SWEAT BIOSENSING DEVICES FOR HEALTH MONITORING

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While most commercial progress regarding the development of wearable sensors has centered around the smart adaptation of existing mechanical, electrical, and optical methods of measuring the body [1], these sensor modalities are of largely non-specific biometrics that are difficult to interpret outside limited applications.

For example, heart arrhythmias can either be an emergency or harmless, and directly measuring concentrations of biomarkers such as C-reactive protein, Interleukin-6, or B-type natriuretic peptide can provide a more definitive diagnosis of a heart condition. Although developing non-invasive chemical sensing of biomarkers is technologically challenging, these novel devices present the most significant biosensing opportunities, including:

- monitoring chemical agent exposure by measuring the agent permeating through skin—like an internal dosimeter for toxins
- tracking human performance (both cognitive and physical) in real time by measuring biomolecular indicators of stress, resilience, or dehydration
- identifying individuals who have come into contact with chemical or biological agents by measuring specific biological markers secreted by the body, reducing conventional reliance on external measurements based on markers that can be washed away or confounded

Multiple components of the Department of Defense (DoD) have highlighted real-time physiological status monitoring (PSM) as a top-tier priority for their research and development (R&D) and science and technology programs. The Army, Navy, and Air Force have set forth an R&D roadmap for Human Systems that focuses in part on delivering "technology capable of objectively measuring warfighter performance in operational environments," that will enable "real-time monitoring" of critical stressors on warfighters and their resulting physiological status [2]. In order to achieve these R&D goals, researchers must develop simple sensors that may quickly, remotely, and non-invasively perform biomarker measurements.

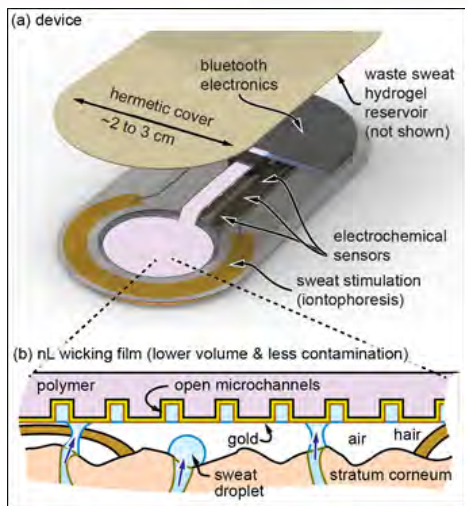

Figure 1. Diagram of an advanced sweat biosensing device, including integrated localized stimulation of sweat (sweat on-demand), advanced wicking materials to work with tiny nanoliter volumes of sweat, and electrochemical sensors to continuously read biomarker concentrations.

Image Credit *Photo Illustration created by HDIAC and adapted from photos by Michele Eaton (U.S. Air Force) and Adobe Stock. (Eaton's photos available for viewing at https://www.wpafb.af.mil/News/Article-Display/Article/818830/bio-sensing-gives-new-meaning-to-breaking-a-sweat/)*

The Air Force Research Laboratory (AFRL) is a notable R&D leader in this space, sponsoring multiple projects seeking to develop skin-wearable biosensing devices. For example, in 2014, AFRL kicked off a multi-year development project in collaboration with the Nano-Bio Manufacturing Consortium to develop a wearable sweat-based biofluid sensor [3]. GE Global Research served as project lead, with industry partner American Semiconductor, Inc., and academic partners Dublin City University, the University of Massachusetts at Amherst, the University of Connecticut, and the University of Arizona. Early prototypes of the patch—which have been tested in the laboratory and in the field—focused on sensing sodium and potassium levels in sweat to continuously monitor hydration levels [4]. The group's ongoing R&D is focused on improving the patch's reliability and stability, as well as extending its shelf life and incorporating additional measurement capabilities, like sweat rate sensing [4].

In 2011, ARFL launched a biochemical monitoring research initiative in collaboration with the University of Cincinnati (UC) to advance the state of the art in biosensing by focusing first on articulating its fundamental challenges. The team investigated the biological mechanisms behind how chemical analytes partition from blood and enter into secreted biofluids like sweat, saliva, or interstitial fluid [5]. For example, it was important to identify early on whether concentrations of the stress biomarker cortisol can be measured in sweat in order to monitor physiological status, similar to how they are used in blood. The team also focused on enabling the controllable secretion of fluids and chemical analytes, while also establishing methods for rapidly and efficiently capturing them in nanoliter-scale volumes for transport to sensors.

The AFRL–UC team developed an open microfluidic platform made out of advanced wicking materials that uses open micro-channels to wick sweat up from the surface of the skin (see Figure 1). These channels cover only 10 percent of the biosensing device's skin-to-sensor surface area, which allows the device to accurately measure analytes using substantially smaller volumes of sweat than previous designs. It also limits contamination of the sweat by dead skin cells—contamination that otherwise would decrease the device's efficiency and ultimate usefulness to the warfighter. AFRL is working with Eccrine Systems, Inc., to test the feasibility of DoD adopting wearable biochemical monitoring on a large scale [6, 7]. As part of AFRL's Tech Warrior 2017 training exercise, Eccrine Systems field-tested a biosensing device capable of continuously tracks and wirelessly reports sweat loss to profile warfighter risk of dehydration [6].

These devices may be used for other applications, the foremost of which is chemical sensing (whether in a continuous and/or repeated modality). It is impossible to imagine modern medicine without the ability to measure the presence, concentration, or functional activity of analytes in biofluids, such as blood and urine. Commercially, however, it is not yet possible to do the same in a continuous and wearable format for any analyte other than glucose. To close the gap, Eccrine Systems is investigating whether cortisol can be monitored in sweat to continuously track levels of stress and recovery.

To further benefit warfighter biosensing applications, two significant areas of future research are investigated. First, expanding capabilities in predictive modeling of analyte partitioning, with a goal of predicting how analyte concentrations change after a physiological event (toxin, injury, fatigue, infection, etc.). The use of predictive modeling is likely to minimize the time needed to develop biosensing technologies and perform on-body validation. Second, investing in new applications, which will invariably require new robust and specific sensors. Combined, these efforts seek to enhance DoD's ability to continuously and accurately monitor the physiological status of its forces in the field.

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