Ultra-Conformable Biodevice for Advanced Medicine and Healthcare

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ABSTRACT

Ultra-conformable biodevices (namely "printed nanofilms") are developed by combining polymeric nanosheets and printing technologies with variety of unique inks. The printed nanofilms allowed for continuous monitoring of biosignals or directing biofunctions, represented by the measurement of surface electromyogram, analysis of neural activity, and wireless delivery of a light into tumors to perform phototherapy.

1 INTRODUCTION

Integration of flexible electronics into nano-biomaterials is expected for advancing medical diagnostics and therapeutics. Such devices should be conformable to the physical and mechanical environment of a living body. And, the information collected from the devices should be transmitted wirelessly for data analysis and processing.

In this regard, we have envisaged the development of free-standing polymeric ultra-thin films (referred to as "nanosheets") for wearable and implantable devices. The polymer nanosheet shows tens- to hundreds-of-nanometer thickness close to the scale of biomembranes [1], in which several polymers (e.g., biodegradable polymers, conductive polymers, and elastomers) can be formed into the ultra-thin structure by spincoating, layer-by-layer and gravure coating processes. The free-standing nanosheet showed flexible and adhesive properties derived from ultra-small flexural rigidity (< 10^{-2} nN m).

In this paper, we show the use of "printed nanofilms" by combining nanosheets and printing technologies with a variety of functional inks represented by drugs, conductive nanomaterials, chemical dyes, bio-mimetic polymers, and cells [2]. The flexible printed nanofilms realize bio-integrated structure and display various functions with unique inks that continually monitor or direct biological activities, such as (i) performing surface electromyography, (ii) measuring epidermal strain, and (iii) treating lesions in wounds and tumors.

2 Conductive nanosheets for ultra-conformable bioelectrodes

Introduction of electrical conductivity into the polymer nanosheets would allow for the development of ultra-conformable skin-contact electronics with flexibility and adhesiveness, while also being less noticeable to the user, than conventional wearable devices. Moreover, the extension of the processing technologies of flexible thin-film devices to scalable industrial fabrication is essential for real-world applications. Towards this aim, we focused on one of the most widely used conductive polymers, PEDOT:PSS. Conductive nanosheets were prepared by a roll-to-roll gravure-printing of PEDOT:PSS dispersion on a mechanically supporting nanosheet made of poly(lactic acid) (PLA) or polystyrene–polybutadiene–polystyrene (SBS) triblock copolymer [3, 4].

As a demonstration of skin-contact applications, the PEDOT:PSS/PLA conductive nanosheets were tested as skin-contact bioelectrodes for the measurement of surface EMG (sEMG) for monitoring bioelectrical signals (Fig. 1). The results showed that such unperceivable nanosheet electrodes successfully recorded the stepwise increase of sEMG signal by the function of the pressure applied by a subject's hand grasping a pressure gauge. It is noteworthy that the conductive nanosheets showed as high a signal-to-noise ratio (SNR = 36.9 dB) as clinically approved standard pre-gelled Ag/AgCl electrodes (SNR = 35.7 dB). This demonstration shows the possibility of the conductive nanosheets not only in healthcare applications but also in other practical or medical fields, such as prosthetics, wearable robotics, and sports science including precise motion analysis of human body movements.

3 Nanosheet electronics for skin-contact devices

The convenient fabrication of electrical circuits on thin-film substrates has been progressed for the development of smart printed flexible electronics. Along the progress of printing technologies on flexible sheet-like substrates, there have been emerged ultra-thin film or tattoo based conformable, printed electronics. For the development of printed nanofilms that detect or monitor the bioelectrical information such as sEMG [3] and neural signals [5], the direct printing of conductive inks is an important technology. While gravure-printing enables the scalable fabrication of homogeneous conductive nanosheets, the patterning of conductive materials on polymeric nanosheets is also required for the development of printed nanofilms with more complex circuits. Hence, we focus on the drop-on-demand inkjet printing of conductive inks, as exemplified by conductive polymers, metallic nanoparticles and carbon nanomaterials, on the polymer nanosheet.

As an example, we developed an ultrathin epidermal strain sensor composed of PEDOT:PSS conductive patterns on an SBS nanosheet [6]. The ultrathin structure and glue-free conformable adhesion of the SBS nanosheet (around 320 nm thick) minimized the obstruction of the skin's natural deformations. With the ultrathin epidermal strain sensor, we successfully measured the skin strain (~2%) on a forearm caused by the extension of the wrist joint. The printed nanofilm-based ultra-conformable epidermal strain sensor should be a powerful tool for precise detection of the motion of the living body, as well as in soft robots [7].

We also demonstrated direct inkjet printing of Ag nanoparticles (AgNPs) on the SBS nanosheet without dewetting and/or agglomerates by coating an ink-absorbing layer (acrylic-copolymer) on the top of the nanosheet to increase its surface wettability as well as water-absorption [8]. Taking advantage of the van der Waals force-based physical adhesion of the SBS nanosheet, we achieved the soldering-free fixation of small electronic elements. As a demonstration, a chip LED was sandwiched between two layers of elastomeric SBS nanosheets (each layer: ~380 nm thick), on one of which AgNPs-based conductive lines (~720 nm thick) were inkjet-printed. With this soldering-free process, electronic elements were physically and electrically fixed on the conductive lines, resulting in the operation of the nanosheet electronics on the human skin (Fig. 2). The present technique to sandwich the electronic element with nanosheets is applicable not only for LED chips but also IC chips and sensors, which will advance skin-contact electronics.

4 Tissue-adhesive nanosheets for implantable devices

Development of implantable medical devices has made a tremendous contribution to the field of biomedical engineering. These devices can monitor the physiological condition of the living body by interfacing with its interior surface as well as intervening in functional body systems through the delivery of drugs or physical energy like electricity and light to the target lesion.

The standard approach for the fixation of implantable devices is surgical suturing; however, it is unsuitable for tissues near major nerves and blood vessels, as well as for fragile organs such as brain, liver, and pancreas, that are mechanically fragile, actively deformed, or moving. Therefore, the development of ultra-conformable tissue-adhesive devices, which stick to the surfaces of living tissues, is anticipated. To this end, we focused on a mussel-foot-protein-inspired bio-adhesive polymer polydopamine (PDA) coating [9]. The surface of polydimethylsiloxane (PDMS) nanosheets were modified with PDA to prepare tissue-adhesive PDA-PDMS nanosheets that allowed for suture-free and long-term stable fixation of small implantable devices on wet internal living tissues. The 650-nm-thick PDA-PDMS nanosheets with an elastic modulus of 14.9 ± 0.60 MPa (flexural rigidity of ~4.5×10^{-4} nN m) showed 25-fold-stronger adhesion (50.7 μJ/cm^2) to chicken muscle than a 0.8-mm-thick PDMS sheet with a flexural rigidity of > 10^5 nN m (2.2 μJ/cm^2).

Taking advantage of the PDA-PDMS nanosheet, we developed a tissue-adhesive wirelessly powered optoelectronic device for fully implantable, metronomic (low-dose and long-term) photodynamic therapy (mPDT) by embedding a near-field-communication (NFC)-based red or green LED chip (Fig. 3). When subcutaneously implanted in the cancer model mice with intradermally transplanted tumors, the device consecutively irradiated the tumor for 10 days, leading to significant antitumor effects. This mPDT device emits light at approximately 1,000-fold-lower intensity than conventional PDT, and thus does not involve the risk of overheating healthy tissues. This implantable and wirelessly powered mPDT system may offer a new path to the application of PDT, especially for deep cancers that are difficult to treat with standard methods.

By integration of emerging printing technologies into the tissue-adhesive nanosheets, the whole structure of implantable/wearable devices can be a thin film type. For example, the light emitting part of the mPDT devices can be replaced by an organic electroluminescence device, that provides broader light irradiation and more conformably fits the surface of target tissues to treat widely diffused lesions. Moreover, antenna coils for wireless communication or organic photovoltaics for self-powering the device can be directly printed on the nanosheets by several printing techniques including inkjet printing, screen printing and transfer printing, to generate fully printed nanofilm electronics.

5 CONCLUSIONS

This paper summarized the seminal technologies of polymer nanosheets and printed nanofilms interfacing with the living body. The mechanical and adhesive properties of the nanosheets, that are derived from their ultra-thin structure (< 1 μm) as well as their low flexural rigidity (< 10^{-2} nN m), not only provide conformal and stable physical adhesion to living tissue surfaces without suture or any adhesive agents, but also solve the mechanical mismatch between relatively stiff materials and soft biological tissues.

Such unique properties of polymer nanosheets are promising as a mechanically compatible platform of wearable/implantable devices interfacing with the living body. Several examples of applications of printed nanofilms demonstrated that a variety of "inks" can be printed on nanosheets and provide an unlimited range of applications. In the future, it is interesting and valuable to generate novel printed nanofilms with a range of functions by printing or embedding wide variety of inks or devices on nanosheets, for example, chemical indicators, such as pH-, potential-, and gas-sensitive dyes; for environmental mapping, organic electronics including transistors, electroluminescent diodes, photovoltaics, and batteries; for flexible electronics, microfluidics for health monitoring devices, antennas for wireless communication, and polymers, proteins and cells for tissue engineering . We believe that the printed nanofilms will contribute to the progress of wearable/implantable devices in the regard of future medicine and healthcare.

"This manuscript is prepared based on the reference [2], in which further details are reported."

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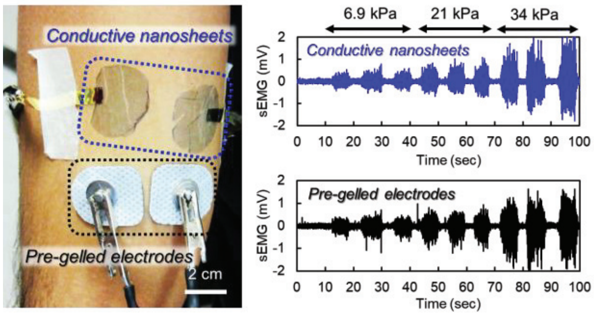

Fig. 1 Conductive nanosheets and conventional pre-gelled electrodes adhered on the forearm of a subject (left) and the obtained sEMG signals (right) through them when the subject was grasping an analog pressure gauge at different levels of pressure. Reproduced from ref. 4.

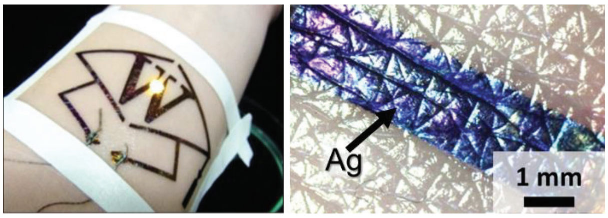

Fig. 2 Image of nanosheet electronics attached to the skin (left). An LED on an Ag-based circuit-printed SBS nanosheet is lit up on the skin. Microscopic image of the Ag line inkjet-printed on the SBS nanosheet adhered to skin (right). Reproduced from ref. 9.

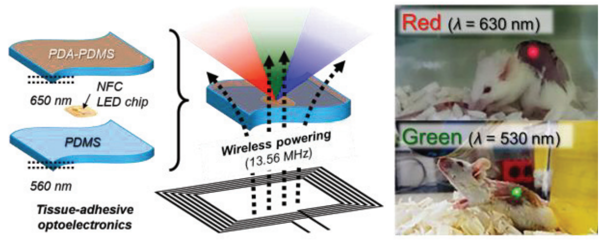

Fig. 3 Tissue-adhesive and wirelessly powered optoelectronic device composed of an NFC-based LED chip sandwiched between PDA–PDMS and pristine PDMS nanosheets (left). Images of red (right, top) and green (right, bottom) lighting emitted from wirelessly powered LED chips implanted subcutaneously in mice. Reproduced from ref. 10.