## A Soft, Wearable Microfluidic Device For The Capture, Storage, And Colorimetric Sensing Of Sweat

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## Background

- As a representative biofluid, sweat is of particular interest owing to its relative ease of non-invasive collection and its rich content of important biomarkers including electrolytes, small molecules, and proteins.
- Despite the importance of sweat analysis in biomedicine, interpreting information from sweat can be difficult due to uncertainties in its relationship with other biofluids, such as interstitial fluid and blood, and due to the lack of biomedical appliances for direct sampling and detection of multiple biomarkers without evaporation.
- Existing systems for whole-body sweat collection have been confined to the laboratory, where standard chemical analysis technologies can reveal the composition of collected samples. Recent attempts to detect and collect sweat simultaneously involve direct contact with sensors on the skin (for example, temporary tattoo) where fabric or paper substrates accumulate sweat for electrochemical and/or optical assessment.
- Colorimetric responses in functionalized porous substrates can yield chemical information, such as the pH of sweat, and further enable simple quantitative assays using devices capable of capturing high-quality digital images, such as smartphones.
- Radio frequency identification systems, which can be integrated on top of porous materials for wireless information transfer, provide additional functionality.
- These and related technologies can quantify sweat generation rate, but because the sweat gland density and overall areas are typically unknown, the total
  sweat rate and volumetric loss cannot be determined accurately. In addition, the most widely explored formats do not simultaneously reveal the
  concentration of multiple chemical components, nor do they offer full compatibility with the growing availability of soft, skin-mounted electronics,
  physical sensors, radio technologies, and energy storage devices.

## Introduction

- In this report a type of thin and soft, closed microfluidic system that can directly and reliably harvest sweat from pores on the surface of the skin is reported.
- The device routes this sweat to different channels and reservoirs for multiparametric sensing of markers of interest, with options for wireless interfaces to external devices for image capture and analysis.
- This type of microfluidic technology builds substantially on epidermal electronic, photonic, and optoelectronic systems through the addition of fluid handling and capture, and biochemical analytical capabilities.
- The devices can be mounted at multiple locations on the body without chemical or physical irritation by use of biocompatible adhesives and soft device mechanics, including flexible and stretchable properties, and watertight interfaces.
- These devices measure total sweat loss, pH, lactate, chloride, and glucose concentrations by colorimetric detection using wireless data transmission.
- Tests included two human trials: a controlled, indoor, mild sweat- inducing study, and a "real-world," outdoor-use study conducted during a long-distance bicycling race.

Fabrication procedures of the epidermal microfluidic device using soft lithography.



### Results



# (E) FEA results of stress distribution associated with devices on phantom skin (PDMS) and respective optical images under various mechanical distortions: stretching at 30%strain, bending with 5 cm radius, and twisting.

## Soft epidermal microfluidic device for sweat monitoring

Schematic illustrations, optical images, and theoretical stress modeling of an epidermal microfluidic biosensor integrated with flexible electronics for sweat monitoring. (A) Schematic illustration of an epidermal microfluidic sweat monitoring device and an enlarged image of the integrated near-field communication (NFC) system (inset). (B) Illustration of the top, middle, and back sides of the device. The reference color (white and black) markers are on the top side, along with the NFC electronics. The microfluidic channels with colorimetric assay reagents (water, lactate, chloride, glucose, and pH) are in the middle. The bottom side consists of a uniform layer of adhesive bonded to the bottom surfaces of the PDMS-enclosed microchannels, with openings that define sweat access and inlets that connect to these channels. (C) Cross-sectional diagrams of the cuts defined by the dashed lines (a) and (b) shown in the top side illustration in (B). (D) Optical image of a fabricated device mounted on the forearm.





## Optimizing the design of the epidermal microfluidic device

of key design features and Analysis demonstration of epidermal microfluidic devices. (A) Sketch of the channel geometry for numerical calculation. The blue and red dashed boxes highlight the dimensions of the serpentine and outlet channels, respectively. (B) Experimentally determined water vapor loss from a microfluidic channel as a function of width (w) and length (L) of the outlet channel with a fixed height of 300 mm. Inner pressure as a function of the outlet channel width was also determined from the model (red line). The orange shading highlights the optimal channel geometry. Data are presented as the average value, and error bars represent SD (n = 3). (C) Model prediction of the change in volume of the serpentine channel as a function of AR [ratio of width a to height h of the serpentine channel in (A), blue dashed box] under various pressures (DP = 100, 200, and 400Pa). DP represents pressure difference between the inside and outside of the serpentine channel. Dotted vertical lines show two representative ARs (10:3 and 5:1). (D) Picture of a fabricated epidermal microfluidic structure corresponding to the theoretical results and cross-sectional scanning electron microscopy (SEM) images of the outlet (red dashed box) and serpentine (blue dashed box) channels



(E) Experimental setup of the artificial sweat pore system. (F) SEM images of the polyimide (PI) membrane mimicking human sweat glands. (G) Demonstration of hydrodynamic fluid flow through the microfluidic device using the artificial sweat pore system at the rate of 5.5 µl/hour.



**Quantitative colorimetric analysis of markers in sweat.** (A) Colorimetric detection reservoirs that enable determination of (B) total water (sweat) loss and concentrations of (C) lactate, (D) glucose, (E) creatinine, (F) pH, and (G) chloride ions in sweat. (B to G) Corresponding quantitative analysis conducted by (i) ultraviolet (UV)-visible spectroscopy and (ii) optical images as a function of analyte concentration. The presented color for (i) each spectrum corresponds to (ii) the color exhibited at the detection reservoir in the device. The insets in the spectra provide calibration curves for each of the analytes. The inset in (E) shows the response over a reduced range of concentrations.



**NFC interface to a smartphone and image processing approaches**. (A) Pictures demonstrating NFC between a sweat monitoring device and a smartphone to launch software for image capture and analysis. (B) Images of the epidermal microfluidic biosensor (left) before and (right) after injecting artificial sweat. (C) Location tracking of sweat accumulation with polar coordinates and their relationship to total captured volume of sweat (inset). (D) Standard calibration curves between normalized %RGB value and concentration of markers for quantitative analysis (n = 3, error bars represent the SD). Each vertical colored bar represents the marker concentration determined from the corresponding reservoirs in the right image of (B) as an example.



Human trials of sweat monitoring devices in a temperature- and humidity-controlled room ( $35^{\circ}C$  at 50% relative humidity). (A) Images of two device designs used for the studies. The brown color corresponds to the adhesive layer on the back sides of the devices, with small and large harvesting areas (inlets). Absorbing pads served as reference controls. (B) Illustration indicating locations of sweat patches on the subjects (volar forearm and lower back). (C) Images of two different types of sweat patches (small and large harvesting areas) applied to the lower back and volar forearm collected at various times during the study. (D) Sweat rate determined at the lower back and volar forearm. Bars represent mean of n = 8; error bars represent SD. \*P < 0.05, two-tailed t test. (E) Correlation of sweat rate between the epidermal microfluidic devices and the reference-absorbing pads (n = 7). (F) Marker concentrations in sweat obtained by image processing of data from the device (unshaded) versus laboratory-based analysis of sweat collected from absorbing pads (shaded) (n = 7). \*P < 0.05, two-tailed t test.



Human trials of sweat monitoring devices on cyclists competing in an outdoor race. (A) Illustration of locations of devices on the cycling subjects (volar forearm and lower back). (B) Histogram of the age distribution of the subjects. (C) Temperature and humidity during the race. (D) Elevation profile of the course. (E) Devices on the volar forearms of several subjects, imaged after ~84 km of cycling (that is, middle point of total race). (The purple ink in the lower part of the image on the right is from a marking formed on the skin using a pen before application of the device.)

## Discussion

- The epidermal microfluidic devices introduced here represent versatile platforms for evaluating athletic performance and monitoring health and disease status.
- The reported embodiments can detect sweat volume and rate, as well as several key markers including glucose, creatinine, lactate, chloride, and pH.
- The systems under discussion are unique in their use of fully integrated, soft microfluidics consisting of a network of functionalized channels and reservoirs for sweat capture, routing, and storage with spatially separated regions for analysis.
- By exploiting advanced concepts in microfluidic total analysis systems and lab-on-a-chip technologies and by integrating skin-conformal electronics, our devices have the potential to provide further quantitative modes of use beyond opportunities afforded by the embodiments reported here or by other approaches.
- Future opportunities could explore the use of these technologies for real-time, in situ sweat analysis and as storage vehicles for ex situ laboratory evaluation.
- The limitations of the current devices are primarily in the range of chemical reagents that are available for accurate colorimetric analysis of markers at relevant ranges of concentration.
- Potential exists for extending colorimetric schemes to include enzymatic reactions or chromogens aimed at a broad range of possible applications for specific clinical diagnosis or for illicit drug use detection.
- In addition to their use in sweat monitoring, similar systems can be used as direct capture and storage vehicles for subsequent colorimetric or conventional laboratory-based analysis for various accumulated biofluids such as tears, saliva, or discharges from wounds, especially for small sample volume collection

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