APPLIED SCIENCES AND ENGINEERING

# Skin-interfaced systems for sweat collection and analytics

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**Recent interdisciplinary advances in materials, mechanics, and microsystem designs for biocompatible electronics, soft microfluidics, and electrochemical biosensors establish the foundations for emerging classes of thin, skin-interfaced platforms capable of capturing, storing, and performing quantitative, spatiotemporal measurements of sweat chemistry, instantaneous local sweat rate, and total sweat loss. This review summarizes scientific and technical progress in this area and highlights the implications in real time and ambulatory modes of deployment during physical activities across a broad range of contexts in clinical health, physiology research, fitness/wellness, and athletic performance.**

## INTRODUCTION

The human eccrine system consists of a collection of glands that excrete sweat to the surface of the skin under control of the sympathetic nervous system. The result helps to provide for thermal homeostasis across a range of environmental and physiological conditions (*1*–*4*). The rich composition of solutes and metabolites in sweat and the relative ease with which it can be noninvasively collected upon excretion from pores in the skin make this class of biofluid highly attractive for diverse applications in ambulatory health diagnostics, sports performance, and monitoring (*5*–*8*). For example, sweat chloride tests are used to diagnose cystic fibrosis (CF) in newborns (*9*), and knowledge of sweat sodium and chloride loss is important in determining fluid intake strategies and in maintaining proper hydration levels and electrolyte balance in athletes (*10*–*12*). Excessive loss of sodium in sweat has been shown to increase risk for hyponatremia (*13*). A noninvasive measure of blood glucose concentration through analysis of sweat could have utility in screening in the context of diabetes in clinical applications (*14*) or energy availability in sports (*15*–*17*). The concentration of blood lactate is an indicator of high physical exertion and represents a key biomarker for pressure ischemia and tissue hypoxia (*18*–*20*). Likewise, uric acid and creatinine levels in sweat could provide insight into kidney disease (*21*, *22*), and changes in sweat pH levels could increase in response to metabolic alkalosis (*23*). In addition to the established framework for analyzing sweat chemistry and composition, localized sweat rate and local loss of sweat are indicators of hyperhidrosis and hypohidrosis and often serve as a basis for evaluating autonomic regulation disorders and stroke (*24*, *25*).

In situ, quantitative analysis of sweat for these and other purposes currently relies on extraction using disposable gauzes, absorbent pads, Parafilm-M pouches, and/or arm bags/gloves (*26*–*32*) and on subsequent insertion into benchtop equipment for liquid chromatography, chloridometry, mass spectrometry, infrared absorption, flame photometry, atomic absorption spectroscopy, electrochemical measurement, nuclear magnetic resonance spectroscopy, or other types of analysis. Additional techniques include gravimetry, infrared gas analysis, and the ventilated sweat capsule for determination of local sweat rate (*20*, *33*–*39*). Although such approaches offer powerful capabilities, the size, weight, capital costs, and complex user interfaces associated with the necessary infrastructure for sample collection, manipulation, storage, and metrology frustrate adoption beyond specialized facilities. Currently, detailed analysis of sweat occurs mostly in hospital or laboratory settings for narrow classes of disease states and for athletes (*6*, *9*, *21*, *24*, *35*, *40*, *41*). These circumstances create clear needs for wearable technologies that can support intimate interfaces to the skin as a means to provide similar capabilities but without the limitations of conventional methods.

Recent advances in active materials, chemical analysis approaches, microsystem designs, and microfabrication/nanofabrication techniques (*42*–*48*) form the basis for unusual, skin-compatible classes of devices that include miniaturized flexible/stretchable electronic systems, wireless communication modules, and electrochemical biosensors. The possibility of coupling such technologies with soft hydrogels and thin, low-modulus microfluidic platforms allows conformal interfaces to the epidermis to facilitate fundamentally differentiated ambulatory modes for sweat extraction, capture, and analysis in real time, outside laboratory environments (*49*–*55*).

This review highlights the underlying, enabling concepts for such systems and summarizes their implementation and demonstrated uses in skin-interfaced multifunctional devices for tracking local sweat loss and for performing continuous physiological monitoring and chemical composition analysis. The results are of direct relevance to clinical medicine, sports, and fitness through the ability to (i) measure key electrolytes and metabolites in sweat using electrochemical and colorimetric assays; (ii) quantify average and instantaneous local sweat rates in real time, with a passive operation that does not rely on externally powered actuators or pumps; (iii) monitor multiple analytes in sweat in a time-sequential manner; and (iv) sense and deliver therapeutic agents transdermally, in a closed-loop fashion. In all cases, physical coupling to the skin provides direct access to sweat, thereby enabling a broad range of operational options, from rapid sweat chemistry analysis to full capture and extraction of sweat and quantification of instantaneous and time-averaged local sweat rates. This review begins with recent advances in flexible electrochemical sensing and epidermal microfluidic (that is, "epifluidic") technologies. The applications that emerge from the convergence of these core technologies appear in the subsequent sections, where the focus is on skin-interfaced epifluidic devices and closed-loop diagnostic/therapeutic systems in physical formats that are thin, lightweight, and ultrasoft to provide

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water-tight, yet physically imperceptible, interfaces to the skin on nearly any region of the body. A concluding section describes future research directions and the potential for commercial adoption.

## FLEXIBLE ELECTROCHEMICAL DEVICES FOR SWEAT ANALYSIS

Platforms that combine electrochemical sensors with conventional or emerging semiconductor device technologies offer attractive capabilities in sweat sensing (*56*, *57*). These systems use flexible printed circuit boards that support the packaged electrodes and associated electronic components. Such devices wrap onto the surface of the skin, where straps, bands, or biomedical adhesives hold them in place. At the skin interface, woven textiles (*58*, *59*) and thin hydrogels of porous chitosan, nafion, or polyvinyl chloride improve mechanical contact with the measurement electrodes to allow continuous monitoring of sweat analytes that emerge from pores in the skin (*46*, *60*, *61*). Although these materials establish coupling to the skin, they do not capture or store the sweat in a controlled fashion, nor do they allow for measurements of sweat rate or total sweat loss (local or global), because the device-skin interface does not form a water-tight seal and the sweat can readily permeate laterally through the hydrogels.

Sensors include amperometric devices for the detection of various metabolites, including glucose (*46*, *61*–*66*), lactate (*46*, *60*, *67*–*69*), and alcohol (*70*, *71*), through enzymatic reactions that generate an electric potential. Ion-selective electrodes (ISEs) serve as the basis of potentiometric means for detecting various electrolytes such as $Na^+$ (*44*–*46*, *50*, *69*, *72*), $K^+$ (*46*), $NH^{4+}$ (*47*), and $Ca^{2+}$ (*73*) and for determining pH (*61*, *69*, *73*–*75*) levels. Alternative strategies based on electrochemical voltammetry provide routes for sensing heavy metal species, such as Zn, Cd, Pb, Cu, and Hg ions (*76*, *77*). In conventional forms, such sensors use bulk electrodes and data acquisition electronics in rigid and planar formats (*44*, *78*) that are poorly suited for skin-integrated, continuous monitoring.

Combining thin sensing electrodes on plastic substrates with integrated electronic components on flexible printed circuit boards bypasses such limitations to allow wearable systems that can bend and adhere onto relevant parts of the body (*46*, *63*, *70*, *73*) without sacrificing signal quality relative to conventional platforms. Javey *et al.* (*46*) recently reported such a system, configured to allow direct lamination onto the skin for continuous measurements of glucose, lactate, sodium, and potassium in sweat (Fig. 1A). Here, a sensor for skin temperature enables compensation for the temperature dependence of the underlying enzymatic reactions. A flexible electrode array that supports this range of functionality (Fig. 1B) connects to an associated electronic module for signal conditioning, processing, and wireless data transmission via Bluetooth protocols (Fig. 1C). The mechanical flexibility allows the system to wrap around the wrist, thereby providing a direct interface with

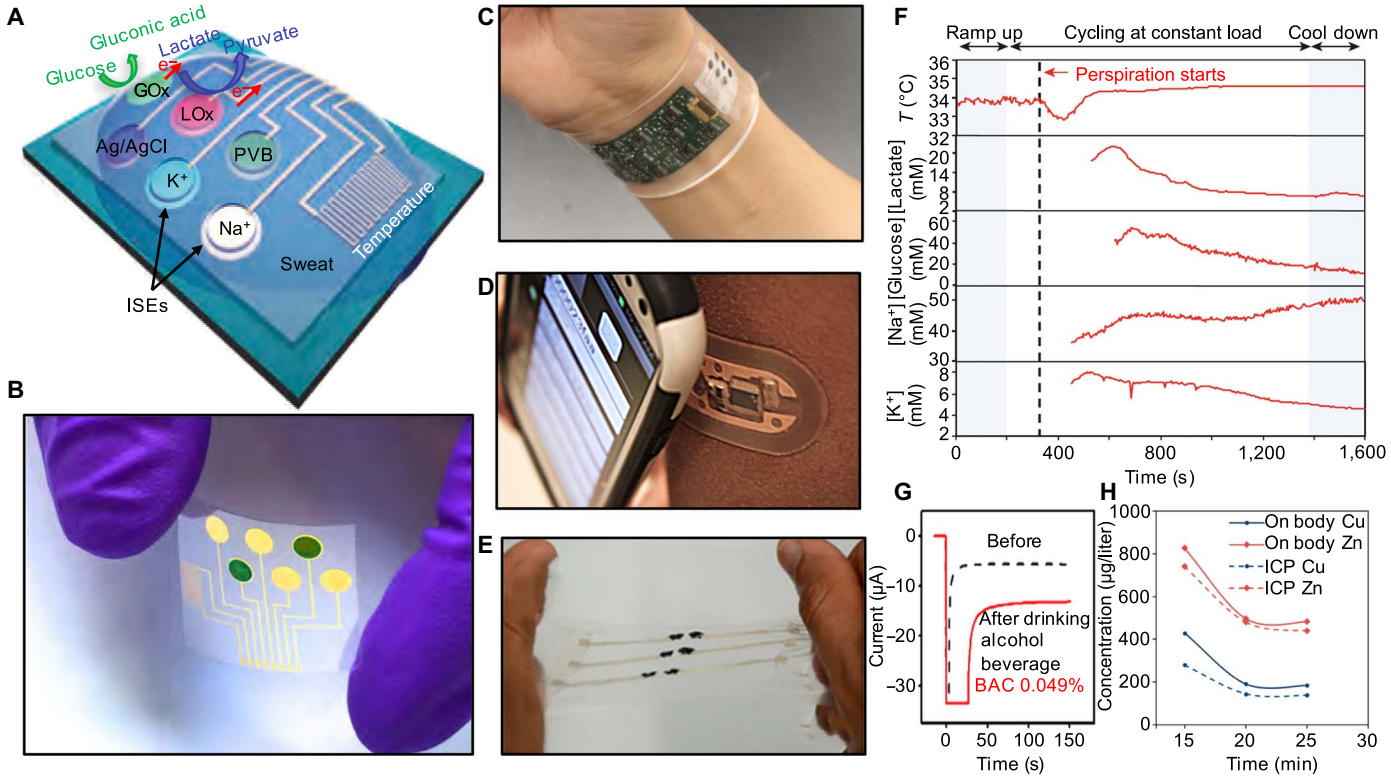


**Fig. 1. Flexible, skin-integrated electrochemical systems for measuring the chemical composition of sweat.** (**A**) Schematic illustration of an array of electrochemical sensors for analyzing the concentration of glucose, lactate, potassium, and sodium in sweat. GOx, glucose oxidase, LOx, lactate oxidase; PVB, polyvinyl butyral. (**B**) Image of a thin, flexible embodiment of the system in (A). (**C**) Wrist-mounted platform that combines the array of sensors in (B) with battery-powered electronics for digital signal acquisition and Bluetooth wireless data transmission. (**D**) Flexible, skin-integrated device for analyzing the concentration of sodium in sweat with a wireless interface to a smartphone based on NFC protocols. (**E**) Image of a stretchable electrochemical sensor under mechanical stress. (**F**) Results from continuous analysis of local sweat glucose, lactate, sodium, and potassium (and skin temperature) with the electrochemical system in (C). (**G**) Alcohol sensing based on a device similar to that in (E) (*70*). BAC, blood alcohol concentration. (**H**) Heavy metal ion sensing with a stripping voltammetric system (platform not shown) (*76*). ICP, inductively coupled plasma (mass spectrometry). Figures were reproduced with permission from Gao *et al.* (*46*) (A to C and F), Rose *et al.* (*45*) (D), Bandodkar *et al.* (*80*) (E), Kim *et al.* (*70*) (G), and Gao *et al.* (*76*) (H).

sweat released from the surface of the skin. Significant reductions in weight, thickness, size, and cost can be achieved through the use of battery-free approaches that exploit near-field communication (NFC) protocols and inductive coupling, enabling attachment and sweat analysis on more body locations. Such systems harvest power through an external device (that is, NFC-enabled smartphone) and transmit data through the same wireless interface. The resulting improvements in form factor enhance the capacity for comfortable, irritation-free integration with the skin (Fig. 1D) (*45*). Together, these wireless sweat-sensing approaches (*45*, *46*, *63*, *69*, *70*, *79*) provide continuous and/or episodic monitoring of changes in sweat metabolites and electrolytes under controlled and ambulatory conditions (Fig. 1, F to H).

A disadvantage of these platforms is that, although they have the ability to flex (that is, they have a low bending stiffness and a robust operation at low bending radii), they cannot stretch (that is, they are not elastic, do not have a low modulus, and do not have the capacity to accommodate large strain deformations), thereby limiting options in integration with parts of the body that present complex contours and/or involve significant deformations of the skin during natural motions. The mismatch between the nonstretchable mechanics of the devices and the intrinsically stretchable mechanics of the skin also leads to interface stresses that can drive delamination, especially during vigorous exercise. Existing efforts to render electrochemical sensors in elastic forms focus on the development of stretchable functional materials that can be patterned by screen printing onto elastomeric substrates. The device in Fig. 1E (*80*, *81*) represents one example, designed to detect glucose (*66*). Advanced concepts in stretchable, skin-like electronics could also be useful in this context (*82*–*87*).

These electrochemical sensing systems and their hydrogel interfaces to the skin provide versatile capabilities, but they require an array of active electronic components and they do not support microfluidic handling, storage, and localized extraction of discrete, measurable quantities of sweat. Recent advances in materials and device designs enable a broad range of lab-on-a-chip–type microfluidic technologies to be rendered into thin, mechanically soft formats for robust, water-tight integration with the surface of the skin. Specifically, these "epidermal" microfluidic systems (herein referred to as "epifluidic systems") can capture, route, and store microliter quantities of sweat with sufficient spatiotemporal resolution to characterize not only the local sweat chemistry but also the average and instantaneous sweat rates and total sweat loss from discrete clusters of sweat glands, down to the single-gland level. In contrast to conventional lab-on-chip microfluidic platforms that rely on pumping or capillary action to drive flow, epifluidic systems leverage the body's eccrine system to move fluid into a network of microchannels through valves, mixers, reservoirs, and other components configured for operation. This body-derived mechanism for pumping eliminates the need for batteries, inductive coupling, or other artificial sources of power. In the context of this self-powered mechanism, colorimetric chemical reagents provide an attractive means for quantitative chemical analysis. Collectively, then, these systems can measure sweat loss and sweat rate, and they can capture, route, and store minute quantities of sweat for real-time onboard analysis and/or subsequent laboratory studies, with the ability to mount on nearly any part of the body. The low-modulus, elastic constituent materials and the thin geometries of these devices are critically important aspects of the design because they allow for irritation-free, water-tight, and robust adhesion to the

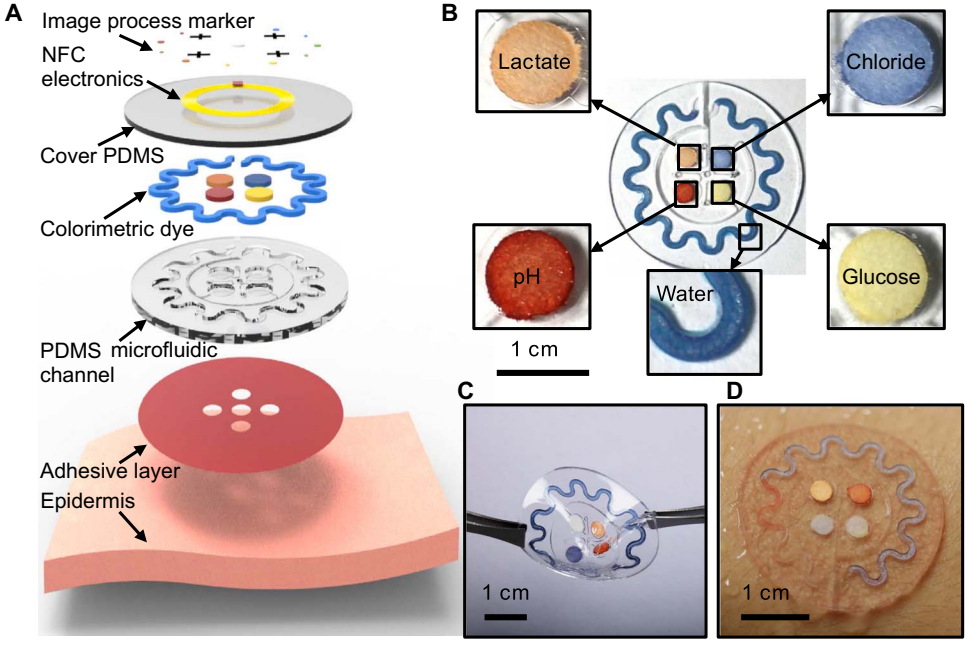


**Fig. 2. Epifluidic devices with integrated wireless electronics and colorimetric chemical reagents for capture, storage, and chemical analysis of sweat.** (**A**) Exploded view schematic illustration of an epifluidic system and its interface with the skin; this device includes microfluidic channels, reservoirs, colorimetric chemical assays, NFC capabilities, and a soft adhesive layer that serves as a water-tight interface to the skin with localized openings that define access of microfluidic inlets to underlying sweat glands. PDMS, polydimethylsiloxane. (**B**) Optical image of a device, with magnified views (insets) of the different regions that provide colorimetric response: a serpentine channel to define sweat rate and total sweat loss (blue; labeled "water"); reservoirs to determine the concentration of lactate, glucose, pH, and chloride ions. (**C**) Optical image of a freestanding device (without electronics) while twisted and stretched to illustrate its low-modulus, elastic mechanical properties. (**D**) Epifluidic system on the skin during sweating, as an illustration of its colorimetric readout for sweat loss, sweat rate, and sweat chemistry. Figures were reproduced with permission from Koh *et al.* (*53*) (A to D).

skin, with options in integration of emerging classes of stretchable electronic components for enhanced functionality.

## SOFT, SKIN-MOUNTED MICROFLUIDIC PLATFORMS WITH COLORIMETRIC ASSAYS

The foundational technologies that underpin this type of technology build on work in skin-like bioelectronics and soft encapsulating materials, for intimate, conformal coupling of microsystems with the skin (*84*, *88*–*90*). The properties of the key constituent materials (modulus, ~145 kPa; area mass density, ~70 mg/cm$^2$) and the biocompatible adhesive interfaces minimize the mechanical and thermal loads on the epidermis [modulus, 0.1 MPa (*91*); area mass density, ~133 mg/cm$^2$ (*92*)]. As a direct consequence, epifluidic systems can follow the natural motions of the skin, without discomfort, irritation, or delamination, while providing a water-tight seal (*53*–*55*, *69*, *79*). These findings are consistent with previous studies in epidermal electronics, where experimental and theoretical findings show that reducing the thickness and effective modulus of the systems yields dramatic reductions in interface stresses associated with various modes of deformation across physiologically relevant ranges (*88*).

This unique design facilitates sweat collection from the surface of the skin through naturally occurring pores, from single or multiple locations at nearly any region of the body (Fig. 2A) (*53*). Figure 2B shows a device with integrated microchannels and colorimetric detection zones for biochemical, electrolyte, and metabolite analysis. The thin profile (~700 μm) and soft material properties of this platform accommodate natural motions that follow from strenuous physical activity, including bending, stretching, and twisting (Fig. 2C).

An exploded view schematic illustration highlights multiple circular microreservoirs, each of which contains a colorimetric chemical reagent for analysis of a targeted biomarker. This example includes assays for glucose, lactate, chloride, and pH, with an additional serpentine microchannel for measurement of sweat rate and instantaneous total sweat loss. The enzymatic reactions use lactate dehydrogenase and diaphorase and glucose oxidase for measuring levels of lactate and glucose, respectively. For chloride and pH levels, detection occurs via reactions with dyes [for example, 2,4,6-tris(2-pyridyl)-*s*-triazine]. In all cases, the changes in color

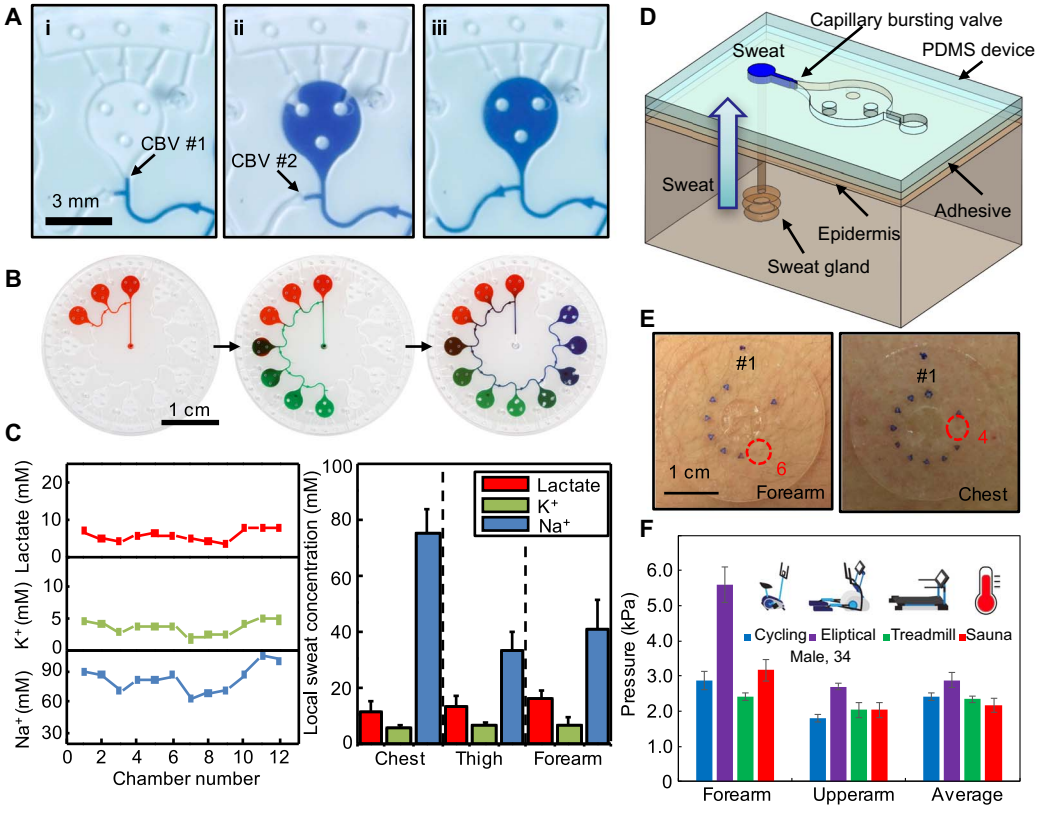


**Fig. 3. Epifluidic systems with CBVs for time-sequential microsampling of sweat and for measuring the surface pressure associated with the action of eccrine sweat glands.** (**A**) Time series images of artificial sweat entering a region of an epifluidic system with three CBVs, an isolated microreservoir, and an interconnecting microchannel, (i) just before entering the microreservoir after passing through CBV #1, (ii) just after filling the microreservoir and before passing through CBV #2, and (iii) just after passing through CBV #2 and moving to the next microreservoir. (**B**) In vitro demonstration of time-sequential microsampling with a device that consists of a circular array of 12 microreservoirs using water dyed with different colors to illustrate the capability for sampling without mixing. (**C**) Concentrations of lactate, potassium, and sodium measured by ex situ analysis of sweat volumes extracted from separate microreservoirs in an epifluidic system mounted on the forearm after a running exercise. (**D**) Schematic drawing of an epifluidic system that contains a collection of CBVs, microchannels, and microreservoirs designed for measuring surface SPSG by eccrine sweat glands. (**E**) Optical images of the colorimetric measurement of surface SPSG from the forearm and chest during exercise, as determined by the maximum bursting pressure among the CBVs that burst during filling. (**F**) Surface SPSG measured under different conditions (cycling, elliptical, treadmill, and thermal exposure in the sauna) and from different regions of the body showing little to no variation in SPSG with the exception of exercise on the elliptical. Exercise duration was limited to 20 min across different exercise conditions, and the relative intensities were not controlled. Figures were reproduced with permission from Choi *et al.* (*54*) (A to C) and Choi *et al.* (*55*) (D to F).

correlate to concentration in an ambulatory mode of use (Fig. 2D). Although, to date, such colorimetric measurements of chloride, glucose, lactate, and pH levels have limitations in accuracy compared to conventional laboratory techniques, they are promising for use in ambulatory exercise settings at a low cost and without requiring capital equipment (*53*), and future advancements can help improve accuracy. Similarly, local sweat volumes and sweat rates can be captured and analyzed in an ambulatory mode using epifluidic devices. Systematic studies establish correlations between the epifluidic sweat rate and chloride measurements and those obtained using standard reference methods based on absorbent pads taped to the skin. The NFC electronics and antenna provide additional functionality in the form of wireless communication with a smartphone for image capture, quantitative color extraction, and data transmission for telemedicine. Similar wireless electronic modules can also include system-on-a-chip modules of biosensors, memory, and power subsystems, thereby expanding the sensing capabilities beyond those summarized here.

These types of devices can support a broad range of components, from valves, pumps, mixers, separation channels, reactors, and reservoirs, some adapted from conventional microfluidic platforms and others specially configured for skin-interfaced applications. As an example, recent studies demonstrate that capillary bursting valves (CBVs) can be used to direct the flow of sweat into microreservoirs in a time-controlled manner (Fig. 3A) (*54*). This mode of "chrono-sampling" of sweat exploits microchannels with low Reynolds numbers (Fig. 3B). Comparative studies show that chrono-sampling of sweat can reveal changes in sweat metabolite/electrolyte concentrations (for example, lactate, $K^+$, and $Na^+$) from several locations on the body as a function of time during exercise (Fig. 3C). This time sequence analysis using a single epifluidic device could provide insight into sweat lactate and electrolyte levels charted over the course of several meals, daily activities, and workouts. Furthermore, with multiple CBVs designed to operate across a range of defined pressures, it is possible to quantitatively measure secretory fluidic pressures generated at the surface of the skin (surface SPSG) associated with the action of eccrine sweat glands (Fig. 3D). Simple colorimetric schemes allow visual detection of bursting of CBVs and, therefore, an immediate readout mechanism for determining the surface SPSG (Fig. 3E). This noninvasive, simple measurement process serves as an attractive alternative to past approaches that use glass capillary needles connected to pressure manometers and interfaced directly to eccrine glands through the sweat ducts. In initial studies of healthy young adults, SPSG measurement using epifluidic devices shows that pressures remain remarkably constant (~2 to 3 kPa) over time and across different exercise routines for a given individual (Fig. 3F).

Epifluidic systems that integrate colorimetric assays with chrono-sampling capabilities and color-responsive temperature gauges provide a useful collection of multimodal analysis capabilities (Fig. 4, A to C). Glucose, lactate, pH, and electrolyte assays leverage existing enzymatic and chemical-based assays. In some instances, the assay for chloride



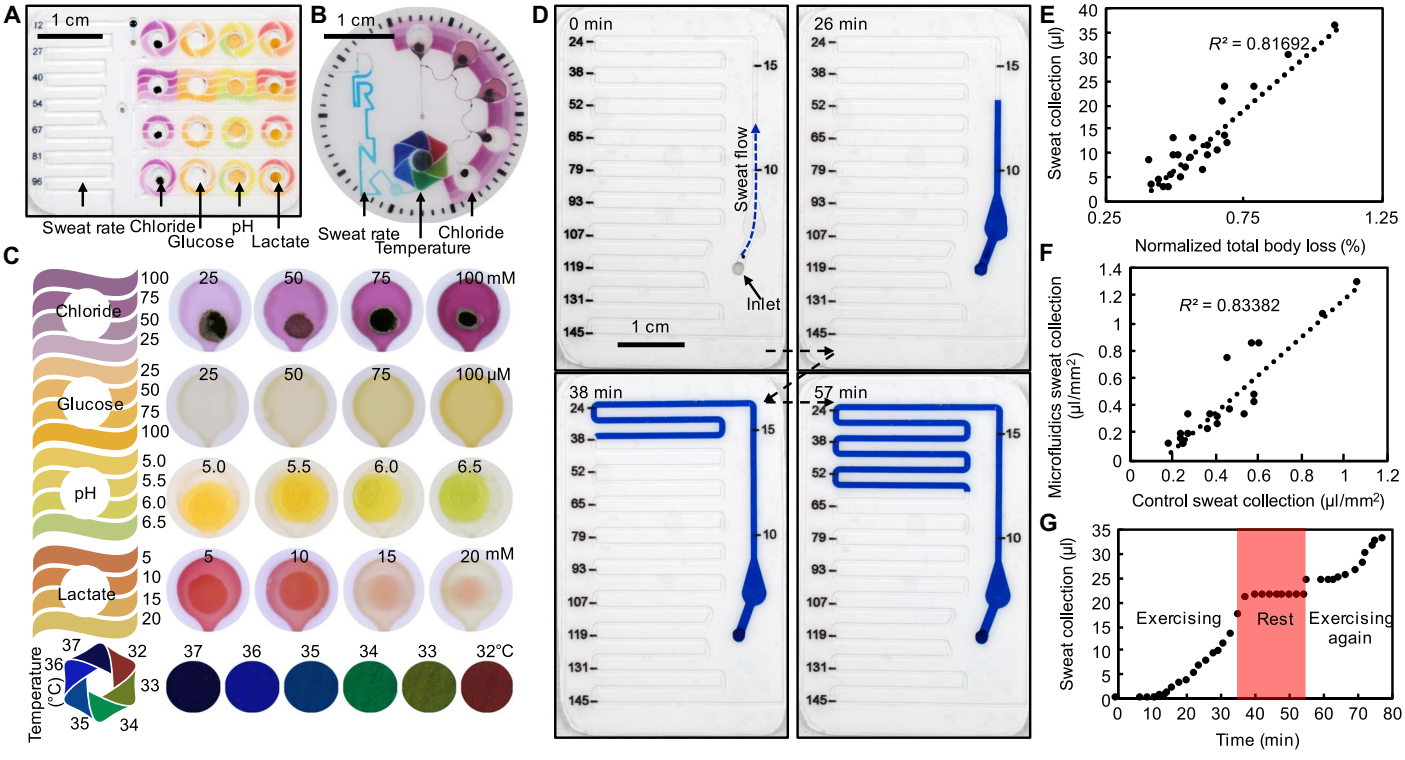


**Fig. 4. Multifunctional, colorimetric epifluidic systems for time-sequential measurements of sweat loss and chemistry.** (**A**) Epifluidic system that includes multiple colorimetric assays integrated with CBVs for analyzing sweat composition and sweat rate in a time-sequential manner. (**B**) Optical image of a related device that also includes liquid crystal sensors for temperature. (**C**) Colorimetric responses and color calibration markers for analysis of sweat biomarkers and skin/sweat temperature. (**D**) Optical image of an epifluidic device spotted with blue dye that mixes with sweat. The extent of blue dye in the channel during sweat provides a measure of total sweat volume at any given instant in time. (**E**) Correlation of sweat collection for an epifluidic device from the anterior forearm versus the normalized total body loss (based on initial weigh-in and final weigh-out with no fluid intake or restroom use during exercise). (**F**) Correlation of sweat collection for an epifluidic device versus an absorbent patch. (**G**) Cumulative local sweat loss versus time measured from the forearm with an epifluidic device during exercise, while at rest, and during a subsequent exercise session.

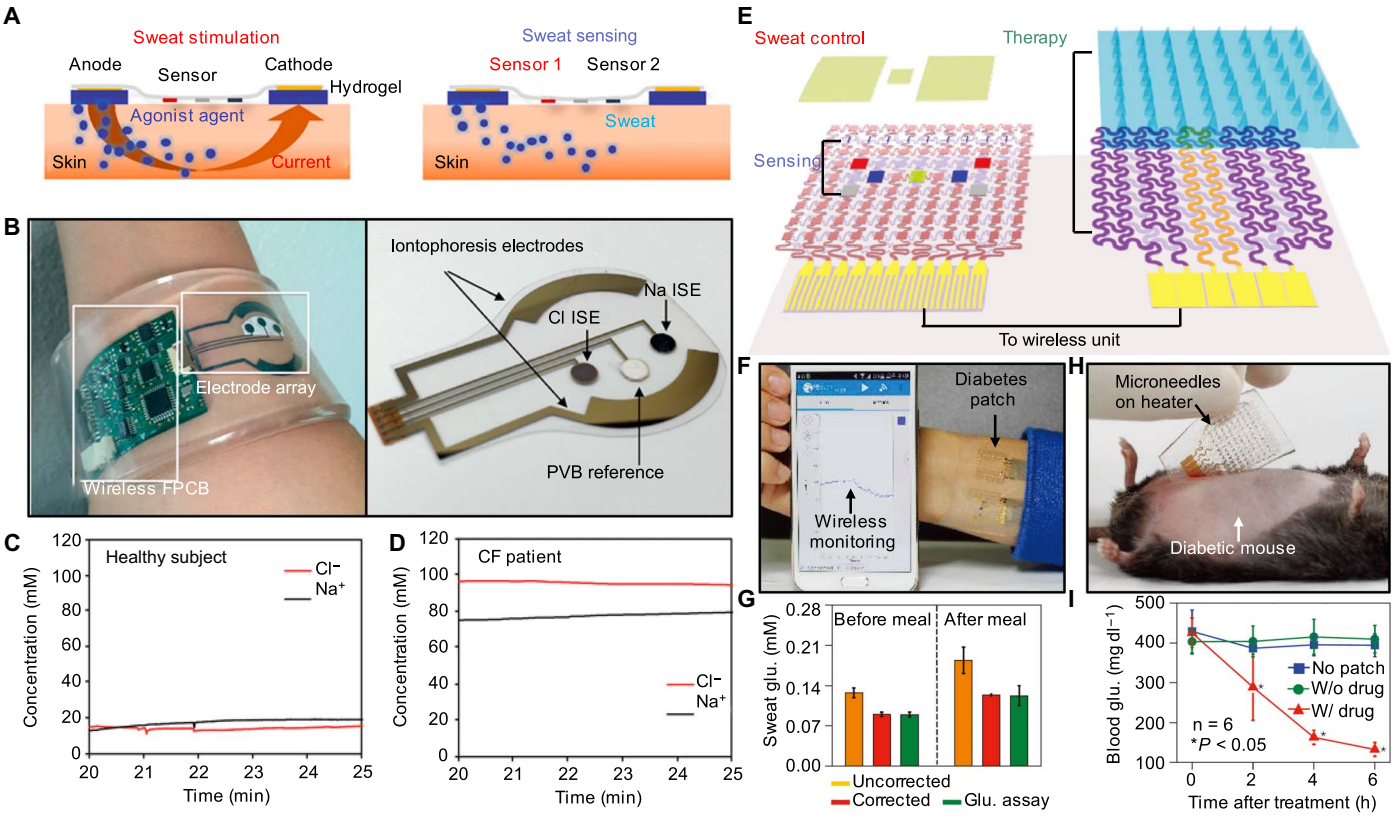


**Fig. 5. Skin-interfaced devices with capabilities for stimulating release of sweat, analyzing sweat chemistry, and delivering pharmacological agents through the surface of the skin.** (**A**) Schematic drawing of strategies for stimulating release of sweat by iontophoresis and for electrochemically analyzing the chemistry of this sweat. (**B**) Optical image of a wearable device with capabilities illustrated in (A), where the sensing involves electrochemical determination of the concentration of chloride and sodium ions (left). Magnified view of electrodes for iontophoresis, chloride, and sodium ISEs and a PVB-coated reference electrode (right). FPCB, flexible printed circuit board. Comparison of concentrations of $Na^+$ and $Cl^-$ in sweat for (**C**) a healthy subject and (**D**) a patient with CF. (**E**) Schematic drawings of a platform for sweat monitoring and pharmacological delivery. (**F**) Optical image of such a system connected to an electrochemical analyzer that is wirelessly controlled with a smartphone. (**G**) Average glucose concentrations before and after correction, accounting for changes in measured pH. (**H**) Optical image of microheaters integrated with microneedles laminated on the skin near the abdomen of a mouse model. (**I**) Blood glucose concentrations associated with mice in a treated group (with drug) and a control group (without the patch and without drug). Figures were reproduced with permission from Emaminejad *et al.* (*63*) (A to D) and Lee *et al.* (*61*) (E to I).

detection requires insertion of hydrogels into the microreservoirs to establish a stable suspension (Fig. 4, A and C) (*93*). For thermal sensing, thermochromic liquid crystals can capture the temperature of both the skin and the sweat (Fig. 4, B and C) (*42*, *94*, *95*).

A key feature of epifluidic systems is the ability to measure sweat rates and losses over targeted, local anatomical regions and to correlate this measure to the total body sweat rate and loss. A simplified device for this purpose is shown in Fig. 4D, where a water-soluble dye inserted near the inlet region colors the sweat to facilitate visual inspection. Comparisons of sweat loss determined using this type of approach from the anterior forearm to the whole-body loss measured by changes in body weight before and after exercise reveal a linear correlation (Fig. 4E). Additional work will help to determine calibration factors to convert the local sweat loss measured using epifluidic systems to total whole-body sweat loss and their dependence on exercise intensity, sex, or other parameters that could influence regional distribution of sweat (*96*, *97*). The local sweat measurement also correlates with evaluation performed via established methods using absorbent pads affixed to the skin (Tegaderm absorbent pad) (Fig. 4F). Because sweat propagation and volume can be tracked through the fluidic channels in real time, the epifluidic systems provide an additional means of measuring instantaneous sweat rates during exercise. Figure 4G shows rates captured at three different intervals in time. During the first session of exercise (labeled "exercising"), there is a constant sweat rate followed by a steady decrease in sweat rate approaching zero sweating when the subject is at rest (labeled "rest"). The instantaneous sweat rate returns to initial levels after a few minutes, once the subject reinitiates physical exertion (labeled "exercising again").

## SYSTEMS WITH CAPABILITIES IN EXTRACTION, ANALYSIS, AND DELIVERY

Techniques that combine pharmacological agents and iontophoresis can trigger the excretion of sweat, thereby allowing its capture without requirements for exercise or exposure to hot, humid environments. Such strategies, performed with traditional hardware, represent the standard clinical procedure in screening for CF (*98*). The associated apparatus, which currently exists in bulk, nonwearable forms (*71*), can be rendered in embodiments similar to those outlined in Fig. 1, as shown in Fig. 5A (*63*, *70*). Figure 5B highlights a wearable device that combines sweat sensing and stimulation. Hydrogels loaded with acetylcholine and iontophoretic electrodes that independently deliver electrical stimulation induce local sweat accumulation (typically, ~1 mA of current for 5 min). The average sodium and chloride levels measured from healthy subjects and CF patients show good agreement with clinical standards

(Fig. 5, C and D) (*99*). Alternative approaches to stimulating sweat release rely on sudomotor axon reflex sweating produced via iontophoresis of a nicotinic agonist using a wearable iontophoretic electrode (*100*). Although these techniques are attractive because they allow spatial separation of the stimulation region from the sensing region, the composition of sweat could be affected by the method of stimulation. Future studies to characterize the effects of iontophoresis compared to passive heating and physical exertion are thus needed.

Extensions in functionality follow from the addition of therapeutic modules for delivering drugs through the skin. Recent work by Son *et al.* (*101*) demonstrates platforms that combine sweat diagnostics and drug delivery. Figure 5E shows an array of sensors and actuators used to monitor glucose levels in sweat to release drugs transcutaneously via microneedles, where demonstrations in animal models illustrate the functionality. The ability to achieve closed-loop diagnostics and therapy on a single platform has important implications for remote health care, particularly when integrated with wireless connections to the Internet via a smartphone (Fig. 5F). In the future, these devices could be used to monitor sweat glucose levels before and after meals (Fig. 5G), as the basis of a prescreening tool for diabetics. In other scenarios, they could be used to deliver metformin as a way to regulate this condition (Fig. 5, H and I).

## CONCLUSIONS

The advances in sweat collection and analytics reported here follow from a convergence of recent progress in flexible/stretchable electronics, electrochemical sensors, and soft microfluidics. The resulting opportunities for investigating sweat in ambulatory modes provide means that were previously feasible only in controlled laboratory settings. The embodiments that now exist in the form of research prototypes can be used to measure local sweat loss, as well as several metabolites and analytes. The potential end applications in clinical medicine, wellness/fitness, and athletic training and competition depend on additional research to determine how measures in sweat relate to those of blood. Future systems that combine soft, skin-like electronics, epifluidics, and multimodal biochemical sensors with capabilities in biophysical monitoring could dramatically expand the functionality. Research in these directions, together with translational engineering efforts, could have significant, positive effects on health care, by reducing costs and improving outcomes, and on athletic performance, by informing nutritional and training strategies.

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