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Flexible sensors for biomedical technology

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Flexible sensing devices have gained a great deal of attention among the scientific community in recent years. The application of flexible sensors spans over several fields, including medicine, industrial automation, robotics, security, and human–machine interfacing. In particular, non-invasive health-monitoring devices are expected to play a key role in the improvement of patient life and in reducing costs associated with clinical and biomedical diagnostic procedures.

Introduction

So far, physiological parameters can be accurately monitored in patients using complex and sophisticated equipment that requires experienced personnel and high costs, limiting the usability to hospital or clinical settings. To overcome these drawbacks, innovative technologies have been recently developed to achieve devices that allow non-invasive, cost-effective and personalized tools for healthcare monitoring. The high performances reached by these devices arise from, among other factors, the ability of the materials and architectures used to conform to the skin, creating an intimate matching with soft and non-planar body surfaces.

In this paper we provide a selected overview of three types of flexible sensors that have been recently applied to biomedical and healthcare purposes through direct application on the human skin: tactile, temperature and biochemical sensors.

Flexible tactile biosensors

Pressure and tactile sensors

Wearable and ultra-conformable devices for non-invasive diagnosis of cardiovascular and cardiac diseases were reported by Bao's group (Fig. 1Aa).[1] These devices consist of a capacitive pressure sensor based on an electrode multilayer followed by a microhairy dielectric layer made of pyramidal-shaped polydimethylsiloxane (PDMS) pillars (Fig. 1Ab). The authors demonstrated the possibility to measure weak signals from the deep-lying internal jugular venous pulses with a high signal-to-noise ratio (SNR) and sensitivity falling in the range 0.55–0.58 kPa^{-1}. Increasing the aspect ratio (AR) of the microhair structures resulted in the amplification of the magnitude of the recorded pulse waveforms, with an ~12 times increase in the SNR observed using AR 10 with respect to flat devices (Fig. 1Ac). This technology promisingly allowed discrimination between a healthy subject and a patient suffering from heart disease according to the waveforms recorded.

The need for less traumatic and easy to implant devices for monitoring physiological parameters has generated a strong research effort towards miniaturized monitoring devices. To this regard, Chen *et al.* developed a wireless, real-time pressure sensing system based on millimeter-scale sensors able to capture human radial pulse waveforms and *in vivo* intracranial pressure (ICP).[2] The mechanically flexible array system contained single sensors as small as 0.1 mm^3, being one and two orders smaller than previously reported research and commercial devices, respectively. The main novelties claimed by the authors were the pressure sensor design, allowing ultra-thin and ultra-small flexible sensors, and the readout scheme that overcomes the low frequency barriers of traditional passive methods.

Another example of a millimeter-sized tactile sensor system was proposed by Nie *et al.*, who described an iontronic microdroplet array (IMA) endowed with capacitive tactile sensing properties.[3] The single sensing elements of the array were made of an ionic liquid nanodroplet sandwiched between two flexible layers containing patterned electrodes. The use of ionic liquids allowed the system to take advantage of the ultrahigh unit-area capacitance established at the interface between the solid electrodes and ionic liquid droplets. Interestingly, a sensitivity of 0.43 nF kPa^{-1} and a minimal detectable pressure of 33 Pa were demonstrated, together with a mechanical response in the range of several milliseconds. The iontronic tactile sensor array was successfully applied to the detection of different surface topologies and the resolution of cardiovascular pressure signals.

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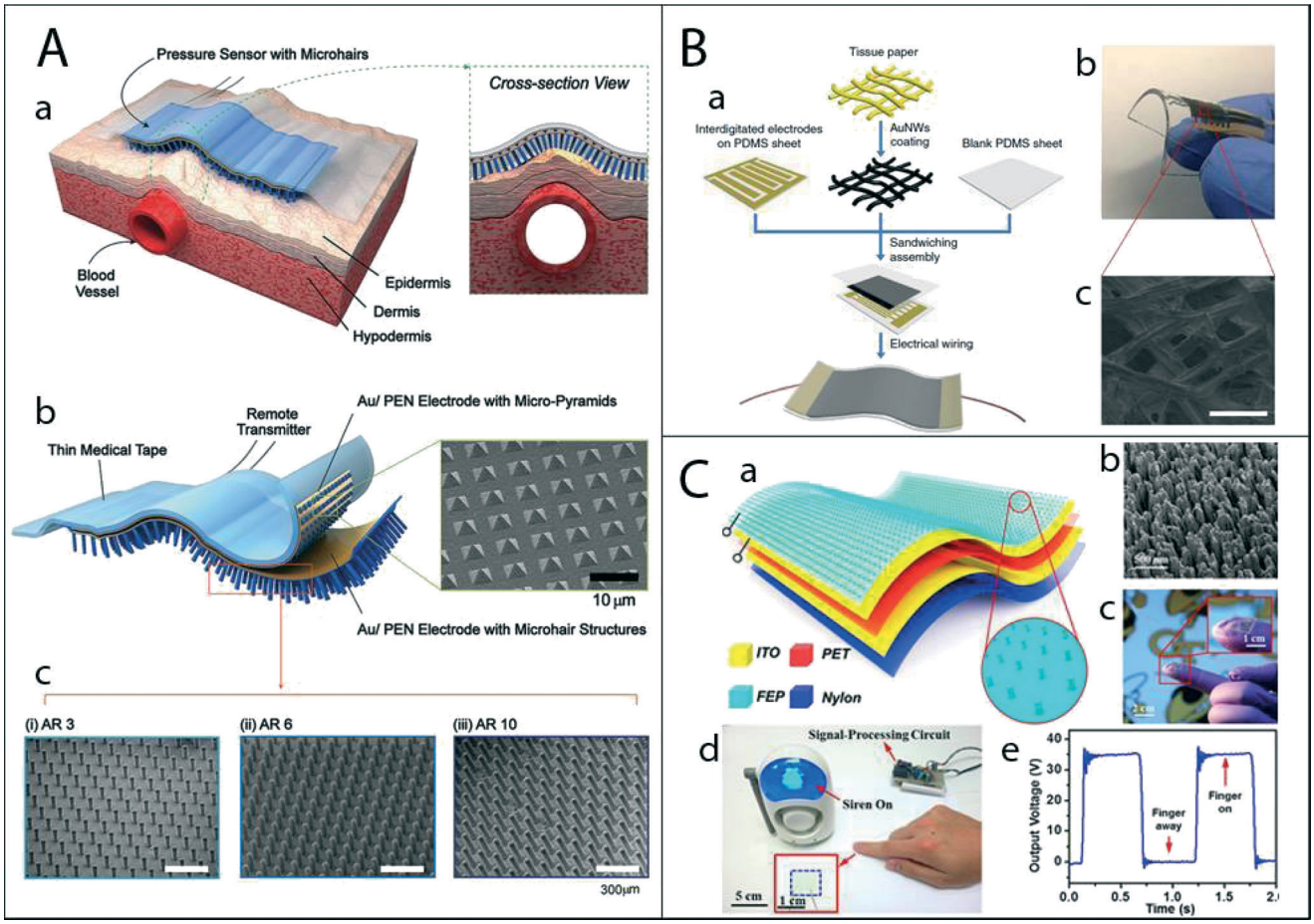


Fig. 1 (A) Highly conformable pulse-detecting pressure sensor based on microhair structures. (a) and (b) Schematic illustration of the sensor, with the pyramid-shaped PDMS dielectric layer placed between two Au electrodes on polyethylene naphthalene (PEN) plastic substrates. (c) SEM images of dense microhair arrays with 30 μm radius and different AR. (B) Pressure sensor based on the AuNWs-coated tissue paper. (a) Schematic illustration of the fabrication of a flexible sensor and (b) photograph showing its bendability. (c) SEM image of the morphology of AuNWs-coated tissue fibers (scale bar, 100 mm). (C) (a) Schematic illustration of the TES with (b) SEM image of polymer nanowires and (c) photograph of an as-fabricated TES. (d) and (e) Complete sensing system based on the TES for practical applications. (d) Triggering a wireless alarm system by gentle finger tapping on a TES (1 cm in side length). (e) Output voltage of the TES generated by finger tapping. Reprinted from ref. 1 (A), ref. 4 (B), ref. 5 (C) with permission.

The combination of nanomaterials and biocompatible elastomers was recently exploited by Gong *et al.* to achieve a highly sensitive and wearable pressure sensor. Gold nanowires (AuNWs) were used as key sensing elements (Fig. 1Ba).[4] The device was based on a AuNW-impregnated tissue paper placed between two thin PDMS sheets where the bottom one was patterned with interdigitated electrode arrays (Fig. 1Bb and c). This AuNW-based pressure sensor could discriminate pressing, bending and twisting forces, and acoustic vibrations. The main advantages of such devices were identified as the scalable fabrication protocol, low energy consumption (<30 μW), high sensitivity (>1.14 kPa^{-1}) and high stability (>50 000 loading–unloading cycles). Biomedical applications were envisaged, like real-time monitoring of blood pulses by application of the sensor on the wrist of a subject.

A self-powered pressure sensing system was developed by Zhu *et al.*, representing an essential breakthrough towards human–machine interfacing and electronic skin.[5] The authors developed a thin-film-based flexible triboelectric sensor (TES) whose operating mechanism was based on a voltage signal generated by contact electrification in response to the physical contact with an external object. The TES consisted of a sandwich structure where a layer of fluorinated ethylene propylene (FEP) acted as an electrification layer (Fig. 1Ca), a functionality provided by vertically aligned polymer nanowires created by plasma dry etching (Fig. 1Cb and c). By integrating the TES with a signal-processing circuit a complete sensing system was obtained (Fig. 1Cd), capable of detecting external excitations (Fig. 1Ce) with exceptional pressure sensitivity in the low pressure region (<0.15 kPa).

Measurement of the elastic modulus of soft biological tissues and organs under various conditions permits assessment of pathophysiological conditions. Conformal and stretchable networks of mechanical actuators and sensors based on nanoribbons of lead zirconate titanate (PZT) were used for spatial mapping of viscoelastic moduli of skin.[6] The authors showed the ability to determine the plasticizing effect induced by a moisturizing and hydrating agent applied

on *ex vivo* skin samples. Other applications of these devices included mapping of pathologies located on various body regions through the analysis of skin with and without lesions, and the *in vivo* evaluation of regional stiffness differences on a skin cancer patient.

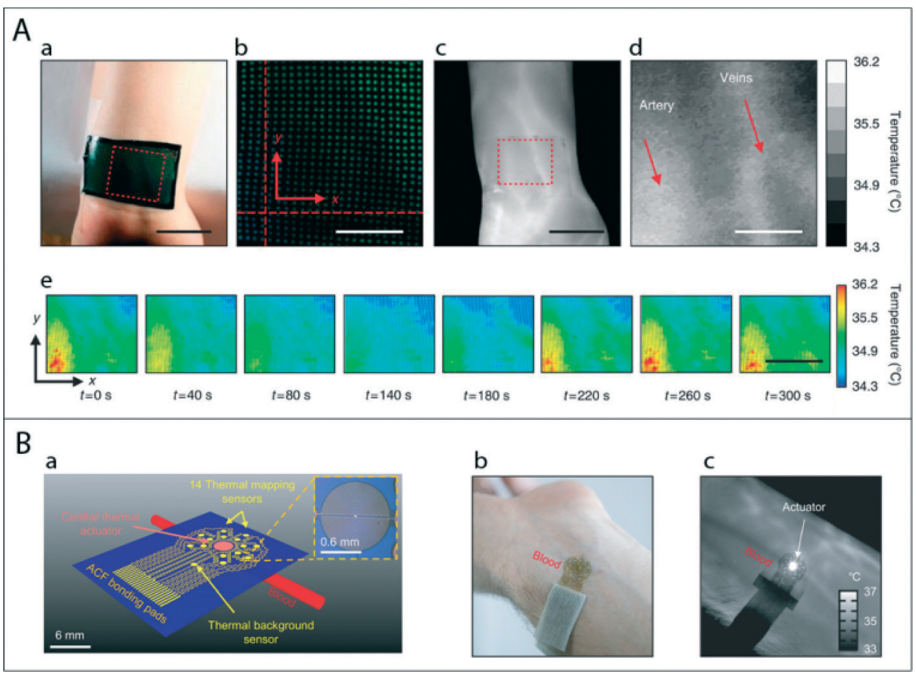
An exciting and innovative field in bioelectronics is the so-called transient electronics field, that deals with biodegradable and stretchable biosensors based on bioresorbable materials that disintegrate in a controlled fashion when exposed to the physiological environment. Among others, Rogers and co-workers have contributed important advances to this area. They reported the application of arrays of stretchable, transient complementary metal–oxide–semiconductor (CMOS) inverters as sensors of pH and electrophysiological (EP) signals.[7] pH sensors showed stable operation at low or near neutral pH when immersed in phosphate buffer solutions for 5 days, while exhibiting a linear decrease in conductance at higher pH (pH 10). The transient electronic materials (Mg and SiO_2) dissolved uniformly without delamination, and with dissolution rates depending on the types and concentrations of ions in solution.

Temperature sensors

The outstanding physical and chemical properties of graphene were recently exploited to achieve a wearable temperature sensor able to monitor in real-time the temperature of human skin.[8] This thermal sensor was based on a composite material consisting of graphene nanowalls (GNWs) vertically standing on a PDMS substrate. The response of the sensor resulted in a dramatic increase in resistance of the GNWs network upon heating over a broad temperature range, originating from the excellent stretchability of the GNWs and large expansion coefficient of PDMS.

A breakthrough in non-invasive mapping of temperature characteristics of human skin was achieved by Rogers' group, in which photonic devices were successfully employed as wearable sensors.[9] Arrays of sub-millimeter pixels made of thermochromic liquid crystals (TLCs) patterned on thin elastomeric substrates were used as sensing elements (Fig. 2Aa and b), with spatial and thermal sensitivities well beyond those required for accurate thermal analysis of the skin. The mechanical properties of the TLC pixels exceeded those of commercially available TLC sheets, with high conformability to the skin as well as small thermal mass and high water permeability of the devices that allow for continuous and long term usage. Assessments related to cardiovascular health (Fig. 2Ac–e) pointed out the potential usefulness of these devices for personalized and easily-accessible clinical analysis.

Techniques based on thermal transport were also used by Rogers' group for epidermal measurement of blood flow as an alternative to existing techniques.[10] Metallic thermal actuators and sensors fabricated on ultrathin and conformable substrates were used to non-invasively monitor the speed and direction of near-surface blood flow of both the macrovasculature and microvasculature of the skin (Fig. 2Ba–c).



Q4 Fig. 2 (A) Use of an e-TLC device in a reactive hyperaemia test. (a) Optical images of an e-TLC device on the wrist during an occlusion test. Scale bar, 3 cm. (b) Magnified view of the device in a. Scale bar, 1 cm. (c) Infrared image of e-TLC device on the wrist. Scale bar, 3 cm. (d) Magnified view of the device in c. Scale bar, 1 cm. (e) Spatial distributions of temperature determined with the e-TLC device at different times during and after occlusion; occlusion starts at t = 0 s and ends at t = 300 s. Scale bar, 2 cm. (B) Epidermal devices for mapping of blood flow. (a) Schematic illustration of the device layout. (b) Photograph and (c) infrared image of a device on the skin over a vein, during application of power to the actuator. Reprinted from ref. 9 (A) and ref. 10 (B), with permission.

Applications of such devices are in clinical and diagnostic settings where diseases, traumas and environmental exposure involve the need for a precise monitoring of changes in the vascular system.

Measurements of the skin temperature can provide complementary information when multifunctional wearable systems are used for diagnosis and therapeutic purposes. An example of a wearable smart device including touch and temperature sensors was demonstrated by Honda *et al.*, who applied a fully printed smart bandage to a male's arm to monitor health.[11] The human-interactive device provided integrated wireless antennas, microelectromechanical systems (MEMS) and sensors, allowing real-time temperature measurements from human skin to discriminate different daily activities (namely, eating and doing exercise).

Non-invasive flexible chemical biosensors

Non-invasive analyses have been receiving significant research interest leading to the development of wearable sensors for *in situ*, rapid, and low-cost detection of biologically and medically important targets. Here, a short description of some of the latest advances reported in the development of biosensors for the diagnosis and possible treatment of patients in real-time are described.

Ultrathin biosensors for the monitoring of metabolites in tears

The use of tear fluids for the determination of metabolites is a relatively new concept, being to date glucose[12–15] and lactate[16] as the most common analytes. Lactate (L-lactate) is an important metabolite with high levels in tears and they are indicative of several diseases such as ischemia, septic shocks, liver diseases, organ failure, stroke and different types of cancer.[16] These facts make tear fluid an appealing matrix for glucose and lactate determination.

B. A. Parviz *et al.* have developed non-invasive and disposable systems that can continuously interface with the human body such as biosensors, radios, and control circuitry in the past years. Firstly, they reported the design and construction of contact lens as lactate and glucose sensors, respectively.[12,13,16] The glucose sensor is based on the immobilization of glucose oxidase (GOD), which is able to recognize and oxidize glucose into gluconic acid and hydrogen peroxide producing an electrochemical signal by its oxidation, on sol–gel film and Nafion. This approach exhibits a fast response, high selectivity and good sensitivity in the range of concentrations of glucose that is found in tears.[12,13] Likewise, the lactate sensor is based on the cross-linkage of lactate oxidase (LOx) which converts lactate into pyruvate and hydrogen peroxide.

Later, the same group developed contact lenses with an integrated telecommunication circuit and sensor for wireless continuous monitoring of glucose in tears with ultra-low power consumption.[16] This lens has obtained good linearity, repeatability and selectivity by the rejection of usual interferences in biological samples. Despite the good responses of the electronic integrated sensors, their implementation in humans is still not reported.

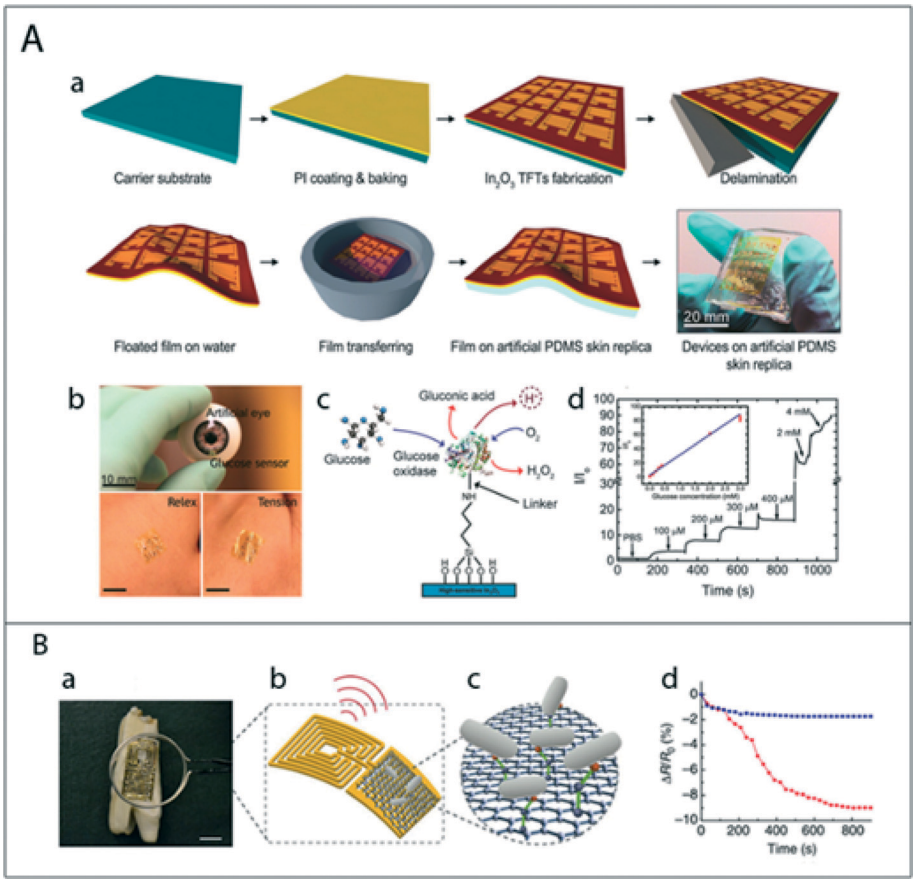
Shleev and co-workers reported a microscale membraneless biofuel cell capable of generating energy using ascorbate and oxygen from human lachrymal liquid as the fuel and oxidant.[14] The bionic contact lens consists of a biocathode modified with AuNPs and bilirubin oxidase (BOx) which reduces oxygen under physiological conditions with direct electron transfer, an anode modified with AuNPs and a tetrathiafulvalene (TTF)–tetracyanoquinodimethane (TCNQ) complex, a glucose biosensor, an interface chip, a display and an antenna. The biofuel cell provides enough electrical power from human basal tears without affecting the glucose concentration, creating a total self-powering glucose sensor. However, the biocompatibility of the biofuel cells still needs to be evaluated before these devices could be ready for human tests.

A simple solution-processing procedure for fabricating ultrathin, sensitive indium oxide (In_2O_3) semiconductor-based FETs as sensors of pH and glucose has been recently described.[15] Fig. 3Aa displays the schematic fabrication of these liquid-gated In_2O_3 FET-based conformal biosensors. These sensors have been successfully adhered to the skin during tension and relaxation states (Fig. 3Ab). The chemical sensing mechanism of the glucose is shown in Fig. 3Ac. The protons generated during the enzymatic oxidation of glucose produce the protonation of the In_2O_3 surfaces varying the current values, as represented in Fig. 3Ad. Therefore, In_2O_3 semiconductor-based FET sensors are potential candidates for further development of simple, affordable, printable, and wearable sensing technologies.

Real-time biosensors for the continuous monitoring of significant metabolites on the skin

Sweat is an acidic, electrolyte-rich fluid whose production is induced by exercise and results in secretion of metabolites including lactate, glucose, uric acid and several electrolytes (Na^+, Cl^-, K^+). Therefore, easy sample collection tools that can be applied for continuous analysis, or those that do not rely on active sample production could result in very useful biosensors, due to the non-invasive nature of sweat analysis. The key limitation is that the sweat production is not easy to control and is also affected by several factors, such as the environment.

One of the first real-time potentiometric biosensors was reported by Rius *et al.*[17] They detected *Staphylococcus aureus* by using a network of single-walled carbon nanotubes (SWCNTs) which act as an ion–electron potentiometric transducer and anti-*S. aureus* aptamers were used as the recognition element. The aptamers were immobilized on the SWCNTs by using two different methods. However, both approaches were able to detect the pathogen with different



Q5 Fig. 3 (A) Liquid-gated In_2O_3 FET-based conformal biosensors. (a) Schematic illustration of the flexible biosensor fabrication procedure. (b) Conceptual images of conformably contacted devices on an artificial eye for glucose sensing in tears are shown. (c) Enzymatic oxidation of D-glucose *via* glucose oxidase to produce gluconic acid and hydrogen peroxide. (d) Representative responses of In_2O_3 sensors to physiologically relevant D-glucose concentrations found in human diabetic tears (lower range) and blood (upper range). (B) (a) Optical image of the graphene wireless sensor biotransferred onto the surface of a tooth. Scale bar is 1 cm. (b) Magnified schematic of the sensing element, illustrating wireless readout. (c) Binding of pathogenic bacteria by peptides self-assembled on the graphene nanotransducer. (d) Change in graphene resistance *versus* time following exposure to ~100 *H. pylori* cells in human saliva (red line). 'Blank' saliva as blue line. Reprinted from ref. 15 (A) and ref. 22 (B) with permission.

sensitivity depending on the aptamer linked content. The detection of *S. aureus* was carried out on a dorsal pig skin where also the selectivity was proven by the presence of other pathogens such as *E. coli*, *S. epidermis* and other microorganisms that could be present in real skin. Despite the sensor showing very satisfactory results on pig skin and its use on human skin not requiring highly trained staff, still it has not been tested on human skin.

Different flexible sensors for monitoring the analysis of ions from sweat have recently been reported by Andrade *et al.*[18,19] Firstly, they proposed a potentiometric K^+ and NH_4^+ sensor made of cotton yarns impregnated with carbon nanotube ink which were partially coated with a suitable polymeric membrane.[18] The sensor was prepared by the combination of screen-printed temporary-transfer tattoo paper with a polymeric membrane selective to ammonium ions. These sensors were tested in volunteers and the satisfactory obtained results showed their ability to sense the change from aerobic to anaerobic exercise which is very attractive for the monitoring of sport performance and healthcare.[19] However, future efforts should be carried out in all these presented skin sensors towards further miniaturization and integration of the electronic interface, data processing, and wireless transmission of the results.

Heikenfeld *et al.* have reported a wearable, medical-grade adhesive radio-frequency identification (RFID)-enabled sensor patch device for the detection of Na^+ and K^+ satisfying the need for developing real wearable sensors controlled by remote systems.[20] The patch is battery-free, powered, and read wirelessly by an Android smartphone and custom-app with all the circuitry solder-reflow integrated on a standard Cu/polyimide flexible-electronic layer which includes an antenna. The potentiometric signals are produced by the difference in potential created across the electrode–ionophore barrier which correlates with Na^+ concentration. The characteristics of these devices were tested for the detection of Na^+ *in vitro* exhibiting a 96% accuracy with a 20–70 mM range by smartphone readout. The wearability of these patches has been stable up to 7 days by using a protective textile. The approach was demonstrated for Na^+ sensing, although using other commercially available ionophores, the sensing of other ions in sweat (Cl^-, K^+, Mg^+, NH_4^+ and Zn^{2+}) is possible.

However, future work still has to be done for the use of these sensors in human skin by increasing their stability.

Park and co-workers reported highly transparent and stretchable electronic devices based on a graphene/silver nanowire (AgNW) hybrid film, which can operate on human skin.[21] The device is a FET sensor with a continuous graphene layer which is monolithically connected through all conductive components. The RLC resonant circuits integrated with FET arrays can work as real-time, wireless sensors for the detection of carbohydrate binding proteins *via* glycolisation of the graphene channel by its non-covalent modification with pyrene-based glyco-conjugates. The graphene FET sensor showed the selective detection of lectins (concanavalin A) and the possible reversibility of the approach. Therefore, this work demonstrated a real-time approach, wireless operation on human skin as a transparent electronic tattoo for applications in wearable electronics.

Nowadays, several wearable sensors in wearable textiles, tattoos and commercial bracelet products have been developed by companies such as Nike or Fitbit. Despite the presented advances in these technologies, the complete wireless sensor which automatically lends itself to maximum time-resolved readings of sweat has not been yet demonstrated.

Mouthguard biosensors for the continuous monitoring of saliva

Saliva, like sweat and tears, is also one of the most useful samples in clinical diagnostics containing a wide variety of biomarkers which are associated with several infections. However, saliva is an extremely viscous fluid which makes its use a challenge for the development of sensing devices. Therefore, up to now, saliva is often collected prior to analysis, limiting its potential for real-time sample analysis.

One interesting work using saliva as a real-time sample is a flexible graphene-based wireless sensor for bacteria detection on tooth enamel.[22] This sensor consists of graphene nanosensors contacted by interdigitated electrodes, which are simultaneously patterned with an inductive coil antenna. Due to the water soluble substrates employed, the graphene/electrode/silk hybrid structure could be transferred to biosurfaces such as different tissues or tooth enamel, as observed in Fig. 3Ba. Then, the graphene surface was modified with antimicrobial peptides (AMP) which are very stable and exhibit broadband detection for a range of pathogenic bacteria (*E. coli*, *S. aureus* cells and *H. pylori* cells) (Fig. 3Bb and Bc). The signal produced by the bacteria presence was registered using a wirelessly remote powering which is battery-free. Fig. 3Bd shows the results of the bacteria detection (red line) against saliva without bacteria (blue line). The change in conductance of the graphene nanosensor by binding of pathogenic bacteria is resolved from changes in the characteristic frequencies and bandwidth of the sensor resonance. The bacteria and cells were observable after their attachment to the sensor by fluorescence showing the detection limits of a single bacterium. Therefore, the remote monitoring of pathogenic bacteria detection has been carried out by the direct integration of extremely sensitive graphene nanosensors on tooth enamel as a battery-free sensor for applications such as point-of-care and diagnostics. However, more improvements should be made for their testing in *in vivo* systems.

More recently, flexible organic electrochemical transistors (OECTs) for the development of highly selective enzyme biosensors employed for saliva testing have been reported.[23] OECTs are a type of organic thin-film transistor and they act as transducers of biochemicals into electronic signals. This work describes flexible OECTs with the gates electrodes modified with a PANI/Nafion–graphene bilayer film for the sensing of glucose and uric acid (UA) levels in saliva. The high selectivity of these sensors is caused by the blocking of the interferences using a positively/negatively charged bilayer film which is very useful for the analysis of biological samples with charged biomolecules (DNA, proteins, ascorbic acid…) in aqueous solution. These devices can be modified with the suitable enzymes for the analysis of uric acid, cholesterol and glucose demonstrating good selectivity and better detection limits than conventional electrochemical methods which also use enzymes. These OECT sensors were fixed on flexible platforms and attached on different surfaces proving their good resistance to the strain.

A mouthguard sampling device for the amperometric monitoring of lactate has been recently developed.[24] It is described as a wearable salivary metabolite biosensor based on the integration of a printable enzymatic electrode on a mouthguard, and is a novel collection device with the potential to convert the current trend of passive, end-point saliva sampling into a minimally-invasive continuous monitoring system. The presented biosensors were fabricated by screen-printing three separate layers on a flexible PET substrate where LOx was immobilized on the working electrode by its entrapment in a polymer. The novel biosensing platform has displayed highly sensitive, selective and stable responses in saliva samples. However, future efforts have to be guided towards continuous in-mouth monitoring and data acquisition by wireless transmission.

Conclusions

Flexible and body-conformable sensors are a promising route for a new generation of personalized biomedical tools. The sensing technologies described in this paper, ranging from physical sensors to biological sensors, show different grades of maturity in terms of reliable operation and interfacing with the human body. The routine application of physical sensors (namely, tactile and temperature sensors) on patients seems to be closer to reality than biosensors. In fact, as in the case of contact lenses or conformal skin biosensors, biocompatibility needs to be investigated in more detail as well as the effective integration with data processing and transmission systems.

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Notes and references

1 C. Pang, J. H. Koo, A. Nguyen, J. M. Caves, M.-G. Kim, A. Chortos, K. Kim, P. J. Wang, J. B.-H. Tok and Z. Bao, *Adv. Mater.*, 2015, **27**, 634–640.
2 L. Y. Chen, B. C.-K. Tee, A. L. Chortos, G. Schwartz, V. Tse, D. J. Lipomi, H.-S. P. Wong, M. V. McConnell and Z. Bao, *Nat. Commun.*, 2014, **5**, 1–10.
3 B. Nie, R. Li, J. D. Brandt and T. Pan, *Lab Chip*, 2014, **14**, 1107–1116.
4 S. Gong, W. Schwalb, Y. Wang, Y. Chen, Y. Tang, J. Si, B. Shirinzadeh and W. Cheng, *Nat. Commun.*, 2014, **5**, 1–8.
5 G. Zhu, W. Q. Yang, T. Zhang, Q. Jing, J. Chen, Y. S. Zhou, P. Bai and Z. L. Wang, *Nano Lett.*, 2014, **14**, 3208–3213.
6 C. Dagdeviren, Y. Shi, P. Joe, R. Ghaffari, G. Balooch, K. Usgaonkar, O. Gur, P. L. Tran, J. R. Crosby, M. Meyer, Y. Su, R. C. Webb, A. S. Tedesco, M. J. Slepian, Y. Huang and J. A. Rogers, *Nat. Mater.*, 2015, **14**, 728–738.
7 S.-W. Hwang, C. H. Lee, H. Cheng, J.-W. Jeong, S.-K. Kang, J.-H. Kim, J. Shin, J. Yang, Z. Liu, G. A. Ameer, Y. Huang and J. A. Rogers, *Nano Lett.*, 2015, **15**, 2801–2808.
8 J. Yang, D. Wei, L. Tang, X. Song, W. Luo, J. Chu, T. Gao, H. Shi and C. Du, *RSC Adv.*, 2015, **5**, 25609–25615.
9 L. Gao, Y. Zhang, V. Malyarchuk, L. Jia, K.-I. Jang, R. C. Webb, H. Fu, Y. Shi, G. Zhou, L. Shi, D. Shah, X. Huan, B. Xu, C. Yu, Y. Huang and J. A. Rogers, *Nat. Commun.*, 2014, **5**, 4938.
10 R. C. Webb, Y. Ma, S. Krishnan, Y. Li, S. Yoon, X. Guo, X. Feng, Y. Shi, M. Seidel, N. H. Cho, J. Kurniawan, J. Ahad, N. Sheth, J. Kim, J. G. Taylor VI, T. Darlington, K. Chang, W. Huang, J. Ayers, A. Gruebele, R. M. Pielak, M. J. Slepian, Y. Huang, A. M. Gorbach and J. A. Rogers, *Sci. Adv.*, 2015, DOI: 10.1126/sciadv.1500701.
11 W. Honda, S. Harada, T. Arie, S. Akita and K. Takei, *Adv. Funct. Mater.*, 2014, **24**, 3299–3304.
12 H. Yao, A. J. Shum, M. Cowan, I. Lähdesmäki and B. A. Parviz, *Biosens. Bioelectron.*, 2011, **26**, 3290–3296.
13 H. Yao, Y. Liao, A. R. Lingley, A. Afanasiev, I. Lähdesmäki, B. P. Otis and B. A. Parviz, *J. Micromech. Microeng.*, 2012, **22**, 075007.
14 M. Falk, V. Andoralov, M. Silow, M. D. Toscano and S. Shleev, *Anal. Chem.*, 2013, **85**, 6342–6348.
15 Y. Seung Rim, S.-H. Bae, H. Chen, J. L. Yang, J. Kim, A. M. Andrews, P. S. Weiss, Y. Yang and H.-R. Tseng, *ACS Nano*, 2015, DOI: 10.1021/acsnano.5b05325.
16 N. Thomas, I. Lähdesmäki and B. A. Parviz, *Sens. Actuators, B*, 2012, **162**, 128–134.
17 G. A. Zelada-Guillen, J. L. Sebastian-Avila, P. Blondeau, J. Rui and F. X. Rius, *Biosens. Bioelectron.*, 2012, **31**, 226–232.
18 T. Guinovart, A. J. Bandodkar, J. R. Windmiller, F. J. Andrade and J. Wang, *Analyst*, 2013, **138**, 7031–7038.
19 T. Guinovart, M. Parrilla, G. A. Crespo, F. X. Rius and F. J. Andrade, *Analyst*, 2013, **138**, 5208–5218.
20 D. P. Rose, M. E. Ratterman, D. K. Griffin, L. Hou, N. Kelley-Loughnane, J. A. Hagen, I. Papautsky and J. C. Heikenfeld, *IEEE Trans. Biomed. Eng.*, 2015, **62**, 1457–1465.
21 J. Kim, M.-S. Lee, S. Jeon, M. Kim, S. Kim, K. Kim, F. Bien, S. Y. Hong and J.-U. Park, *Adv. Mater.*, 2015, **27**, 3292–3297.
22 M. S. Mannoor, H. Tao, J. D. Clayton, A. Sengupta, D. L. Kaplan, R. R. Naik, N. Verma, F. G. Omenetto and M. C. McAlpine, *Nat. Commun.*, 2012, **3**, 763.
23 C. Liao, C. Mak, M. Zhang, H. L. W. Chan and F. Yan, *Adv. Mater.*, 2015, **27**, 676–681.
24 J. Kim, G. Valdes-Ramirez, A. J. Bandodkar, W. Jia, A. G. Martinez, J. Ramirez, P. Mercier and J. Wang, *Analyst*, 2014, **139**, 1632–1636.