Medium-distance affordable, flexible and wireless epidermal sensor for pH monitoring in sweat

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ABSTRACT

In the last decade, wearable sensors have gained a key role on biomedical research field for reliable health state monitoring. A wide plethora of physics marker sensors is already commercially available, including activity tracker, heart rate devices, and fitness smartwatch. On the contrary, wearable and epidermal sensors for chemical biomarker monitoring in several biofluids are not ready yet. Herein, we report a wireless and flexible epidermal device for pH monitoring in sweat, fabricated by encompassing a screen-printed potentiometric sensor, an integrated circuit, and antenna embedded onto the same Kapton substrate. An iridium oxide film was electrodeposited onto the graphite working electrode providing the pH sensitive layer, while the integrated circuit board allows for data acquisition and storing. Furthermore, a radio frequency identification antenna surrounding the entire system enables data transmission to an external reader up to nearly 2 m in the most favourable case. The potentiometric sensor was firstly characterised by cyclic voltammetry experiments, then the iridium oxide electrodeposition procedure was optimised. Next, the sensor was tested toward pH detection in buffer solutions with a near-Nernstian response equal to \(-0.079 \pm 0.002\) V for unit of pH. Interference studies of common sweat ions, including Na\(^+\), K\(^+\) and Cl\(^-\), showed any influence on the pH sensor response. Finally, the integrated epidermal device was tested for real-time on-body pH sweat monitoring during a running activity. Data recorded for a running subject were wireless transmitted to an external receiver, showing a pH value close to 5.5, in agreement with value obtained by pH-meter reference measurement.

1. Introduction

In 2015, several countries adopted the 2030 Agenda with 17 Sustainable Development Goals to face traits for sustainable development in several sectors including the biomedical one. In detail, the Goal 3 “Good health and well-being” has the overall objective to save the lives of millions of people by promoting well-being for all at all ages, increasing life expectancy and eradicating a wide range of diseases. In the continuous transformation of the practices in clinical field, research efforts have been devoted to revise the “one-size-fits-all approach”, in which disease treatment strategies are developed for the average person, with the “precision medicine approach”, which accounts for individual variability in genes, environment, and lifestyle for each person. Furthermore, the advancement in technology has boosted the physicians in using cutting-edge technological devices for treatment, automate dictation during surgery progresses, and diagnosis (e.g. wearable device) [1–3]. In the last years, wearable sensors have gathered a huge attention due to the awareness in remote health monitoring with the aim to replace the current hospital-focused model with individual-centric management of health [4]. So far, the main research activities have been focused on wearable sensors aimed at physical sensing to monitor physiological parameters including heart rate, electrical activity of the brain from the scalp, and oxygen saturation in arterial blood but missing in providing any information at molecular levels. To accomplish this issue, research efforts have been already dedicated to develop chemical sensors for biomarker monitoring in sweat to realize a non-invasive
biomarker detection, avoiding the need to collect blood samples [5–7].

Up to date, several electrochemical (bio)sensors have been developed for painless monitoring of electrolytes and metabolites in sweat as indicators of health status, with the advantage of higher sensitivity in respect with colorimetric-based sensors. For instance, the innovative temporary-transfer tattoos including electrochemical biosensors have been reported by Wang group for continuous monitoring of lactate and glucose in sweat [8,9], combining the tattoo electrochemical biosensors with laboratory set-up instrument or with an electronics board [10]. The first fully integrated wearable flexible system was recently published on Nature, in which a flexible printed circuit board is combined with a sensor panel for the detection of clinical biomarkers in sweat. The continuous monitoring of glucose, lactate, sodium, and potassium ions was carried out thanks to electrochemical integrated (bio)sensors combined with a skin temperature sensor, necessary to calibrate the biosensor response [11]. However, the reported device requires a battery for continuous monitoring. Furthermore, data retrieval is based on the Near Field Communication (NFC) architecture at 13,56 MHz that enables a rapid and simple communication with smartphones without pairing (unlike Bluetooth). However, as the read distance is limited to a few centimetres, the reading device has to be brought rather close to the sensorized body so that a manual procedure is needed [12–14]. Accordingly, this kind of reading modality is collaborative and does not allow an automatic data retrieval during sport activity, especially when multiple sensors are involved on the body.

In addition to the previously cited biomarkers i.e. lactate, glucose, sodium, potassium, pH is a useful parameter to monitor in sweat giving important information on health conditions including metabolic alkalosis, hydration, skin diseases, cystic fibrosis, among others [15,16]. The reference method encompasses the use of one of the most prominent electrochemical sensor i.e. pH glass potentiometric sensor. However, for its dimension and rigidity this sensor is not suitable for application as epidermal sensing tool. A wearable sensor for real-time pH monitoring on-body was developed by Bariya et al. [17]. The sensor was printed by roll-to-roll gravure technique and modified with polyaniline to sense pH with a near-Nernstian response of 0.054 ± 0.001 V/pH. In addition, the electrode was combined with printed circuit board and battery-assisted Bluetooth Low Energy (BLE) connection at 2450 MHz for longer read distances (up to 10 m) and an automatic data exchange in moderately large environments.

Nyein et al. [18] developed a fully integrated headband device, still exploiting a wireless BLE connection, allowing for the real-time detection of calcium ions and pH in body fluids, including sweat and tears. The sensor was fabricated by photolithography technique to create a patterning of Au electrodes onto a flexible polyethylene terephthalate substrate. Furthermore, modification of the Au working electrode surface by polyaniline electropolymerization provides a sensitive layer for pH detection with Nernstian response of 0.062 V/decade. The integration with a printed circuit board allowed for data acquisition and transmission to a smartphone receiver during physical activity.

Overall, the above referred sensing platforms exhibit some limitations or critical issues such as: i) sensor and transmitters are generally separate modules made by different materials that need to be interconnected through wires of other means; ii) a relevant number of electronic components are required onboard, thus preventing a low-cost manufacturing; iii) NFC requires a nearly contacting interaction with the sensor and to extend the communication beyond the few centimetres batteries are required.
Herein, we report an innovative flexible epidermal sensor, suitable to be used in both battery-less and battery-assisted modes, with minimal integrated electronics to evaluate pH value in sweat sample and transmit it up to a couple of meters. To deliver a miniaturised and affordable device we exploited i) the printing technology to directly deposit the sensor on the same material used in electronics (Kapton) to deliver a whole printed Kapton-based patch, ii) a biocompatible sensing element (iridium oxide) deposited directly onto the working electrode surface by electrodeposition; iii) a cotton-based material for sampling and placing in contact the sweat with the working electrode by means of paper-based microfluidics avoiding any external pump or high-cost microfluidic system; iv) the Radiofrequency Identification (RFID) platform working in UHF band to enable a much longer read range than NFC and a better power autonomy than BLE, as it can be also used in fully battery-less mode for real-time measurements.

2. Experimental section

2.1. Reagents and equipment

Ferric chloride, sodium chloride, iridium chloride, oxalic acid, sodium carbonate, potassium ferricyanide, potassium dihydrogen phosphate, dipotassium hydrogen phosphate were purchased from Sigma Aldrich. Kapton® HN Polyimide substrate was purchased from RS Components Srl. Cyclic voltammetry (CV) and potentiometry were performed using a portable PalmSens® instrument (PalmSens, Netherlands) in connection with a laptop and controlled by PSTrace 5.3 software.

2.2. Fabrication of printed sensors

A three-electrode system (screen-printed electrode, SPE) was screen-printing using an Ag/AgCl ink (Electrodag 477 SS) to print the pseudo-reference electrode and a graphite-based ink (Electrodag 421) to print the counter and working electrode. All the conductive-inks were purchased from Acheson. Successively, the electrodes printed on Kapton were modified with iridium oxide by electrodeposition, carried out using cyclic voltammetry in iridium chloride solution by 60 scans in a range of potential comprised between 0 V and 0.8 V, with a step potential of 0.05 V and scan rate of 0.05 V [19].

2.3. The RFID microchip transponder and backscattering modulation

The heart of the chemical sensor sampling is a sensor-oriented (5 mm × 5 mm) Integrated Circuit (IC) RFID transponder (AMS-SL900A IC AMS SL900A Tag Chip Datasheet [Online]. Available:https://ams.com/ger/content/download/755603/1912935/file/SL900A Da tashlee_t_EN_v5.pdf), that embeds a 10-bit ADC and an internal temperature sensor. The chip works in the UHF RFID band (860–960 MHz) and can be used in fully battery-free mode (minimum activation power –6.9 dBm) as well as in Battery Assisted Passive (BAP) mode (–15 dBm) that allows for a longer read distance and even data logging modality (up to 841 data samples) in the absence of an external reader, with more than two years autonomy. The external port of the RFID IC, to be connected with the pH sensor which has a programmable range of 0.96 V.

More in details, the IC transponder accomplishes the RF to DC conversion, it samples the sensor output and modulates the backscattered field. With reference to the block-diagram of Fig. 1A, the incoming RF signal, is first rectified to DC to and regulated (Power Management Unit) to feed the whole circuitry. The External Sensor Front-ends senses the signal variation produced by the sensor that is hence conveyed to the internal automatic gain control unit (AGC) to ensure a reliable analog to digital conversion. Then, binary digitized data reaches the Processing Digital Control unit for encoding by means of an internal solid-state switch to produce a controlled change of a reference impedance load. When the IC is connected to an antenna, the load modulation produces a modulation of the radar-cross-section of the overall tag that in turn induces a backscattering modulation (ISO 18000-6C standard) of the impinging electromagnetic field that comes back to the reader for demodulation and decoding.

2.4. The integrated wireless epidermal device

The final layout of the integrated device is shown in Fig. 1B. The antenna fills most of the board surface and is made by a 3 × 3 cm open-loop (Miozzi et al., 2019) whose layout was optimised to maximize the efficiency of the electromagnetic energy harvesting when the sensor is directly attached onto the human skin. The antenna is tuned by a lumped inductor, and two ferrite beads are used for the RF isolation of the analog port (where the sensor is connected). As the board is also suited to host a coin cell battery for read range boosting, an additional ferrite bead is then used for RF-DC isolation at the battery port. Overall, just five low-cost electronic components are required, including the RFID chip.

A manufactured prototype is shown in Fig. 1C. The antenna and the circuit traces were fabricated by etching of a copper-laminated Kapton substrate (thickness 50 μm). The pH sensor, produced by screen-printing technique, was deposited on the same layer. The three-electrode configuration of the sensor was manufactured by electrochemical deposition of pH-sensitive layer using portable PalmSens® instrument. Being a potentiometric measurement, only the working and the reference electrodes were interconnected with the electronic circuit.

The resulting Printed Circuit Board (PCB) hence hosts the IC transponder and some additional electronic components for tuning and isolations and the optional battery. Once the sensor is in put in contact with a solution, the H⁺ ions activity generates an electrical potential between the Ag/AgCl pseudo-reference electrode and the iridium oxide modified graphite working electrodes that are connected to the external port of the RFID chip and it is hence measured as electric potential difference generated at the solution/electrode interface.

The wireless board can work either as real-time monitor system or as data logger. In the first case, the board is fully passive (no battery needed) and the required energy to drive all the tasks described in Section 2.3 are provided from remote by an RFID interrogator module (in our case a ThingMagic M6e reader) and conveyed to the RF port of the IC by the harvesting loop antenna.

In data logging mode, instead, the battery is used to enable the IC transponder to sample the sensor and automatically store data into the integrated EEPROM at regular intervals defined by the programmable internal RTC Oscillator, without the presence of the external RFID reader. Activation of the data logging functionality is enabled in a single interaction with the reader. The data gathering procedure is similar to the real-time one, except for the encoding task, which is skipped since data are not directly sent back to the reader unit. Indeed, at each clock cycle, the converted data flow from the ADC to the EEPROM passing through the Processing Digital control unit. The whole process requires a battery to keep the IC active for data sampling. To download sensor data, a specific command sent by the reader will stop the data logging activity and starts the data transfer. At this point the IC encodes the entire content of the EEPROM and gradually transmits it to the reader via backscattering communication. The whole interaction with the reader, from the stop command to the data download, takes 2–4 s, without wasting the battery charge. Accordingly, as the battery charge is only drained during the sampling of the chemical sensor, the autonomy of the device will be much longer than any BLE module and can last up to a couple of years i.e. it encompasses the realistic lifetime of the device so that no battery replacement or recharge is required. The maximum read distance of the resulting radio-sensor, when attached onto the arm of a volunteer, was measured (Fig. 1C) by a reader emitting an EIRP of 3.2 W. Depending on the working frequencies, the device can be read from a distance up to 0.6–1 m in case of battery-free mode and up to 1.4–2 m in battery assisted mode. Such distances are all compatible with an automatic data retrieval when the user crosses a gate, with no manual effort.
2.5. pH measurement of standard solution using portable potentiostat

Cyclic voltammetry technique was used for sensor characterisation and optimisation by connecting Kapton-printed electrodes to portable PalmSens® potentiostat. CVs were performed by dropping 80 μL of 5 mM ferro/ferricyanide in KCl 0.1 mM onto three-electrode system. Potentiometric measurement of pH was carried out by dropping 80 μL of standard solution at known pH on only working and reference electrodes (two-electrode system, being a potentiometric measurement), obtaining the signal in less than 30 s.

2.6. pH measurement of standard solution using integrated device

Measurements were performed by using the proposed integrated wearable device, which includes the screen-printed electrode and the circuit board that are embedded in the same Kapton substrate.

In detailed, 80 μL of pH standard solution were dropped onto the working and reference electrodes, and pH of samples was measured. Data were then instantly wireless transmitted to the ThingMagic M6e RFID reader, connected to a laptop for fitting and analysis.

2.7. pH measurement of collected sweat solution using the portable potentiostat

In order to simulate the on-body measure, an adsorbent cotton pad (Cien, Lidl Stiftung & Co. KG, Switzerland) was placed onto the surface of the working and reference electrodes, to add the sample on this pad. In detail, sweat was collected from a volunteer after running activity by scratching the runner wet skin belly with microtubes. After, 80 μL of collected samples without any treatment were dropped onto the cotton pad placed in contact with the working and reference electrode, and the pH of samples was measured.
Fig. 3. A) Calibration curve obtained by measuring 80 μL of citrate buffer pH 3, 4 and 5, and phosphate buffer pH 6, 7 and 8, after potential treatment. OCP parameters: $t_{\text{interval}} = 0.01 \text{ s}$, $t_{\text{run}} = 30 \text{ s}$; B) Potentiometric response obtained after potential treatment, by measuring 80 μL of citrate buffer pH 3, 4 and 5, and phosphate buffer pH 6, 7 and 8. OCP parameters: $t_{\text{interval}} = 0.01 \text{ s}$, $t_{\text{run}} = 30 \text{ s}$; C) potentiogram obtained by measuring of 80 μL of citrate buffer pH 5 with 2 h of acquisition time. D) Hysteresis study testing different pH values from 4 to 7 and vice versa in the selected working conditions; E) Histogram bars for potentiometric measurements of 80 μL of phosphate buffer pH 5, in presence of K$^+$ 15 mM, Na$^+$ 70 mM and Cl$^-$ 40 mM. OCP parameters: $t_{\text{interval}} = 0.01 \text{ s}$, $t_{\text{run}} = 30 \text{ s}$. Measurements carried out in triplicate; F) Histogram bars for potentiometric measurements of 80 μL of citrate buffer pH 5 in absence (red) and in presence of BSA (green) 6% (w/v). OCP parameters: $t_{\text{interval}} = 0.01 \text{ s}$, $t_{\text{run}} = 30 \text{ s}$. Measurements carried out in triplicate. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
2.8. Real-time on-body pH measurement of sweat using integrated epidermal wireless sensor

On body continuous measurements were performed during the running activity of a volunteer. The integrated wearable device was encapsulated in a breathable 22 μm-thin polyurethane membrane to isolate the electronic components from the skin, and then it was stuck on chest skin by a Tegaderm™ film. Moreover, to facilitate sample collecting during running and to avoid contact between the skin and the modified electrode, the cotton pad was placed between the epidermal surface and electrode.

For this experiment, the epidermal sensor was equipped with a coin cell battery to store pH data inside the microchip internal memory during a running period of 60 min. After the physical activity, data were retrieved, following a customized RFID interrogation, when the runner passed through a gate that was equipped with the ThingMagic M6e reader.

Battery could be however avoided whether the only initial and final values of pH are collected.

3. Results and discussion

3.1. Electrochemical characterisation of Kapton-based printed sensor

To evaluate the suitability of Kapton as substrate for screen-printed electrodes, an electrochemical investigation was carried out by cyclic voltammetry varying the scan rate from 20 to 1000 mV/s in 5 mM [Fe(CN)₆]³⁻/⁴⁻ + 0.1 M KCl solution.

As depicted in Fig. 2A both anodic and cathodic current peaks increase proportionally with the square root of the scan rate,
Fig. 6. A) Scheme of the different layers used to assemble the flexible device on body for pH measurement. B) Time required to wet the cotton-based pad by using a colored aqueous methylene blue solution. C) Real-time on-body pH measurement. D) pH measurement during running activity by using the integrated wearable device. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
demonstrating an electrode reaction controlled by mass transport-controlled reaction (semi-infinite diffusion) [20,21]. The inset shows the plots of the current density vs the square root of the scan rate for the anodic (red) and cathodic (black) peaks current, with a regression line equation equal to \( y = (0.04 \pm 0.01) + (0.014 \pm 0.001) x \), \( R^2 = 0.982 \) for anodic peak.

Furthermore, the electroactive surface area of the electrodes was calculated employing the Randles-Sevck equation: \( I_p = (2.69 \times 10^3) n^{3/2} A \theta^{1/2} C v^{-1/2} \), where \( I \) is the current peak intensity, \( n \) (number of electrons exchanged) = 1, \( D \) (diffusion coefficient of \( \text{Fe(CN)}_6^{3-}/4^- \)) = \( 5.9 \times 10^{-5} \text{ cm}^2 \text{ s}^{-1} \), \( C \) (concentration of \( \text{Fe(CN)}_6^{3-}/4^- \)) = 5 mM and \( v \) (scan rate) = 50 mV/s.

An electroactive area equal to 0.033 cm\(^2\) was obtained, which is lower than the ones found in case of screen-printed electrodes printed on office paper, Whatman #1 paper, and polyester, \((0.21 \pm 0.03, 0.15 \pm 0.03, \text{ and } 0.11 \pm 0.01 \text{ cm}^2\), for respectively) with same geometrical area [22]. These results demonstrated the capability of Kapton to be used as substrate, even if electrodes characterised by lower electroactive area than one obtained with supports usually employed. However, the effectiveness of Kapton relies on use of the same support for production of an embedded device containing both the electrochemical and electronics components on same flexible support.

3.2. Optimisation of iridium oxide electrochemical deposition

Electrodeposited iridium oxide was used as sensing element to deliver a sensitive and accurate sensor for pH detection in sweat. In pH sensor development, the optimal metal oxide layer formation is a key step to obtain reproducible measurement. Indeed, when using metal oxides as pH sensitive element, the pH response not only depends on the sensitivity but also on the oxidation state of the deposited metal. In detail, after the electrodeposition process, a mixed anhydrous/hydrated iridium oxide film composition is usually created, with the following continuous steps of oxidation and reduction as reported in literature [25]. In order to optimise iridium oxide electrodeposition, several parameters were investigated, including the number of voltammetric cycles and the potential window of the cyclic voltammetry. A citrate buffer solution at pH 4 was measured by using electrodes modified with iridium oxide electrodeposited by different numbers of voltammetric cycles, namely 40, 60, 80, and 100. As depicted in Fig. 2B, when 60 cycles were used, a higher sensitivity was obtained, while with more deposition cycles i.e. 80 and 100 or lower i.e. 40 cycles, a lower sensitivity was recorded. This can be probably ascribed to the formation of thin sensitive layer when using only 40 voltammetric cycles, and a thicker oxide layer when using deposition cycles higher than 60 [19].

Then, the deposition potential window was investigated by measuring the same pH 4 citrate buffer solution with electrodes modified with iridium oxide electrodeposited at different potential ranges, namely between 0 V and 0.8 V, −0.2 V−1 V and −0.4 V−1.4 V. Fig. 2C shows a higher sensitivity and repeatability when an electrodeposition from 0 V to 0.8 V was carried out. The use of wider potential windows brings the formation of several iridium oxide compounds, generating a lower sensitivity. For this reason, a potential window between 0 V and 0.8 V was chosen for the iridium oxide electrodeposition.

3.3. Effect of treatment and analytical features of sensor in standard solutions

As previously described, sensitivity of iridium oxide layer lies on \( \text{Ir}^{3+}/\text{Ir}^{4+} \) ratio. In order to ensure a significant amount of both \( \text{Ir}^{3+} \) and \( \text{Ir}^{4+} \) oxidation states [25] an oxidative step consisting of applying a potential of 200 mV for 3 min in a pH 7 phosphate buffer solution is required, as reported in literature [19].

As consequence of the potential treatment (Fig. 3A), a higher repeatability was obtained, compared to the measurements performed without treatment (Fig. S1); for instance, in case of pH 4 citrate buffer solution measurement, a Relative Standard Deviation (RSD %) decrease was observed from 6.4% to 1.1% (n = 3). A linear correlation between pH value and potential was recorded using three different sensors, with a regression line equation equal to \( y = (-0.079 \pm 0.002) x + (0.83 \pm 0.01) \), \( R^2 = 0.992 \). In Fig. 3A a typical response of sensor at different pH values was reported. The recorded super-Nernstian response, namely a slope equal to \(-0.079 \pm 0.002 \) (RSD% = 2.5), is a consequence of the sensitive iridium oxide layer composition, as previously described, and it is commonly obtained when this system is employed [26].

Thus, the electrode requires to be treated before the use. To deliver a sensor ready to use, the treatment was carried out before the measurement and the storage stability of treated sensor was evaluated as reported in Section 3.4.

We further investigated the stability of the measurement during 2 h of continuous pH monitoring, by analysing 80 \( \mu \)L of pH 5 citrate buffer solution. Fig. 3C showed a small decreasing of potential value, confirming the satisfactory working stability of the developed sensor.

Finally we evaluated the hysteresis of the sensor, testing solution at the following pH values, namely 4, 5, 6, 7, 6, 5, 4. The study was carried out recording the potential values of the sensor when the pH was increased from 4 to 7. After, we recorded the potential values decreasing the pH from 7 to 4 using the same electrode, and the same experiment was carried in triplicate using three different sensors. As shown in Fig. 3D, any hysteresis effect was observed, demonstrating the capability of this sensor to test different pH values without any memory effect.

3.4. Storage stability study

A key feature for an affordable sensor is its stability. In order to deeply investigate this parameter, potentiometric measurements were carried out after three and six days from the iridium oxide electrodeposition. Results in Fig. S2 show a decreasing in term of sensitivity when the measurement was performed three and six days after the electrodeposition. This can be probably ascribed to the oxidation of the iridium (+3) oxide layer changing the ratio when the sensor is stored in normal atmosphere condition.

With the aim to overcome this drawback, modified electrodes where stored in vacuum and pH measure was carried out after 28 days, observing a quite stable signal within 6 days, with a decrease of the potential response in the following days. However, the slope (0.068 \pm 0.003 V/pH) is quite stable during the period tested as reported in Fig. S3. Thus, in this storage condition, before the measurement, the sensor need to be calibrated for accurate measurement. In order to avoid the calibration before the use, the sensor has been maintained at −26 °C for 20 days observing the unvaried potential response (RSD% = 1.2), improving the storage stability when storage at low temperature.
3.5. Interference study

An evaluation about interference of the most common sweat electrolytes was also performed. Investigation on Na⁺, K⁺, and Cl⁻ interfering action was carried out by measuring these elements in pH 5 citrate buffer solution, at a physiological concentration equal to 70 mM, 15 mM and 40 mM respectively [27]. As depicted in Fig. 3E, any interference was recorded when pH 5 buffer solution was measured in presence of these elements, showing a high selectivity of the iridium oxide layer for H⁺ ions. In sweat sample different proteins are present including dermcidin, apolipoprotein D, clusterin, prolactin inducible protein, and serum albumin [28]. The response of the sensor using three different electrodes was tested using citrate buffer at pH 5 in absence and in presence of serum albumin at concentration of 6% w/v. As depicted in Fig. 3F no variation of response was observed, demonstrating the resistance of the sensor to the inactivation of surface in case of level protein present in sweat.

3.6. Portable potentiostat vs printed circuit board for pH measurement

To deliver a sensor patch able to sense pH, register and transmit data, we printed electrodes close to printed circuit board on Kapton. After electrochemical iridium oxide deposition, the integrated device was tested by analysing solution at pH 3, 5, and 7. In detail, we tested the analytical performances of sensor using both the portable potentiostat (Fig. 4A) and the printed circuit board (Fig. 4C), in which the data were instantly wireless transmitted to the ThingMagic M6e RFID reader. As shown in Fig. 4B, the potentiometric responses using Palm Sens instrument (i.e. potentiogram output) were found in agreement with the data obtained using the printed circuit board (i.e. response highlighted as dot in Fig. 4B), obtaining a correlation value of $R^2 = 0.997$. These results demonstrated the effectiveness of the embedded sensor in printed board to detect accurately pH of the analysed solution.

3.7. Sensor for pH detection in collected undiluted sweat

For sweat analysis, a small size cotton pad ($1 \times 1 \text{ cm}$) was placed onto the two electrode system (working and reference electrodes) with the aim to simulate the “on-body” configuration, where the pad absorbs and collect the sweat produced under physical activity. In addition, the cotton pad ensures an optimal collection of the produced sweat and avoids the direct contact between skin and electrode, eluding the working electrode fouling by e.g. proteins present in the sweat. As depicted in Fig. 5A, using cotton pad a stable signal was observed, even if with a slight decrease of values. A pH sweat value of $5.3 \pm 0.3$ was obtained by interpolation method (Fig. 5B), in accordance with the measurement performed by a commercial pH meter equal to $5.2 \pm 0.2$.

3.8. Continuous pH monitoring in sweat with the integrated epidermal wireless sensor

As reported in Fig. 6A, the sensor was in contact with body through a cotton-based pad for an easy management of sweat. To estimate the time the pad needs to get fully filled of sweat, a 300 μL of distillate water-based methylene blue solution was dropped over it and the color change was observed along with time. Fig. 6B shows that the cotton-based pad became completely wet (colored) after 60 s. Accordingly, we expect some minutes for a change of the baseline voltage that is detectable by the epidermal board after the running start, due to the runner begins sweating and the pad becomes wet to finally interact with the printed electrochemical pH sensor.

To test the suitability in field of the developed device, it was stuck onto chest skin of the subjects performing running activity (Fig. 6C). On-body real-time measurement was performed during 30 min running (Fig. 6D) and at the start the epidermal board collected only noise signal as the cotton-based pad was not yet wet. Then, the pad was wet and the board recorded a pH close to 5.5, in agreement with the value obtained by pH-meter measurements equal to $5.4 \pm 0.2,$ thus demonstrating the effectiveness of the cost-effective wearable device developed.

4. Conclusions

Within the consolidating trend of close synergy among analytical chemistry and electronic/mechanical engineering, we developed an integrated epidermal device comprising a screen-printed electrode electrochemically modified with iridium oxide combined with a flexible integrated circuit board for pH measurement in sweat and wireless transmission of data in the medium range. The device was conceived as a patch in which the electrochemical sensor, some electronics components, and the antenna are all printed on the same substrate, namely Kapton, to deliver a body-conformable epidermal device. The optimised sensor in terms of iridium oxide modification and electrochemical pretreatment was tested in vitro, demonstrating a comparable accuracy in respect to classical bulk glass-pH sensor as well as other pH sensors, with the advantages to be cost-effective, to need of only few μL of sweat sample, to be miniaturised, and to provide real-time data (Table S1). When the board is applied on the skin, the sampled pH data can be remotely retrieved up to 1 m in fully battery-less mode and up to 2 m in battery assisted mode with a power autonomy that generally encompasses the true life of the specific application since thin skin devices are mainly considered as disposable. Such read distances are intermediate between that of state-of-the-art low-cost NFC skin sensors (1–5 cm) and the more versatile BLE boards (<10 m). Hence, taking the benefit of both those platforms, but with a remarkable improvement to their current drawbacks, namely the limited short range of NFC and the high cost of BLE, the proposed UHF-RFID pH sensor is a valid candidate for the massive automatic monitoring of patients/users inside a house, thus contributing to moving from hospitals to “home-spitals”, and above all of multitude of athletes in sportive events.

Credit author statement

Vincenzo Mazzaracchio: Investigation, Methodology, Formal analysis, Writing - review & editing; Luca Fiore: Investigation, Methodology, Formal analysis, Writing - review & editing; Simone Nappi: Investigation, Methodology, Formal analysis, Writing - review & editing; Gaetano Marrocco: Conceptualisation, Supervision, Funding acquisition, Project administration, Writing - review & editing; Fabiana Arduini: Conceptualisation, Supervision, Funding acquisition, Project administration, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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