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Hydrogel-Based Cytocompatible Electrode Systems

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Abstract

A stretchable organic conductor, a composite of PEDOT and polyurethane, was tightly attached to the surface of a hydrogel. The resulting moist, molecular permeable electrode device shows superior cytocompativility, and can be directly combined with cells, tissues and body to measure the bioelectric signals and to stimulate the bioelectric functions.

1. Introduction

Recent rapid progress in the fabrication of electrodes on flexible substrates has opened a new prospect in the field of future electronics. Hydrogels are excellent candidates of flexible substrate due to their stiffness comparable to that of living tissues (a few ~ tens kPa) and the molecular permeability that guarantees synergy to the physiological milieu. We have developed an electrochemical technique for micropatterning stretchable electrode PEDOT/polyurethane on hydrogels to provide a fully-organic, moist electrode [1-3]. As the substrate hydrogel, soft but strong double-network (DN) hydrogels, with rupture stress exceeding 1 MPa, was adopted. A tighter bonding between the components is therefore critical to minimize failure during exposure to high stress environments. We utilized electropolymerization of PEDOT as an adhesive to get tough adhesion. The DN hydrogel substrates were desiccated with shrinkage to approximately 25 % size of the original, accompanied by wrinkling of the PEDOT/PU electrode. The desiccated substrates show excellent re-swelling property to recover the original condition. This implies that our devices can be stored in the dry condition, allowing easy handling and transportation, making it more compliant with marketing to distant consumers. Significantly, the adhesion of the PEDOT/PU to hydrogel and the conductivity of the electrodes were both maintained after autoclave for sterilization. We will present examples of applications of this hydrogel-based flexible electrodes in variety of biomedical fields (In-Vitro, On-Skin, and In-Vivo).

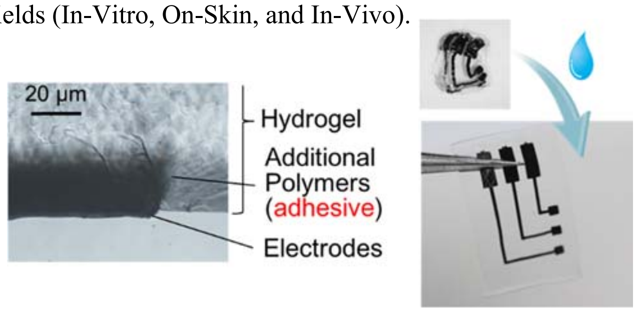

Fig. 1 Cross section of the hydrogel-based electrode, which can be dried and re-hydrated to recover its original size and shape.

2. In-Vitro Applications

In-vitro bioassay using cultured cells becomes increasingly important as the alternative to animal experiments in biological basic research and drug discovery. The bioassay systems fabricated by combining the microelectric devices with cell-micropatterning techniques have enabled localized electrical regulation and long-term monitoring of electrophysiological responses from the cells such as a neural, cardiac, and skeletal muscle cell cultured on the device. We have coupled the hydrogel-based electrode with skeletal muscle cells for studying complex mechanisms of type-2 diabetes that closely associates with defection of glucose uptake in skeletal muscle cells [4-6]. Since the muscle cells are sensitive to the stiffness of culture substrate, we developed first the technique to culture micropatterned C_2C_{12} myotubes on soft, moist fibrin gel sheet, that showed stable contractile activity for a longer period of time (more than a week). By laminating the myotubes-patterned gel and the PEDOT electrode on hydrogel, the resulting contractile muscular chip enables the site-specific investigation of the effects of electrical stimulation-mediated contraction, which could mimic the metabolic events in skeletal muscle tissue under exercise. We successfully demonstrated the fluorescent imaging of the contraction-induced translocation of the glucose transporter, GLUT4, from intracellular vesicles to the plasma membrane of the myotubes. This device would be applicable for quantitative bioassay of various contraction-induced metabolic alterations in myotubes.

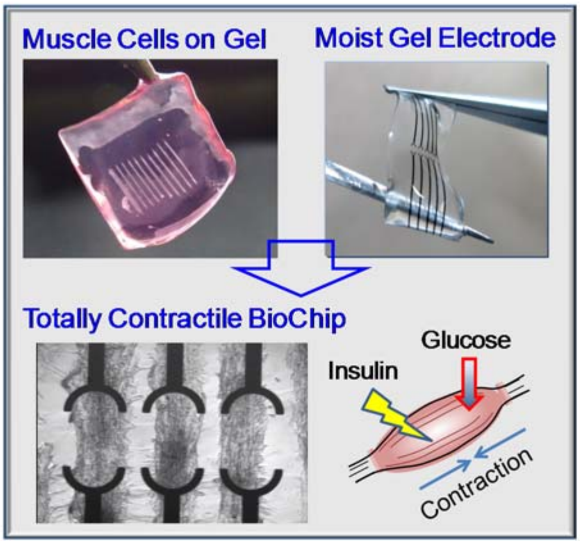

Fig. 2 The totally contractile muscular chip could be a research tool for type-2 diabetes.

3. On-Skin Applications

Electrophysiological measurements such as electrocorticography, electrocardiography, and electromyography on the human body surface have been widely performed for medical diagnosis, medical monitoring, and neuron-to-machine interfaces for prostheses. These electrophysiological measurement systems have recently been integrated into wearable devices for daily health monitoring and therefore, much effort has been paid for the development of flexible and stretchable electric devices in order to ensure the motion adaptivity. For stable monitoring, it is necessary for electrode devices to maintain electric contact with the curvature of a skin even during body motion. Therefore, soft electrolyte gels are practically used as an interfacial material between the solid electrode devices and the soft skin. In fact, a commercially available Ag/AgCl patch is combined with an adhesive electrolyte gel. By combining stretchable electrode devices and stretchable DN hydrogels, a totally shape-conformable electrode device could be realized for stable electrophysiological measurement at any parts of a body with motions.

We fabricated a shape-conformable electrode/hydrogel composite shown in Fig. 3, in which a stretchable Au electrode was tightly attached to the surface of a DN hydrogel sheet [7]. The electrochemically deposited PEDOT serves as a stable adhesive layer. This PEDOT adhesive layer showed the advantage of low-impedance and low-noise measurement.

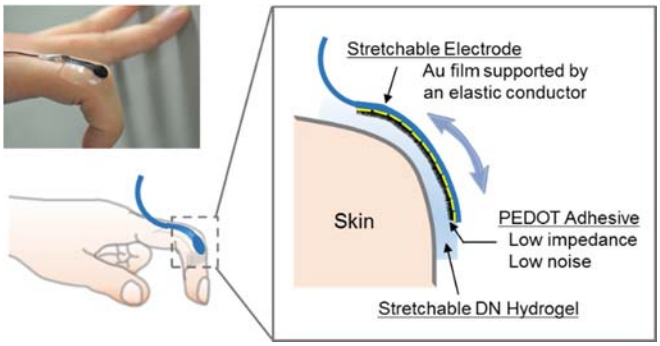

Fig. 3 Schematic illustration of the developed shape-conformable electrode/hydrogel layered composite on a forefinger.

This electrode/hydrogel composite showed stable resistance of $35 \pm 5\ \Omega\ \mathrm{sq}^{-1}$ even during successive 20 % stretching because of the pre-formed, designed cracks in the Au film. The large interfacial electric double layer capacitance ($9.5 \pm 0.3\ \mathrm{mF\ cm}^{-2}$) of the PEDOT adhesive layer at the interface of the layered composite was found to stabilize the electrode potential against external noises, and decrease the electric impedance. For example, at 5 Hz which is in the typical range of electrophysiological signals, 27 times lower electrode/hydrogel interface impedance was obtained for the PEDOT adhesive than that of bare Au film. The totally stretchable composite stably adhered to the skin surface even upon 90-degree bending of the finger without any additional adhesive material (the strain at the forefinger joint: 20 %). The spectra of contact impedance without significant change during 10 cycles of bending. The robustness of the electrode/hydrogel composite for EMG measurement was demonstrated on the moving forefinger joint. The spike signals were obtained, which was synchronized with the 90-degree bending motion of the forefinger. This proves stable EMG monitoring even at the drastically moving parts of a human body.

4. In-Vivo Applications

The most characteristic feature of the hydrogel-based microelectrodes should be its molecular permeability, which enable the direct combination with living systems without hindering biofluid circulation. The electrode equipped on the soft contact lens serves as the device for monitoring movement of eyeball that reflect mental condition. The hydrogel-based electrode adhere onto the surface of organ such as spinal marrow to monitor its activity during brain surgery. We believe the hydrogel-based electrode device can become a standard low-invasive surgical tool, and are exploring the possible applications to other kinds of organs including brain and hart.

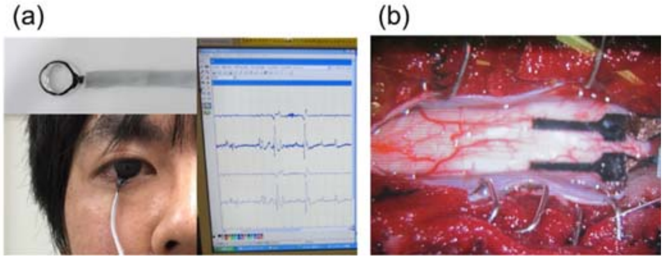

Fig. 4 (a) Monitoring of eyeball movement. (b) Monitoring of spinal marrow responses during brain surgery (experiment using a pig).

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