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Development of an alginate/TiO_2-based microfluidic biosystem for chrono-sampling and sensing of glucose in artificial sweat

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ABSTRACT

Glucose is an analyte of great importance, both in the clinical and sports fields. As an alternative to standard blood analysis, sweat arises as an easily accessible, non-invasive biofluid, as well as a great candidate to monitor human health and sport performance of athletes. However, there is a current need for the fabrication of low cost, easy to use technologies capable of sequential analysis of sweat biomarkers at different times. In this research, we developed a chrono-sampling microfluidic platform integrated with an alginate/TiO_2 biosystem for sweat glucose determination. Glucose concentrations ranging from 10 to 1000 μM in artificial sweat were detected and quantified, both in a bead format and in the device, where the whole system was calibrated and verified. The PDMS microfluidic platform allowed chrono-sampling over more than 42 min. This research is oriented towards the development of a miniaturized device for fast analysis at the point and place of need. The integration of the chrono-sampling capacity opens the possibility for a continuous monitoring of sweat biomarkers during exercise, allowing a personalized-oriented training to improve the performance of athletes.

1. Introduction

There is an increasing need to develop novel approaches that permit the use of non-invasive biofluids as alternatives to blood analysis. In this regard, sweat outperforms other non-invasive biofluids such as urine, saliva and tears due to its ease of obtaining and highly informative character [1–5], which highlights the diagnostic potential of this biofluid. In this regard, glucose monitoring is of high importance to detect a great variety of disease conditions, such as hypoglycemia and diabetes [6]. In fact, some studies have suggested that the detection of sweat glucose could be applied to detect big changes in blood glucose [7,8]. Glucose levels in sweat are established to be between 10 μM and 1000 μM, with the physiological range being 60–110 μM [6,9].

Therefore, tracking an athlete during exercise, for instance, could prevent any health issues that may arise during the process, as well as be a potential, reliable way of improving his/her performance. However, sweat rate and composition change over time due to several factors, such as gender [10,11], race, age, fitness conditions and exercise intensity [4], and sampling area [12], which hinders the possibility of standardizing sweat sensing. This highlights the need for the development of new approaches for real-time detection and quantification of sweat biomarkers at different times, thus allowing a continuous and personalized tracking of individuals.

Most of the microfluidic platforms developed so far focus on single measurements of sweat biomarkers. However, in order to carry out a reliable and useful real-field application, sweat sensing technologies have to allow the continuous monitoring of athletes. For this purpose, chrono-sampling has been studied in microfluidic devices as a potential methodology to fulfil this sport science requirements, since it allows quantitative measurements at defined time intervals [13]. In this regard, Jungil, C. *et al.* [14] developed a PDMS platform integrated with capillary bursting valves (CBVs) which opened at different pressures and guided passively the flow through the device, allowing a sequential detection of Na^+, K^+ and lactate. Two years later, the same group

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optimized the CBVs, which, when integrated in the microfluidic platform, directed the flow towards separated detection chambers [15]. They were able to detect and quantify chloride, glucose, pH, lactate, temperature, sweat rate and sweat loss in the same device. However, further research needs to be done in this field since the current available technology is not yet mature enough to reach the potential end users and be integrated into wearable platforms for sports science.

As a proof-of-concept technology for sweat analysis in sports medicine, previous research was developed by us on glucose and lactate detection using alginate beads. We were able to develop a biosystem, based on an alginate hydrogel, capable of measuring lactate in real sweat samples within the physiological range 10 – 100 μM, setting the detection time to 13 min [16]. In order to be used in real field applications, however, faster biomarker determinations are preferable so that decisions regarding the performance or health of the athlete can be taken at the time needed. Therefore, we explored the use of a superhydrophilic material to enhance the sensing time by integrating TiO_2 nanotubes in the alginate bead biosystem. Using this novel biomaterial, we developed a biosystem for glucose and lactate sensing in sweat, lowering the detection time to just 5 min [17]. The integration of the TiO_2 nanotubes resulted in an improvement of alginate-based systems for sweat sensing, demonstrating their potential towards a personalized-oriented training to improve the performance of athletes.

Considering the increasing need for a fast and personalized oriented sports medicine, and taking into consideration our previous results, in this research we explore the fabrication of a biosystem for a continuous glucose sensing at different times during exercise. For this purpose, we calibrated an alginate/TiO_2 bead biosystem for glucose 10 – 1000 μM sensing in artificial sweat. Moreover, we developed a microfluidic platform capable of performing chrono-sampling for glucose sensing in artificial sweat using the calibrated bead biosystem. This research aims at increasing the number of available technological tools towards a personalized sports medicine, in order to be applied at the time and place needed for tailored training of athletes.

2. Materials and methods

2.1. Artificial sweat

Artificial sweat was prepared by dissolving NaCl 60 mM (≥ 99.5%, Sigma-Aldrich) and urea 60 mM (99%, Fisher BioReagents) in distilled water [16]. Solutions of artificial sweat 60 mM with spiked *D*-(+)-glucose (≥ 99.5%, Sigma) concentrations at 10, 20, 40, 50, 60, 70, 80, 90, 100, 110, 150, 250, 500, 600, 750 and 1000 μM were prepared and the pH was adjusted to 6.5. The solutions were stored between 2 and 8 °C for later use.

2.2. Fabrication of the biosystem

The alginate beads were fabricated by mixing 5 μL of GOx 0.8 mg mL^{-1} (*Aspergillus niger*, Sigma), 5 μL of HRP 0.04 mg mL^{-1} (Sigma Aldrich) and 1.5 μL of TMB (Sigma Aldrich) dissolved in dimethyl sulfoxide (DMSO, Sigma) with 30 μL of sodium alginate (Sigma-Aldrich) 1.5% or 30 μL of Alginate/TiO_2. TMB was prepared by dissolving 10.7 mg in 1 mL of DMSO. Alginate/TiO_2 was prepared by dissolving 5 mg mL^{-1} of TiO_2 nanotubes (TiO_2) [17] in alginate 1.5%, and it was left under stirring conditions for 48 h until its complete dissolution. All solutions were stored between 2 and 8 °C for later use.

For the formation of the biosensor, 17 μL of the alginate mixture was taken and dropped into a 400 mM $CaCl_2$ solution (≥ 93.0% Sigma-Aldrich) and left there for 1 min, which led to the consequent formation of the final alginate/TiO_2 bead biosystem. Afterwards, the newly formed beads were wiped and washed with distilled water for 3 min before wiping them again.

2.3. Fabrication of the microfluidic platform

A PMMA mold was fabricated following a layer-by-layer approach, which was used later as a mold for the final PDMS device. It was formed by 5 layers, which from bottom to top were 1.1 mm-thickness PMMA (ME303010, clear, Goodfellow, United Kingdom) with the negative of our device, a frame of PSA 8939 (ARcare® 8939, Adhesive Research, Ireland), a frame of 4 mm-thickness PMMA (ME303040, clear, Goodfellow, United Kingdom), a frame of PSA 8939 and a frame of 4 mm-thickness PMMA. The PDMS was made with silicone elastomer base and silicone elastomer curing agent, both from SYLGARD™ 184 Silicone Elastomer Kit, in a 10:1 ratio. This mix was poured into the mold, degasified for 45 min and cured at 62 °C during 2 h. Once unmolded, circular PSA 8939 was attached at the bottom to provide a higher contrast for the later image analysis, and PSA 92712 (ARcare® 92712, Adhesive Research, Ireland) was added at the top of the device.

PSA layers were designed with CorelDRAW Graphics Suite X7 and cut using a Graphtec cutting Plotter CE6000–40 (CPS Cutter Printer Systems, Spain). PMMA layers were designed with CorelDRAW Graphics Suite X7 and cut with a CO_2 Laser System (VLS2.30 Desktop Universal Laser System, VERSA Laser, USA).

2.4. Calibration and verification of the sensor

For the initial calibration of the biosensor in plate, a 96-well white plate (Non-Treated Surface, Thermo Fisher Scientific) was used. One bead was placed in each well and 150 μL of the different glucose solutions in artificial sweat were added to the alginate beads. For the calibration in the microfluidic platform, the different glucose concentrations were tested in different devices.

Likewise, the verification of the sensor was done both in plate and in the device. *In vitro* unknown glucose concentrations were spiked in artificial sweat, and after the colorimetric analysis of the images, the calibration curves were used for the determination of the glucose concentrations of the different samples. The accuracy and the precision of the obtained values were discussed attending to the standard deviation (SD) of the measured black and white (B/W) values, compared to the real glucose concentration, see Section 2.5 for colorimetric analysis specifications.

Four different beads were measured for the calibration of the biosystem (n = 4) and three (n = 3), for the verification. In plate, the analyzed beads for each glucose concentration were placed in individual wells, while in the device, the analyzed beads for each glucose concentration were placed in different reservoirs of the same device.

For the calibration and verification experiments in the device, positive pressure was applied using a syringe pump (Harvard Apparatus Pump 11 Elite) at a constant flow rate of 5 μL min^{-1}. The entire process is summarized in Fig. 1. All the calibration and verification experiments were carried out at room temperature, both in plate and in device.

2.5. Colorimetric analysis

The experiments were recorded with a 64 MP camera (Sony IMX682 1/1.73″, f/1.89, PDAF) in a white chamber under the same light conditions. Images at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 13, 16, 19, 25 and 30 min were subtracted from the video and were, afterwards, analyzed with the image processing program ImageJ freeware software (National Institutes of Health, USA) in the grey scale. For the grayscale analysis, the image was turned into an 8-bit image and the B/W value of each bead was measured, where 0 stands for black and 255, for white. To facilitate the interpretation of the data, the measured B/W values were subtracted to 255, so that the more intense the color of the bead, the higher B/W value.

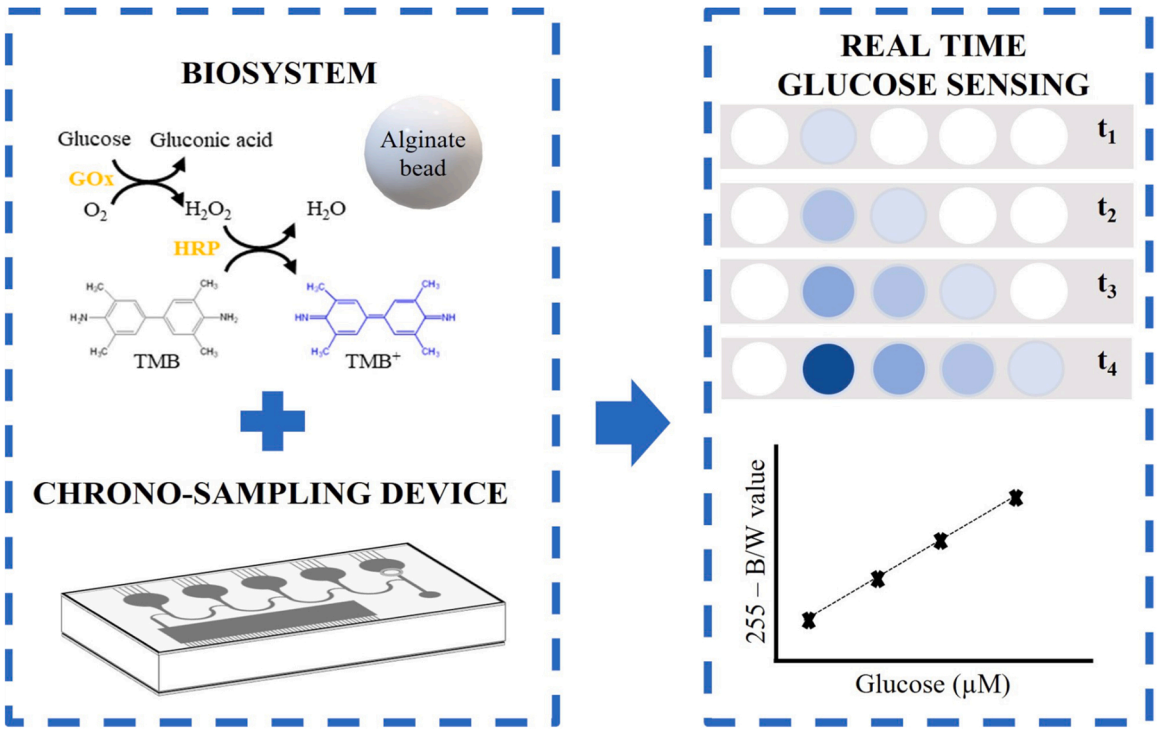

Fig. 1. Workflow of the development of a microfluidic bead based biosystem with chrono-sampling capacity to detect glucose. The biosystem (top left image) consists of an enzymatic assay integrated into an alginate/TiO_2 bead for the determination of glucose 10 – 1000 μM. The oxidation of TMB yielded a blue colored product. Thus, beads with a higher blue color intensity were obtained as the analysis time and glucose concentration increased. A PDMS microfluidic platform (bottom left image) was designed to achieve chrono-sampling. Then, the alginate/TiO_2 biosystem was integrated in the microfluidic platform to sequentially detect and quantify glucose in artificial sweat, at different times (right image). After measuring different glucose levels in artificial sweat, a calibration curve for chrono-sampling inside the device can be obtained.

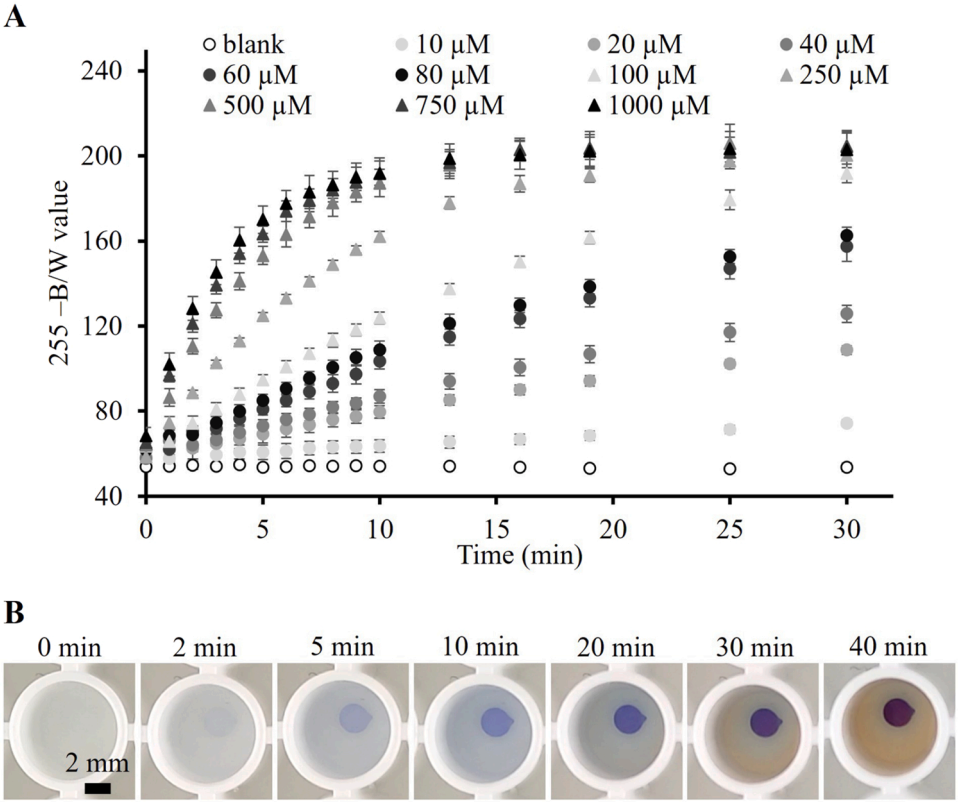

Fig. 2. Calibration of glucose in alginate/TiO_2 beads using artificial sweat. **(A)** B/W values of glucose 10 – 1000 μM at different times for 30 min (n = 4). **(B)** Images of an alginate/TiO_2 bead over 40 min after the addition of 150 μL of 80 μM glucose in artificial sweat.

3. Results and discussion

3.1. Calibration and verification of the biosystem in plate

The detection of glucose was carried out through an enzymatic assay consisting of a mix of GOx, HRP and TMB integrated in an alginate/TiO_2 bead (see Section 2.2). The fabricated alginate/TiO_2 beads had a dimeter of 2.0 ± 0.1 mm and showed a homogeneous white color. Indeed, this characteristic was found to be appropriate for detection applications through colorimetric approaches since it provided better contrast for image analysis procedures [17].

The detection approach was similar to the one previously described for lactate sensing with an alginate-based biosystem [16]. In brief, when a glucose solution is poured over the bead, it penetrates the alginate/-TiO_2 bead due to the porosity of the material, and it is oxidized by the GOx, yielding gluconic acid and H_2O_2. Then, the HRP uses the H_2O_2 as an electron donor for the oxidation of the TMB, which is oxidized to a diimine, and it can undergo either a one- or two-electron oxidation, yielding a blue- and yellow-colored product, respectively [18].

For the calibrations of the biosystem (see Section 2.4), glucose concentrations ranging from 10 to 1000 μM were used to ensure that the reported physiological range of glucose in sweat was tested [6]. Fig. 2A shows the calibration of the biosystem over 30 min, with solutions of artificial sweat 60 mM with spiked glucose concentrations of 0, 10, 20, 40, 60, 80, 100, 250, 500 and 1000 μM. We measured the B/W value of the beads, where higher glucose concentrations showed higher intensity values, since more glucose diffused inside the alginate bead. Fig. 2B shows real images of the alginate/TiO_2 beads over 40 min when 150 μL of glucose 80 μM in artificial sweat was added to the biosystem. As more glucose entered the biosystem over time, the blue color intensity of the bead increased due to a higher amount of TMB being oxidized inside the biosystem. Moreover, the added artificial sweat solution covered all the bead, thus, yielding a homogeneous color distribution. It can also be appreciated that the beads maintained their spherical shape during the analysis time, demonstrating their structural stability.

The calibration curve for the B/W analysis (Fig. 3A) was done at time 5 min, since this was the minimum time at which the measured concentrations were distinguishable from each other, within the error. A calibration curve was obtained for the B/W analysis, as described by the Eq. (1), obtaining a R^2 of 0.998. These results reinforced our previous research [17], in which we demonstrated that the superhydrophilic character of the integrated TiO_2 nanotubes in the alginate hydrogel allowed fast detection times.

$$y = 191.1 + \frac{60.1 - 191.1}{1.0 + \left(\frac{x}{247.8}\right)^{1.2}} \quad (1)$$

Since the glucose solutions used for the calibration of the biosystem covered a very extensive range of concentrations, the calibration curve shown in Fig. 3A was divided in two different regions for an easier interpretation and application of the data, depending on the desired range of operation. At low glucose concentrations (Fig. 3B), a linear calibration range of glucose 10–100 μM was determined, where the measured B/W values linearly increased, proportionally to the glucose concentration of the solution. At high glucose concentrations (Fig. 3C), however, glucose in artificial sweat was detected in a logarithmic calibration range from 100 μM to 1000 μM, which shows the saturation of the biosystem. Fig. 3D shows real images of several beads at 10 –

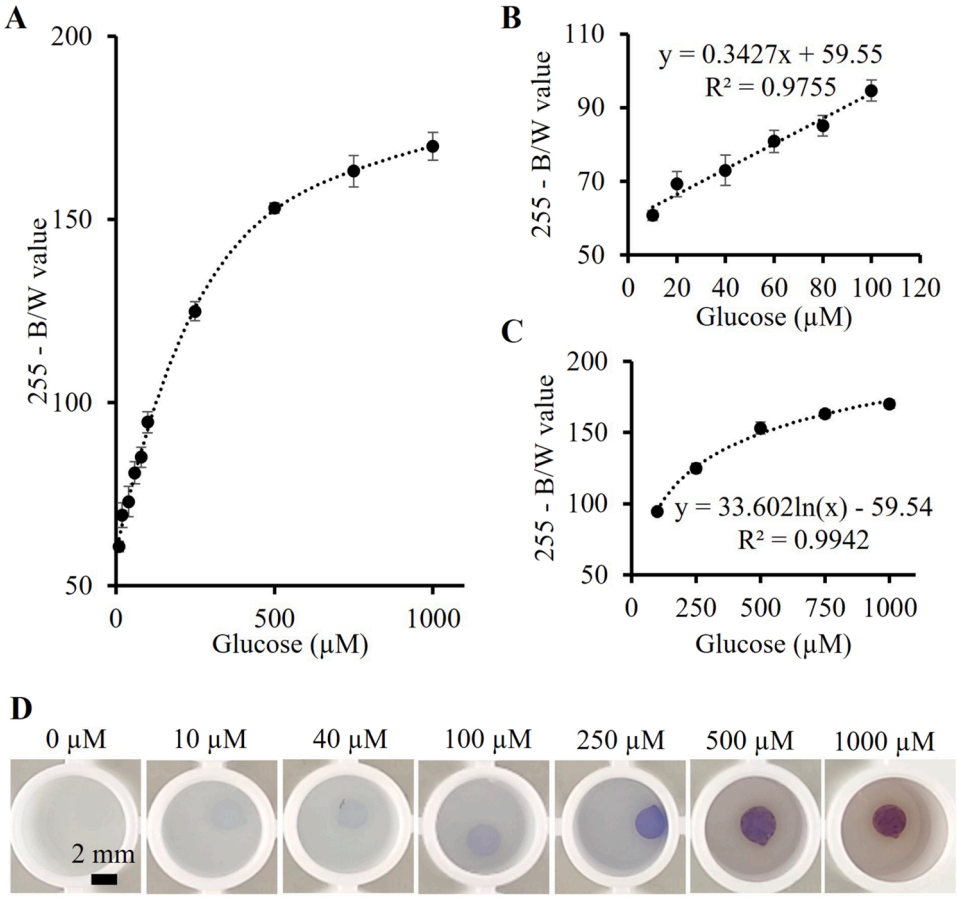

Fig. 3. Calibration of glucose in alginate/TiO_2 beads using artificial sweat. Calibrations curves of the alginate/TiO_2 beads at time 5 min using the B/W values for **(A)** glucose 10 – 1000 μM, Eq. (1), (B) glucose 10 – 100 μM and **(C)** glucose 100 – 1000 μM in artificial sweat (n = 4). **(D)** Images of the alginate/TiO_2 biosystem for glucose 10 – 1000 μM at 5 min, which correspond to the B/W values of the calibration curve.

1000 μM glucose concentrations taken at 5 min, when the calibration curve was carried out.

The limit of detection (LOD), which was calculated as three times the standard deviation (SD) of the blank, and the limit of quantification (LOQ), which was calculated as ten times the SD of the blank, were determined for our biosystem. An LOD of 4.1 μM and an LOQ of 13.6 μM were obtained for glucose sensing in alginate/TiO_2. Therefore, we have demonstrated that our biosystem is capable of detecting and quantifying sweat glucose with high sensitivity within the physiological range, reinforcing the reliability of this approach for personalized sports medicine.

To further demonstrate the efficiency of this sensing approach, the alginate/TiO_2 biosystem was verified and the results were analyzed by measuring the B/W value of the beads. For this purpose, artificial sweat samples with glucose 70, 90 and 110 μM were tested using the beads and the obtained B/W values were plotted in the calibration curve described in Fig. 3B for the first two glucose solutions, and in Fig. 3C for the third glucose solution. The obtained values were of 79 ± 4 μM, 92 ± 2 μM and 105 ± 3 μM, respectively. In fact, a precision of the measurement of at least 95% and an accuracy of 87% were achieved for the three glucose concentrations that were tested. These results demonstrate that the alginate/TiO_2 biosystem developed in this research can be used for the quantification of glucose in artificial sweat within the physiological range with high accuracy and precision. This, together with the homogeneity of the color, led to an increased sensibility and robustness during color analysis, obtaining reliable and reproducible results.

3.2. Chrono-sampling microfluidic device

Since sweat glucose levels change over time during exercise and are different for each individual [1], it is of high importance to develop a technology capable of measuring biomarkers at different times, this is, chrono-sampling. For the development of a final functional device, a total of five different microfluidic platforms were designed and fabricated through an optimization process (see Supplementary Information, SI-1). A PMMA mold was fabricated through a layer-by-layer approach (Fig. 4A) (see Section 2.3), which was later used as a negative for the fabrication of the final PDMS microfluidic device (Fig. 4B). The dimensions of this device are shown in Fig. 4C. The microfluidic platform was composed of an inlet, 5 reservoirs, a sweat storage trench and the microfluidic channel connecting these features (see Supplementary Information, SI-1.3). Figs. 4D and 4E show both the PMMA mold which was used for the fabrication of the device and the PDMS device itself, respectively. The final microfluidic prototype was operated with positive pressure, simulating the physiological sweat rate by eccrine glands [9]. A constant flow rate of 5 μL min^{-1} was applied throughout the time the experiment was running.

Chrono-sampling was achieved by designing three different channel diameters within the device (Fig. 5 A): the main channel with a diameter of 400 μm, the bifurcation channel with a diameter of 200 μm, and the air channel with a diameter of 100 μm. This approach, which followed a similar configuration than the one previously reported by Jungil *et al.* [14], is based on the liquid flowing through the channel with the lowest resistance, this is, the channel with the higher diameter. Therefore, when the liquid flowing through the main channel reached the bifurcation, it stopped at the bifurcation channel and flowed towards the reservoir since it offered less resistance to the flow (Figure 5B, t_1). It was not until the well was filled that the liquid reached enough pressure to continue flowing through the bifurcation channel (Figure 5B, t_2). However, this pressure was not enough to overpass the resistance of the

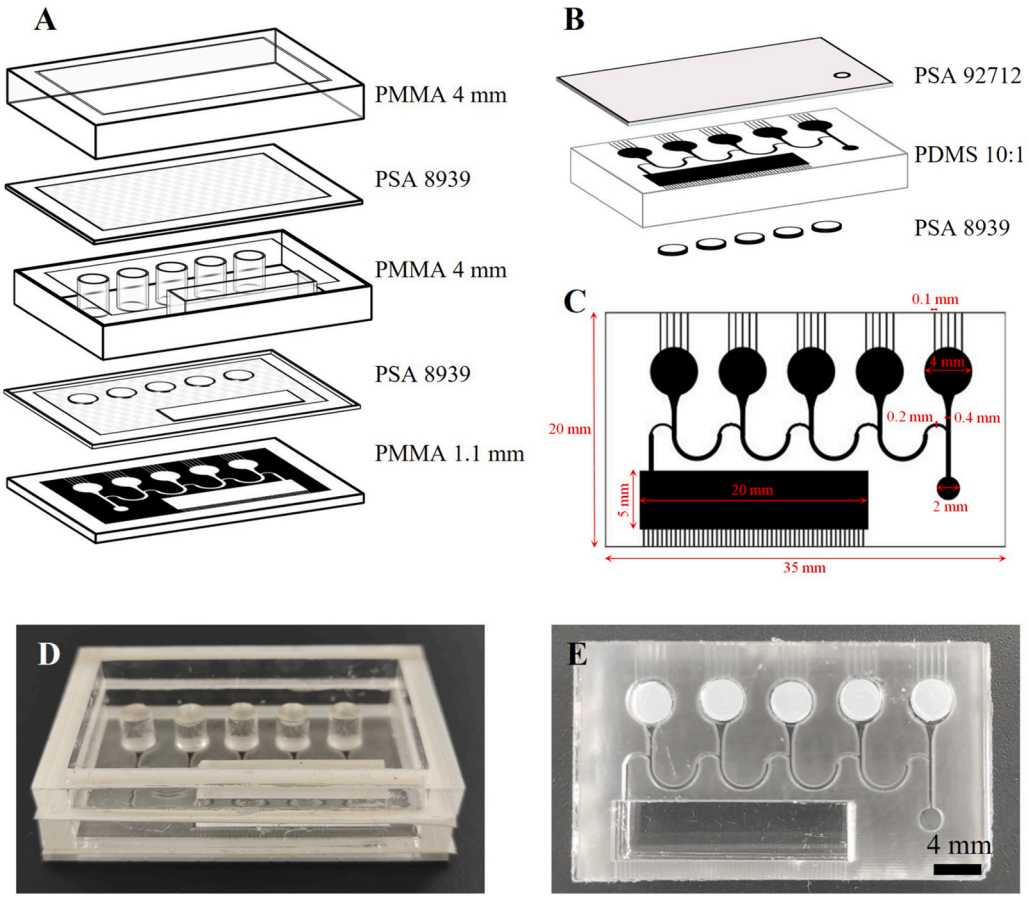

Fig. 4. Microfluidic platform for chrono-sampling. Schematic diagram of the different layers of the **(A)** PMMA mold (grey dotted surface represents an open space), **(B)** the PDMS device and **(C)** the dimensions of the platform. Real images of **(D)** the PMMA mold and of **(E)** the final PDMS device.

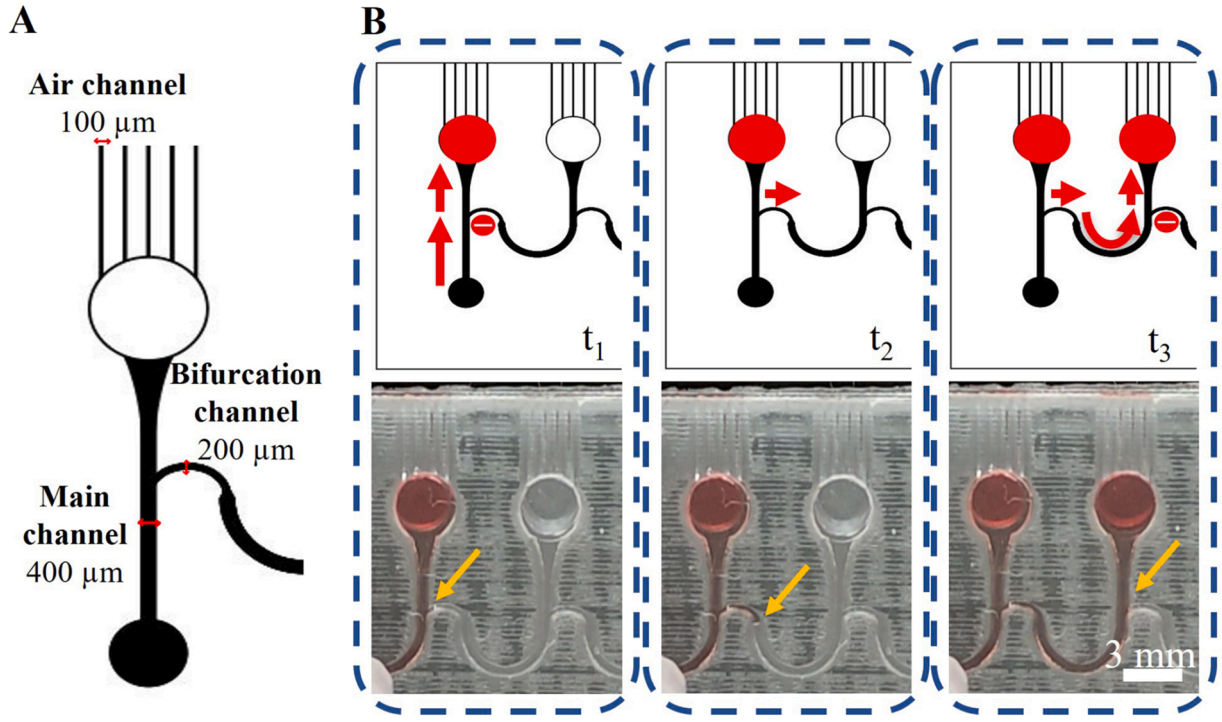

Fig. 5. Chrono-sampling in the microfluidic platform. **(A)** Schematic diagram of the three different channels diameters that were used in order to allow chrono-sampling in the device. **(B)** Working principle of chrono-sampling. As the liquid flowing through the main channel reaches the bifurcation, it will flow towards the reservoir (t_1) since it offers the lower resistance. Only when the reservoir is filled, the liquid inside reaches the necessary pressure to overcome the resistance on the bifurcation channel (t_2), so it flows towards the next reservoir (t_3). The yellow arrow in the real images shows the liquid front.

air channels, so it flowed towards the second reservoir and filled it (Figure 5B, t_3) until overcoming the pressure needed to flow towards the next reservoir. This process was repeated until all the reservoirs were filled. Then, the liquid reached the trench, which acted as a storage reservoir, allowing a continuous flow throughout the whole device during the time the experiment was carried out, avoiding sweat accumulation, and thus, measuring always fresh sweat. The sequential filling of the reservoirs provided an effective chrono-sampling function for independent sweat glucose determinations in each reservoir (see Supplementary Information, SI-2). For a further demonstration of the chrono-sampling principle, see Supplementary Information SI-3.

3.3. Calibration and verification of the biosystem in the microfluidic platform

The alginate/TiO_2 bead biosensor was integrated in the reservoirs of the microfluidic device before closing them with the PSA top layer. The control bead placed in the first reservoir was used as a color control to standardize the measurements of the colorimetric analysis. The other four reservoirs contained the enzymatic mix and were replicas of each concentration. Each glucose concentration was calibrated in a different device, as a proof of concept, at room temperature and under the same light conditions.

The measurements of the beads in the reservoirs were done taking time 0 min as the time at which sweat started entering the well, since it was then when the enzymatic reaction starts. The observed filling times were 361 ± 12 s for each of the reservoirs, with a delay between them of 20 ± 2 s, and measured times for each well were 16.0, 22.5, 29.0, 35.5 and 42.0 min, from the moment the device started the filling process.

The calibration in the microfluidic device was done with glucose solutions of 10, 60, 100, 250, 500 and 1000 µM in artificial sweat, as shown in Fig. 6A. The obtained calibration curve (Fig. 6B) is described by the Eq. (2), with an R^2 of 0.996. Unlike the calibration in plate, the calibration curve in the device was done at 16 min due to the delay in the filling of the reservoirs, which was found to be 6 min. The beads in the device were analyzed at 16 min from the beginning of the filling of each reservoir, at the same time to study the precision of the measurement.

$$y=0{\cdot}1x+36 \quad (2)$$

The LOD and LOQ were calculated as explain above (see Section 3.1) and the values obtained were 7.7 and 25.6 µM, respectively. Compared to those values obtained for the calibration of the biosystem in plate, 4.1 and 13.6 µM respectively, we can state that higher LOD and LOQ were obtained in the device. This can be due to a lower volume of sweat needed to cover each bead, since the space for the bead in the device was more reduced than in the plate, which led to a lower amount of glucose available. Nevertheless, similarly to what happened in plate, a lower limit of detection was obtained regarding the values reported in literature on sweat glucose sensing through colorimetric approaches in microfluidic platforms. For example, Xiao, J. *et al.* [19] reported a LOD of 0.03 mM, similarly to that reported by Xiao, G. *et al.* [20], who obtained a LOD of 35 µM using the same enzymatic reaction that the biosystem developed in this research. Although lower LOD and LOQ can be obtained with electrochemical detection approaches [21,22], colorimetric detection offers easy-to-read and easy-to-use systems.

The verification of the biosystem for chrono-sampling in device was also performed. The obtained values were 45 ± 12 µM, 197 ± 25 µM and 631 ± 49 µM, for the samples of 50, 150 and 600 µM, respectively. Likewise, with the calibration in plate (see Section 3.1), the precision and accuracy of the measured values were discussed. Considering the deviation of the measured value, more precise measures were obtained at higher glucose levels compared to the precision of the measurement at lower glucose concentrations, with a precision of 92.2% and 73.4%, respectively. Moreover, the highest accuracy (95.0%) was achieved at higher glucose concentrations. These results demonstrate the potential to further develop this chrono-sampling platform and its implementation in wearable technology towards a tailored-oriented training of

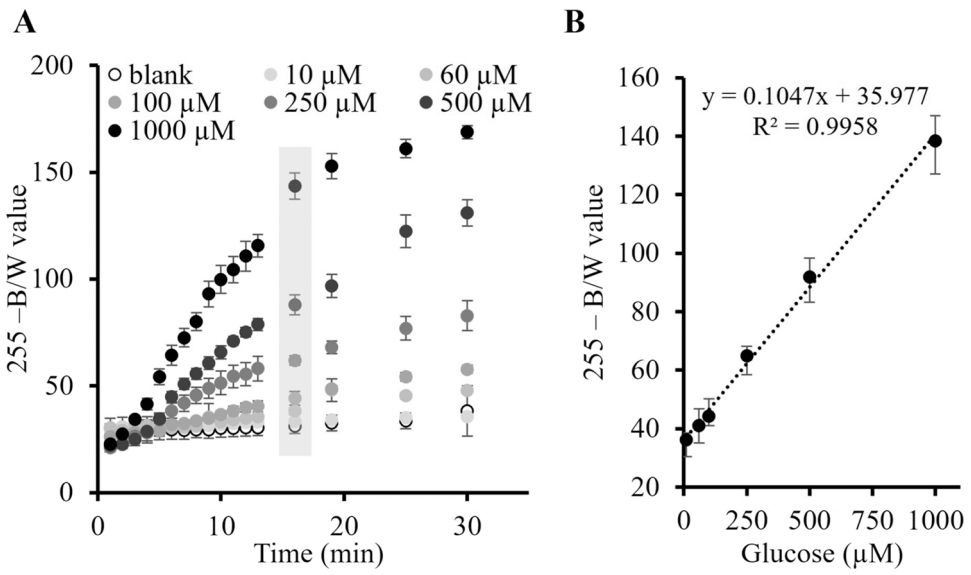

Fig. 6. Calibration of glucose in alginate/TiO_2 beads in artificial sweat in the chrono-sampling microfluidic platform. **(A)** B/W values of glucose 10 – 1000 µM at different times for 30 min (n = 4). The shadowed values correspond to those at time 16 min **(B)** Calibration curve of the alginate/TiO_2 beads at time 16 min using the B/W values (n = 4).

athletes.

4. Conclusions

Since sweat composition changes between individuals, there is a difficulty for sweat sensing standardization towards diagnostic medicine. However, contrary to what it may seem, sweat sensing postulates as a powerful tool as a tracking biofluid for each individual in sports medicine, since the training can be tailored to each athlete based on her/his own biomarker levels. It demonstrates its potential to tailor training exercises according to the necessities of each athlete, in order to increase their performance and avoid injuries.

Moreover, the capacity of continuously measuring sweat biomarkers in athletes while exercising is crucial for ensuring an efficient training routine to enhance their performance, as well as to prevent injuries. In this regard, we have developed a microfluidic platform for chrono-sampling of sweat glucose within the physiological range 10 – 1000 µM. Specifically, glucose levels at time 16.0, 22.5, 29.0, 35.5 and 42.0 min were measured in each device, which provided an advantage over other microfluidic devices that only allow single measurements. The sequential measurements of the different beads were done in independent reservoirs, and no cross-contamination between adjacent reservoirs was observed.

Fast detection times were achieved due to the integration of TiO_2 nanotubes within the alginate sensing scaffold. Due to the super-hydrophilicity of this material [19], detection times of 5 min in plate and 16 min in device were achieved, opening the possibility to further develop this technology as a tracking device for sweat glucose sensing. The higher detection time obtained in the chrono-sampling platform was due to the filling time of the reservoirs.

This research opens the possibility of continuous monitoring the performance of athletes, providing a personalized health tracking method. Moreover, the measuring times could be adapted to the duration and type of exercise by modifying the microfluidic platform, as well as integrated with a biosensor for other metabolites apart from glucose. In the near future, more research with real sweat samples will be done stating the high potential of this novel biosensing material, with the interest of developing a marketable microfluidic platform.

CRediT authorship contribution statement

Sandra Garcia-Rey: Conceptualization; Methodology; Validation; Formal analysis; Investigation; Writing – original draft; Writing – review & editing. **Eva Gil-Hernandez;** Validation; Investigation. **Udara Bimendra Gunatilake:** Methodology; Investigation. **Lourdes Basabe-Desmonts:** Conceptualization; Methodology; Writing – review & editing; Visualization; Supervision; Funding acquisition. **Fernando Benito-Lopez:** Conceptualization; Methodology; Formal analysis; Investigation; Resources; Data curation; Writing – review & editing; Visualization; Supervision; Project administration; Funding acquisition.

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.

Data availability

Data will be made available on request.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.snb.2023.133514.

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