based on the concentration measured in the sensing capsule. Therefore, the sensor is integrated in a ventilated capsule system, which is commonly used by physiologists for measuring sweat rate [12].

2. Method

2.1. Design

It is estimated that a sensor with a detection range between 0 and 100 ppm is required, by using data about [NH_4^+] in sweat found in literature [7], sweat rate and volumetric flow rate of air through the capsule. Based on measurement range, price, and ability to integrate this sensor in a wearable, the MICS-5914 semiconductor metal oxide gas sensor (SGX Sensortech, Switzerland) was selected. This sensor consists of a Si/SiO_2 substrate with 4 gold-platinum electrodes. Two electrodes are used for heating the sensor and two are for performing the measurement. The metal oxide sensing layer including tungsten nano-plates, is placed on top [13]. When the sensor is exposed to NH_3, the resistance across the sensing electrodes will drop. Next to NH_3, the sensor is sensitive to C_2H_5OH, H_2, C_3H_8 and C_4H_{10}. These gases will not be formed during sweating in general conditions. Figure 1 shows a schematic overview of the entire measurement system. We use a series-series feedback circuit to read-out the sensors (Figure 2a). This circuit has a linear response, which facilitates calibration. It also reduces noise, distortion, and variations due to temperature influences. The circuit includes the precision operational amplifier LTC2057 (Analog Devices, USA) and the MCP3421 (Microchip, USA) analog to digital converter with differential input is used. These electronics with a single NH_3 sensor and a humidity and temperature sensor (HDC1080, Texas Instruments) are placed at a small PCB (34 mm × 28 mm), that is designed to fit in a capsule (Figure 2b,c). The capsule can be taped to the skin of the athlete. The sensors are placed inside the capsule and the other supporting electronics of the readout circuit are placed at the other side of the PCB, outside the capsule. The capsule PCB is connected to a shield that contains the current source for the heater circuit, the connection to a power supply and a multiplexer to switch between different capsules. Data of four sensor capsules can be read out with an STM32F411RE microcontroller board (STMicroelectronics, Switzerland) (Figure 2d). It was chosen to place the sensors as close as possible to the collection surface, to prevent that NH_3 is absorbed by the materials of the capsule and the tubing, before the NH_3 molecules are detected. A thin gold layer was sputtered on the inside of the capsule to prevent absorption in this area. The capsule itself is made of a 3D printed flexible photopolymer (Connex 3, Objet 350, Stratasys, Israel) and has a collection surface diameter of 26 mm. The airtight capsule will be placed at the skin with a double-sided acrylate adhesive (3M 1522, [14]) During the in-situ experiments, the capsule can be ventilated with dry air at a flow rate between 0.2 and 1.2 l/min, depending on the type of exercise test that will be performed.

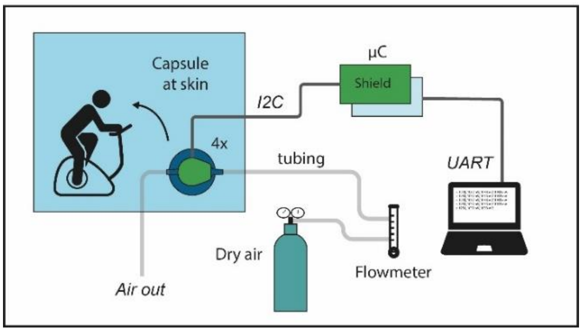


Figure 1. An overview of the sweat NH3 measurement system. Four capsules with sensors are placed at the skin and can be read out by the microcontroller. Data can be retrieved through a UART connection.

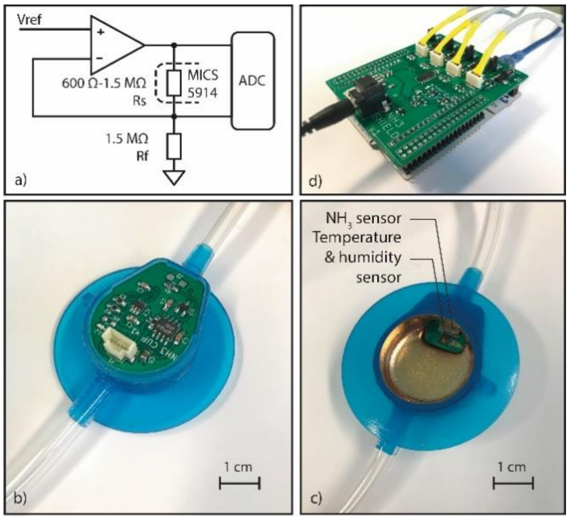


Figure 2. (**a**) The series-series feedback circuit used to read out the MICS-5914 sensor. (**b**) Top view of the capsule. (**c**) Bottom view of the capsule. (**d**) The shield for reading out 4 capsules**.**

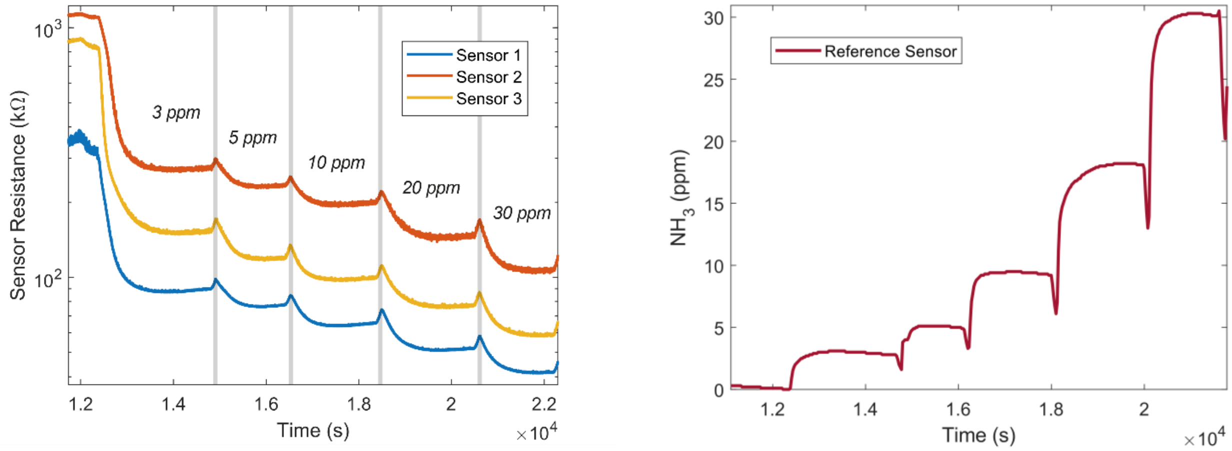
2.2. Sensor Characterization

Each of the MICS-5914 sensors has a different resistance in air and the sensitivity will also differ [15]. Therefore, each individual sensor needs to be calibrated. A calibrated electrochemical NH_3 sensor for air quality monitoring (S900, Aeroqual, New-Zealand) was purchased to calibrate the sensors. The sensor modules and the reference sensor are placed in a closed box with tubing to an Erlenmeyer flask. The air is ventilated with a small fan through the glass and through the box. First, the sensor resistance must stabilize before NH_3 can be measured reliably. Therefore, the sensors are started up 2 h before the measurement. One sensor is covered with aluminum foil, to keep an eye on the effects of temperature and humidity changes. An ammonia solution is made in the Erlenmeyer flask from household ammonia and demineralized water. With this solution different NH_3 concentration levels can be created in the closed ventilated box. Measurements of 30 to 40 min are performed at concentration levels of 3, 5, 10, 20 and 30 ppm NH_3.

During sweating, humidity levels in the measurement capsule will increase. These humidity changes will influence the NH_3 measurements. To quantify the influence of humidity, the Erlenmeyer flask is removed and beakers with different diameters with water are placed in the setup. In this way, different humidity levels can be created in the box.

3. Results & Discussion

Figure 3a shows the raw data of the resistance change of the sensors during the NH_3 experiment. The temperature is 25 °C and the humidity level is 60%. The baseline resistance highly differs for each sensor (from 360 kΩ to 1140 kΩ). Furthermore, the sensor readings show a transient behaviour. In literature it was found that metal oxide gas sensors have a fast response time compared to other types of gas sensors [16], and in experiments with ethylene, the MICS-5914 has a sorption and desorption time constant of $\tau_s = 29$ s and $\tau_d = 43$ s [13]. On top of that, the reference sensor shows a very similar transient response (Figure 3b). It is expected that the transient is mainly originating from the rising NH_3 concentration in air, since the NH_3 is evaporating from the flask, and it will take some time before an equilibrium at a certain concentration is reached. The small peaks between each concentration level originate from the moment that we change the flask and box is circulating air from the environment for a few minutes. During this moment, [NH_3] and humidity levels will decrease, and sensor resistance will increase. When a new flask with an NH_3 solution is connected, the resistance will immediately decrease again.



(**a**) (**b**)

Figure 3. (**a**) Sensor resistance plotted over time during the calibration experiment. The sensors are exposed to an environment with different concentrations of NH_3. The sensor resistance is plotted on a logarithmic scale. (**b**) The reference measurements during the calibration experiment with the calibrated S900 sensor (Aeroqual, New-Zealand)**.**

A calibration plot can be made using data from the MICS-5914 sensors and the reference sensor measurements. This calibration plot is shown in Figure 4. A clear difference in sensitivity between sensors can be seen, which emphasizes that each individual sensor needs to be calibrated. In all experiments, it was found that the baseline sensor resistance drifts over time. This drift varies in each measurement. In further experiments, these measurements will be repeated multiple times, to test the stability of the sensors during NH_3 measurements. A sensor with excellent stability would be beneficial if physiologists and clinicians want to know the absolute concentration levels in sweat. However, in studies about the relationship between [NH_3] and muscle fatigue, measuring relative changes in [NH_3] would already give valuable information.

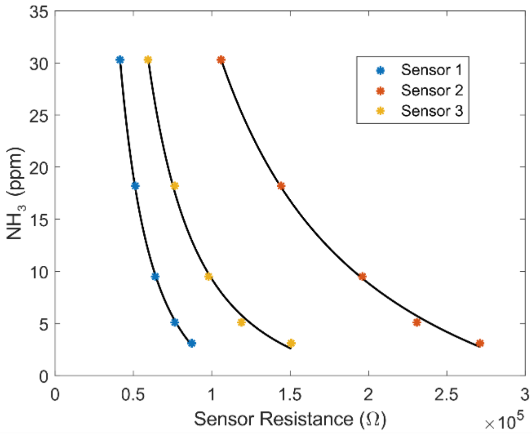


Figure 4. NH_3 concentration plotted against sensor resistance. Data were fitted using a power function: y = a ∗ xb + c. (R2 > 0.99 for all fits).

When exposing the sensor to a changing humidity level from 38% to 50%, a clear drop in resistance, which varies between sensors (from 25% to 60%), can be seen. These changes are comparable to the changes measured by Krivec et al. [13]. Water molecules can be adsorbed at the sensor surface in a similar way as the volatile gas. These molecules reduce the baseline resistance and the sensitivity of the sensor because the available surface area for adsorption of NH_3 molecules decreases. The humidity measurements show the necessity of compensating for humidity influences during sweat NH_3 measurements. Future experiments will include researching the environmental conditions (temperature and humidity) in the capsule during sweat experiments and calibrating the sensors in these conditions. Sweat rate and skin temperature will influence humidity and temperature conditions. This confirms our choice of directly integrating a temperature and humidity sensor in each capsule. Furthermore, it would be beneficial to place a hydrophobic PTFE membrane between the sensor and the capsule opening, to protect the sensor against sweat droplets.

After quantifying temperature and humidity effects in the expected conditions, the sensors will be tested in a physiological experiment in which athletes will perform a high intensity cycling exercise of 1 h. In this experiment we will validate the use of our NH_3 ventilated capsule system for NH_3 sweat measurement. Trends in NH_3 levels in the capsule during exercise at a cycling ergometer will be researched. Based on the insights from these experiments, further improvements of the system will be made.

4. Conclusions

In this research, a new approach to measure NH_3 levels in sweat is presented. A metal oxide gas sensor is placed in a small ventilated capsule that is placed at the skin. The sensor measures the NH_3 molecules that evaporate from the sweat. At the same time humidity and temperature measurements are performed in the capsule. These measurements can be used to compensate for humidity and temperature effects on the metal oxide gas sensor. Calibration experiments showed that the sensors can detect NH_3 levels in the desired range of 3 to 30 ppm. Experiments also showed that humidity changes have a significant effect on baseline resistance. Future experiments should therefore focus on measuring temperature and humidity variations in the capsule during exercise and calibrating the sensors within this range.

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Conflicts of Interest: The authors declare no conflict of interest

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