Soft electronics go for three-dimensional health monitoring in deep tissue

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Daily health monitoring is a critical aspect of maintaining good health. It provides timely physiological information, allowing individuals to better understand their physical condition and achieve early diagnosis of any potential health issues. The ability to monitor vital signs, such as heart rate, blood pressure, and body temperature, can help identify changes in health status and enable healthcare professionals to devise appropriate interventions. Nursing care activities based on documentation, such as vital signs and activities of daily living monitoring, are critical in identifying a patient's condition and ability to meet their daily needs. Health tracking apps and wearable electronics have made it easier for individuals to proactively participate in this process by recording their own data and sharing it with healthcare providers. However, current commercial electronics encounter hurdles such as weight, portability, and flexibility when being applied on human skin.

Soft electronics, also known as flexible electronics, is a rapidly growing field

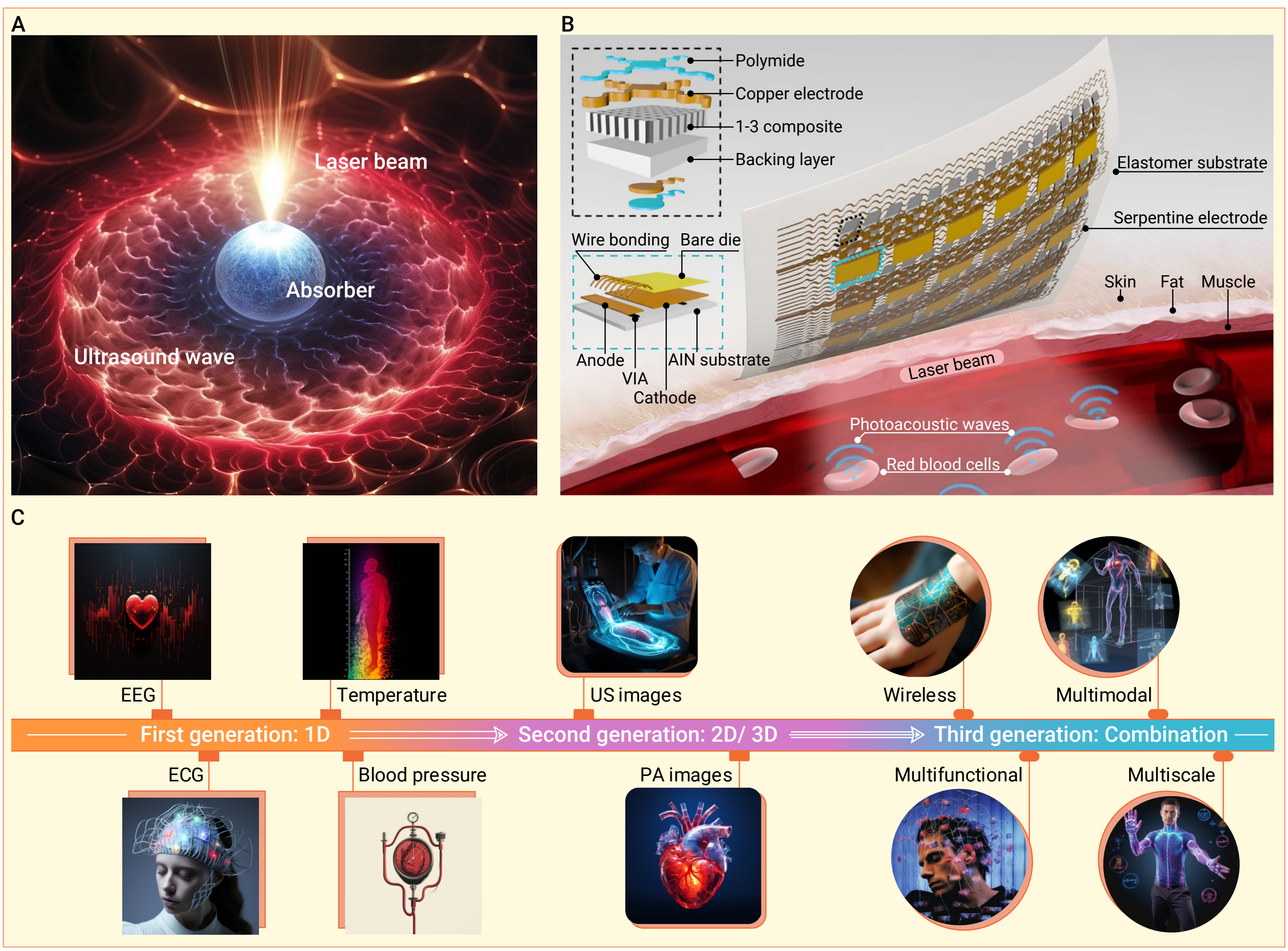

Figure 1. Current photoacoustic soft electronic patch and development of soft electronics (A) Principle of photoacoustic imaging. (B) Design of the photoacoustic soft electronic patch.[4] (C) Development of soft electronic patches for health monitoring.

of research that involves the development of electronic circuits and sensors that can be bent, stretched, folded, and twisted. Along with the development of flexible materials and processing technologies, it has become possible to apply flexible electronics seamlessly to human skin for continuous and comfortable wear and use. This technology has become increasingly popular in health monitoring due to its light weight, sensitivity, etc., which has been widely used to monitor important physiological indications such as heart rate, blood pressure, body temperature, respiration, and exercise. Recently, the commercial development of wearable electronics has been progressing at a rapid pace, showcasing immense potential across various industries. Soft electronics, in particular, are leading a revolution in the realms of wearable technology, healthcare, robotics, and flexible displays. Notably, the global market size of wearable technology is projected to experience a staggering improvement of 300% over the next decades.

The history of soft electronics for health monitoring can be traced back to the early 20th century when researcher began exploring the use of sensors to monitor heart rate and respiration. Since then, there have been significant advancements in the field, which have enabled real-time tracking of physiological signals. There are several important milestones along this journey. A significant breakthrough occurred in 2011. Prof. Rogers's group developed a flexible sensor by photolithography and metallization that matched to the epidermis from thicknesses, effective elastic moduli, bending stiffness, and areal mass density aspects, which can measure electrical activities produced by heart, brain, and skeletal muscles in real time.[1] This development paved the way for the creation of wearable electronics that could be integrated into clothing and accessories, allowing for continuous monitoring of vital signs and other health-related data. In 2014, Prof. Bao's group developed a wearable, flexible, and highly sensitive pressure sensor using micro electromechanical systems (MEMS) that can provide information about cardiovascular health, emotional state, and other aspects of human physiology.[2] In 2020, Prof. Rogers's group proposed a highly integrated electronics system for conformal, high-density, and multimodal sensing and actuation in hearts.[3]

These exciting advancements have built upon the intrinsically flexible nature of soft electronics that can perfectly meet the needs of skin-fitting and easy to operate, which has greatly boosted the convenience of daily health monitoring. The integration of chemical and physical sensors with wearable electronics involves various methods and techniques to ensure seamless functionality and user comfort, such as photolithography, MEMS, metallization, and so on.[1-3] It is not difficult to notice that most soft electronic patches in health monitoring to date are based on one-dimensional sensing information, such as electrocardiography (ECG), electroencephalography (EEG), electromyography (EMG), respiration, blood pressure, blood oxygen, sweat on the skin surface, temperature, pH, etc. If two-dimensional informational (2D) or three-dimensional (3D) information of the target can be profiled through the soft electronic patch, it will extend the broadness and depth of the information, making it clearer, more intuitive, and easier to understand. Also notably, bioinformation yielded by current flexible electronic patches is mostly detected from skin or shallow tissue region beneath the skin; high spatiotemporal resolution probing of deep tissue remains challenging, although it is more closely and directly related with the physiological state of human body than the superficial feedbacks.

Most recently, Gao *et al.* in Prof. Xu's group proposed a photoacoustic platform integrated with flexible and wearable patch that allows for three-dimensional mapping of hemoglobin in deep tissues.[4] The work cleverly marries the merits of absorption contrast of light and deep penetrating capability of ultrasound (Figure 1A). As shown in Figure 1B, on a flexible substrate (total area: 3 cm^2), the platform integrates 24 (4 × 6) interconnected vertical-cavity surface-emitting laser (VCSEL) diodes at wavelength of 850 nm to function as the photoacoustic excitation source, which can emit high-power pulses to penetrate into deep tissue beyond 2 centimeters. The *in-situ* hemoglobin molecules are excited by the laser pulse (although diffused at depths), generating mechanical vibrations and hence ultrasonic waves due to the photothermal effect. The generated ultrasonic waves propagate, with no- or weak scattering, to tissue surface and are received by 240 (15 columns × 16 rows) 2 MHz lead zirconate titanate (PZT) piezoelectric transducers. Note that the ultrasonic transducers are arranged between the vertical-cavity surface-emitting laser columns. The performance of this soft photoacoustic patch is verified through *ex-vivo* and *in-vivo* experiments. For example, this photoacoustic patch can image cysts embedded in a porcine tissue at a depth of 2 cm *ex vivo*. As the amplitude of photoacoustic signals is linear to the medium temperature within a large range, the photoacoustic patch can also be used to measure the local temperature with high spatial resolution and high accuracy in the static blood. This photoacoustic patch is then applied for imaging the three-dimensional veins in the hand, foot, thigh, forearm, and neck in human body, resulting in clear structural images of blood vessels at different locations. The cross-sectional vein information suggests a change with cuff inflation, which is meaningful to timely discover the blood vessels' abnormalities.

Collectively, the captioned work presents an innovative platform for biomolecule monitoring, offering an accurate and efficient strategy to evaluate vessel functions, diagnose vascular diseases, and monitor human physiological status. On the other hand, typical impression of photoacoustic imaging system is usually accompanied with bulky modules such as pulsed laser source and ultrasound receiving transducer or array. Although there is already a miniaturization trend in the field, existing photoacoustic implementations are unlikely suitable for portable or even wearable daily health monitoring. The proposed concept via such a soft electronic photoacoustic patch provides an inspiring strategy for the development of photoacoustic imaging with the further advancement of wireless and wearable electronics.

As seen, bioinformation provided by soft electronics has thus far advanced from one dimension (in a form of signals) to two dimensions and even three dimensions (in a form of images), which may represent a progress trend of the field (Figure 1C). The first generation of soft electronic patches is mainly based on one-dimensional signals, such as electrocardiography, electroencephalography, electromyography, sweat on the skin surface, pH, *etc.* The second generation targets at two-dimensional / three-dimensional images inside deep tissue, such as ultrasound and photoacoustic images,[4,5] which is more intuitive and easier to understand. Within the body, not only two-dimensional figures, like photoacoustic images mentioned above, are important for health monitoring, one-dimensional fluidic information, such as body fluids, blood parameters (total hemoglobin, blood flow and oxygen saturation, etc.), and tissue fluid, and the parameters mentioned in this commentary, are of clinically significance for health monitoring. Thus, the third generation, the one yet to come, may be a combination of the former two generations, providing more comprehensive information of human body. Meanwhile, the next generation will probably evolve into epidermal format, integrating wireless, multiscale, multimodal, and multifunction features for biosignal acquisition, transmission, and processing.

Finally, in order to achieve large-scale production of epidermal electronics, it is essential to develop cost-effective fabrication protocols and enhance the stability of these electronics when operating under diverse conditions. The soft patch can offer not only target images, but also various key physiological parameters, allowing for home-based health monitoring and examination. The potential is bound only by imagination.

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DECLARATION OF INTERESTS

The authors declare no competing interests.