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A stress test for bioelectronics

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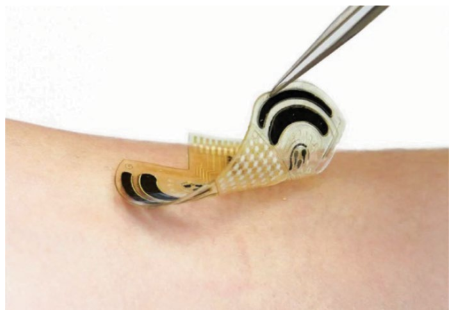
Advances in wearable and ingestible electronics are rapidly expanding the health-monitoring capabilities of bioelectronic devices.

The idea of using an electronic device to track your health and well-being is already an established practice for many. The latest smartwatches – such as the Apple Watch, which had 50 million sales in 2022 alone[1] – can measure temperature and heart rate, check blood oxygen levels and take electrocardiograms. But this is likely just the start of what bioelectronic devices can do in terms of continuous health monitoring and personalized medicine.

For one, such devices can take on a variety of forms, from wearable to implantable to ingestible. Work on devices that can be swallowed – and then provide readings from inside the body – can be traced back to 1957, when an ingestible capsule capable of internal pressure and temperature readings was reported[2]. But it is in the past 25 years or so – and following the introduction of the PillCam capsule endoscope[3] – that research activity in the field has gained a more prominent momentum.

Ingestible electronic devices could be used to track and treat different diseases in the gastrointestinal tract. In recent years, advances have been made at the sensor, circuit and system level, and devices have been created that can measure gastrointestinal gases[4] and biomolecules[5]. In a Review article in this issue of *Nature Electronics*, Yasser Khan and colleagues examine the development of ingestible electronics.

Through their analysis, the researchers – who are based at the University of Southern California and Georgia Institute of Technology – provide a step-by-step guide for the design of ingestible electronic capsules at the system level. They explore the key components and functions of such devices, which include sensors and actuators, integrated circuits, communication, power, packaging, localization and locomotion. They also assess the issues that currently restrict the wider application of the technology.



Optical image of the electronic skin developed by Gao and colleagues, which can be used to monitor responses to stress.

Ingestible electronic devices are typically made of hard, rigid materials. This is also the case with commercial wearable technology. But the potential of flexible and stretchable materials in the design of wearable devices is a focus for the research community, and one that could notably expand the capabilities of such devices. The approach can allow devices to form an intimate contact with the skin and can provide – via sweat sensing – molecular insights into the body. The expanding sophistication of such systems is illustrated elsewhere in this issue of *Nature Electronics*, where Wei Gao and colleagues report a wearable sensor that can monitor and classify stress responses.

The researchers – who are based at the California Institute of Technology, Hong Kong University of Science and Technology, and the University of California, Los Angeles – used a scalable inkjet-printing approach to build an electronic skin that can be worn on the wrist. Containing a microfluidic module and a range of sensors, the device continuously monitors molecular biomarkers in human sweat (such as glucose and sodium ions) as well as various vital signs (such as skin temperature and pulse waveform). It also integrates a miniaturized iontophoresis module that can be used to induce sweat (providing the necessary samples without the need for vigorous exercise).

Gao and colleagues show that the electronic skin can continuously monitor a person's daily activities – from eating and sleeping, to working and exercising – over a period of 24 hours. Moreover, data from the device can classify responses to distinct stressors with high accuracy. Three different physiological and psychological stressors were used (a cold pressor test, a virtual reality challenge and intense exercise), and, with the help of machine learning, the different stressors could be differentiated with an accuracy of 98.0%. They could also quantify psychological stress responses with a confidence level of 98.7%.

As H. Ceren Ates, Cihan Ates and Can Dincer explain in an accompanying News & Views article, the work provides "a foundation for the development of wearable-based stress management technology". They also note that the approach is based on the idea that sympathetic neuron activity and the release of stress hormones leave a unique fingerprint on the measured variables (such as heart rate and sweat metabolites). However, there is currently no database correlating these measurements with stress hormones. Thus, "clinical studies are vital to precisely quantify the complex relationships between physiological parameters and stress".

Notably, Ates and colleagues – who are based at the University of Freiburg and Karlsruhe Institute of Technology – go on to consider how such technology could be used to create future personalized stress management systems. Here though they caution that more than just sensor data are needed to understand stress: insight into a person's subjective experience is also required, and thus self-reported data need to be integrated into any system.

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