Biofuel Cells

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Epidermal Biofuel Cells: Energy Harvesting from Human Perspiration**

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The healthcare industry has recently experienced a major paradigm shift towards wearable biomedical devices.[1] Such devices have the ability to monitor vital physiological parameters, such as heart rate or blood pressure.[2] Particular recent attention has been directed towards skin-worn electronic devices fabricated by novel hybrid techniques for the measurement of these vital signs.[3] Despite dramatic technological advances, further progress in the arena of on-body biomedical devices has been hindered by the lack of effective wearable power sources able to scavenge sufficient energy from the wearer. Major efforts have thus been directed towards the identification of a suitable wearable power source that offers conformal integration with the wearer's body. This activity has resulted in the development of flexible thin-film batteries, piezoelectric nanogenerators, wearable solar cells, mircosupercapacitors, and endocochlear-potential-based biobatteries.[4] Nevertheless, new body-worn conformal power sources able to extract biochemical energy from the wearer's body (and his/her epidermis, in particular) are still highly desired.

Herein we demonstrate the ability to generate substantial levels of electrical power from human perspiration in a non-invasive and continuous fashion through the use of epidermal biofuel cells based on temporary transfer tattoos (tBFCs). Enzymatic BFCs have attracted considerable interest owing to their ability to generate power from the bioelectrocatalytic reaction of common chemicals and metabolites, such as glucose and alcohol, under physiological conditions.[5] Recent efforts resulted in implantable glucose BFCs that can generate significant power densities in small animals, such as snails, insects, and rats.[6] However, there are no reports on harvesting the chemical energy from a human in connection with the rapidly developing field of wearable electronics.

The successful development of non-invasive tBFCs requires the judicious integration of new manufacturing processes and advanced surface functionalization for efficient power generation from lactate present in the wearer's perspiration. The development of the tBFC builds on our recent introduction of epidermal electrochemical sensors.[7] The two electrode constituents of the new wearable tBFC were designed in the shape of "UC" (acronym for "University of California"; Figure 1; see Figure S1 in the Supporting Information for an illustration of the tBFC fabrication and transfer process). We carried out close visual examination of the tBFC on the dorsal region of a human wrist during repeated bending, stretching, and twisting movements for a total of 50 such iterations (see Figure S2). The resulting screen-printed transfer-tattoo electrodes are compatible with the nonplanarity of the epidermis and can withstand repeated mechanical deformations.

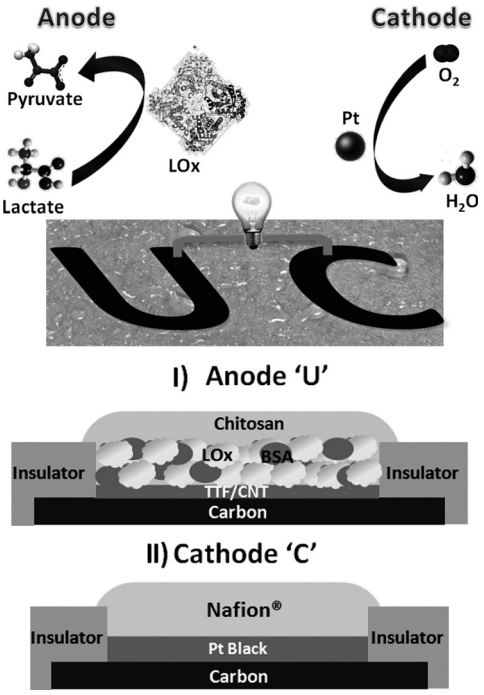

Figure 1. Illustration of the epidermal tBFC and the constituents of the anode (I) and cathode (II).

Lactate was selected as the biofuel since it is present in abundant levels in human perspiration[8] and can be readily oxidized by commercially available enzymes. Moreover, sweat lactate is also a widely recognized biomarker for

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exercise intensity and muscular exertion.[9] Accordingly, the power density produced by the new epidermal tBFC device can be correlated with the fitness level and aerobic capacity of an individual on the basis of the selective oxidation of lactate present in the perspiration by a lactate oxidase (LOx) functionalized bioanode (Figure 1 I). To date, all reported studies of lactate-powered BFCs have exploited the lactate dehydrogenase enzyme.[10] This enzyme requires nicotinamide adenine dinucleotide (NAD^+), which represents a significant challenge, as this cofactor must be regenerated and immobilized on the electrode without leaching while ensuring access to the active site of the enzyme.[11] Although LOx-based BFCs, to the best of our knowledge, have not been used in vitro/vivo, they offer greater promise for epidermal power generation.

Electrochemical mediators have been widely employed to promote the low-potential bioelectrocatalytic conversion of lactate by LOx in sensing applications.[12] We evaluated various common mediators for their suitability for use in the wearable tBFC, including ferrocene derivatives, Meldola blue, and tetrathiafulvalene (TTF), and found that TTF yielded the lowest oxidation potential, showed the most stable performance, and enabled the most straightforward handling. TTF does not cause skin irritation[13] and has been widely used as a mediator for biosensor applications. To improve the efficiency of the tBFC, we relied on a TTF/carbon nanotube (CNT) composite as an effective and insoluble electron shuttle (Figure 2 a). The TTF/CNT complex was employed earlier as an efficient electron shuttle.[14] The adsorbed TTF/CNT film was subsequently coated with the biocatalytic LOx/albumin layer. A biocompatible chitosan (Chit) overlayer on the bioanode prevented the efflux of the biocatalytic backbone from the electrode surface onto the underlying skin. Prevention of leaching was further enhanced by cross-linking with glutaraldehyde. The CNT/TTF/LOx/Chit matrix was thus selected as the modifier for the bioanode ("U") of the tBFC (Figure 1). The cathode ("C") consisted of the printed carbon electrode modified with platinum black and coated with a protective biocompatible Nafion layer[15] to avoid direct platinum–skin contact.

Given the aim of harnessing lactate from perspiration as the biofuel for epidermal power generation, the tBFC must be able to catalyze the oxidation of lactate with fairly high turnover. The mediated oxidation of lactate is initiated at around −0.1 V with a peak potential of 0.14 V (versus Ag/AgCl; Figure 2 b); thus, the CNT/TTF/LOx/Chit system exhibits high catalytic activity towards the oxidation of lactate. Such a low lactate-oxidation onset potential reflects the efficient electron-donor–acceptor TTF/CNT interaction,[16] which promotes the shuttling of electrons between the redox center of the enzyme and the electrode surface. The performance of the tBFC is further demonstrated by the power density generated from the tBFC (Figure 2 c). The power density approached 25 $\mu W\,cm^{-2}$ at a lactate concentration of 8 mM and increased to 34 and 44 $\mu W\,cm^{-2}$ at higher lactate concentrations of 14 and 20 mM, respectively. Minute power output was observed during a control experiment without lactate; this effect has also been reported for other BFCs.[6b,17] The observed concentration dependence of the generated power enables a promising alternative application of the device as a novel self-powered, non-invasive lactate sensor.[18]

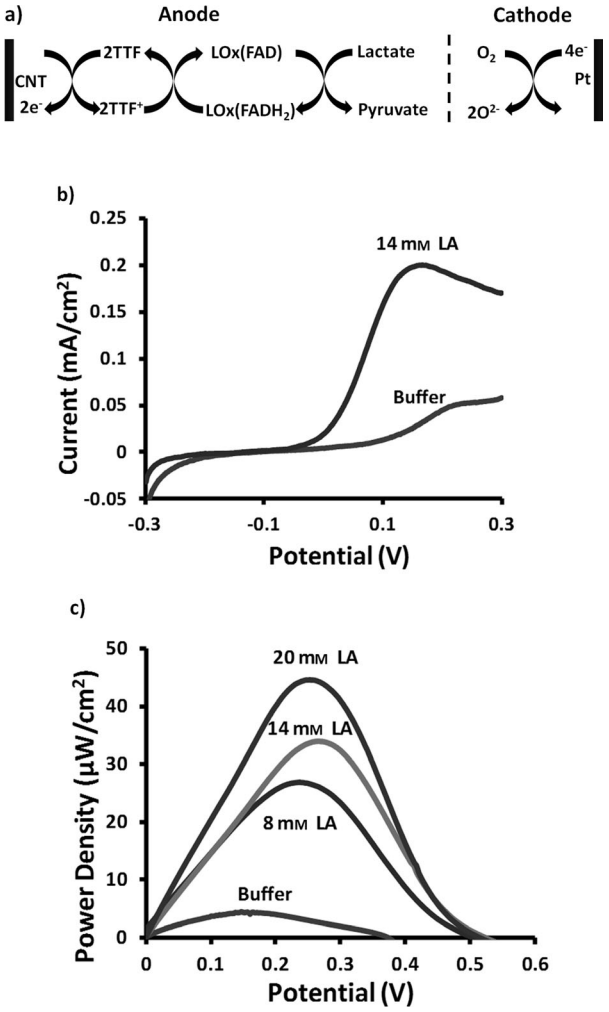

Figure 2. a) Redox reactions that occur within the tBFC. b) Polarization curves for the CNT/TTF/LOx bioanode in the absence and presence of lactate (14 mM) in 0.2 M McIlvaine buffer solution (pH 5.5). c) Power density of the tBFC at varying lactate (LA) concentrations in 0.2 M McIlvaine buffer solution (pH 5.5). FAD = flavin adenine dinucleotide.

A formidable challenge facing epidermal bioelectronic devices is the requirement for resiliency against mechanical stress and strain caused by continuous body movements. The mechanical resiliency and power output of the tBFC were further examined in vitro on a Gore-Tex textile during repeated bending and stretching motions. The electrochemical behavior of the tBFC during these stretching and flexion deformations (see Figure S3) showed that the tBFC is able to withstand repeated stress characteristic of epidermal wear. A relatively minor loss/fluctuation in the original power levels (ca. 15 %) was observed following the 50 stress iterations. These results show that the tBFC can maintain its electrochemical performance (as well as its structural integrity) in the face of complex mechanical deformations, which are even more severe than those encountered during epidermal applications.

Prolonged stability is a major prerequisite for the successful long-term use of BFCs. The electrochemical stability of the tBFC was examined in vitro over a 4 week period by the use of artificial sweat[8] containing lactate at a concentration of 14 mM (pH 5.3, with intermittent storage at 4 °C). The tBFC remained active throughout this investigation; its power output decreased by less than 10 % during the initial 14 day period and was retained at over 50 % of the original value at the conclusion of the 4 week investigation. These results imply that the tBFCs remain relatively stable for considerable durations. They are thus expected to operate over extended periods with no major deterioration in their performance. Whenever required, tBFCs can be replaced rapidly and easily.

The compelling results obtained during the course of our in vitro evaluation of the tBFCs established the groundwork for their epidermal integration. The tBFCs were applied to 15 healthy, consenting human subjects and examined during intense physical activity. It is widely known that during physical activity, the aerobic metabolism is incapable of satisfying the energy demands of the body.[19] Under such conditions, the human body instigates the more efficient anaerobic metabolism, which provides the body with energy through the glycolytic breakdown of blood glucose and glycogen in the eccrine sweat glands to produce lactate.[20] As a result, sweat lactate excretion is directly correlated with the intensity of the physical activity pursued: higher lactate levels correspond to increased muscular exertion during periods of anaerobic exercise.[9a] The tBFCs were applied to the volunteers' right deltoid (Figure 3 a), as this region remains mostly unperturbed during the cycling activity, and the tBFC can thus be connected to the recording instrumentation.

Subjects were divided into three groups according to their fitness level: group 1—low fitness level (<1 bout of physical activity per week); group 2—intermediate fitness level (between 1 and 3 bouts of physical activity per week); group 3—high fitness level (>3 bouts of physical activity per week). The clear distinction observed in the power density generated by the three fitness groups reflects differences in the real-time lactate dynamics of the subjects (Figure 3 b). Maximum power densities of 70 and 55 $\mu W\,cm^{-2}$ were obtained from two of the volunteers who populated the "low-fitness-level" group (Figure 3 b I). For subjects that engaged in moderate physical activity, the "intermediate-fitness-level" group, the maximum power output obtained resided within the 10–20 $\mu W\,cm^{-2}$ range (Figure 3 b II), a substantial decrease as compared to that of the low-fitness-level group. Among those subjects that engaged in frequent physical activity (exercise enthusiasts, Figure 3 b III), power densities were typically less than 5 $\mu W\,cm^{-2}$. The onset of power delivery differed among the individual volunteers and reflects the duration of time required until perspiration began to form.

The power generated by each volunteer was dependent on the anaerobic capacity of the subject (Figure 3 b). More specifically, a strong inverse relationship between power density and fitness level is apparent. This relationship implies that less fit individuals excrete greater amounts of lactic acid. Such behavior is in agreement with earlier exercise-physiology studies[19,20a] and reflects the more rapid onset of muscular fatigue among such individuals. Additionally, high sweat-excretion rates could result in diminished (diluted) lactate concentrations in the perspiration[9a,20b] and hence decreased power output.

Apart from the ability to generate power from the perspiration, the tBFCs should be able to withstand repeated usage associated with prolonged physical activity. One volunteer was requested to perform two 20 min bouts of intense cycling separated by a 2 h interval of rest while the tBFC was applied to the deltoid. The tBFC generated reproducible power output (ca. 13 $\mu W\,cm^{-2}$) during this repeated activity over an extended duration (Figure 3 c). Furthermore, no signs of skin irritation or inflammatory response were observed among the volunteers, even for one volunteer who wore the tBFC for 8 h. This result suggests that the tBFCs can harvest power from

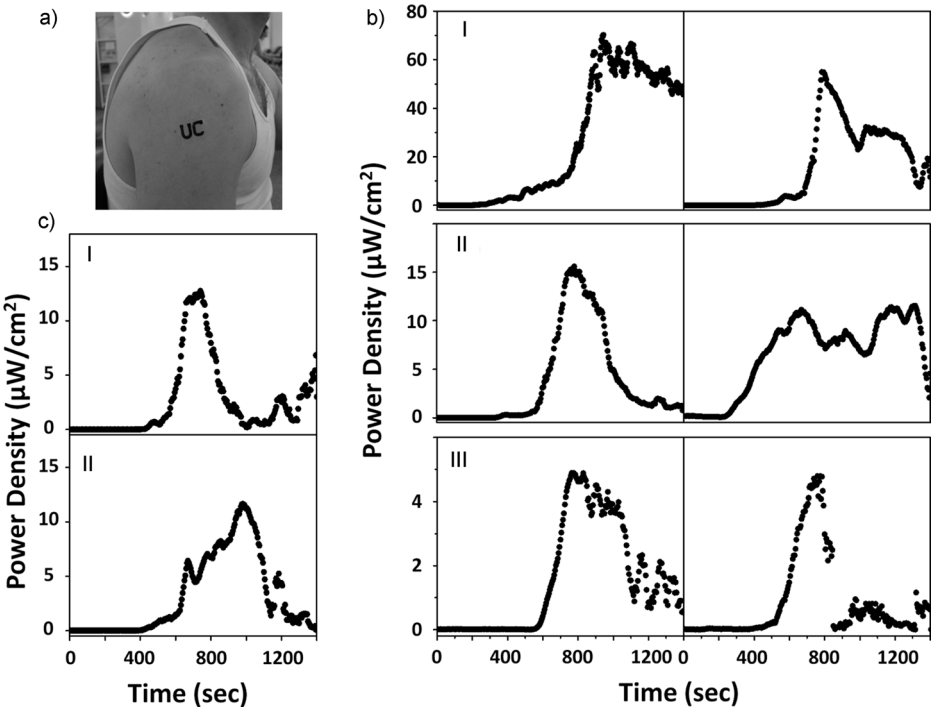

Figure 3. Harvesting of the biochemical energy of lactate during physical activity. a) A "UC"-inspired tBFC on the deltoid of a volunteer. b) Real-time power-density profiles during cycling for 6 subjects: I) low fitness level, II) intermediate fitness level, III) high fitness level. c) Repeated power-density measurements with a single tBFC: I) first measurement, II) measurement 2 h later.

sweat lactate for a prolonged period in an innocuous manner.

In conclusion, we have demonstrated a new skin-conformable epidermal BFC that can be successfully implemented for the harvesting of biochemical energy from perspiration lactate during physical activity in a completely non-invasive fashion. Power densities during non-invasive on-body studies ranged from 5 to 70 $\mu W\,cm^{-2}$ and thus reflected the wide range of lactate levels secreted in the perspiration of individuals with varying fitness levels. As expected for on-body BFCs,[6a] the new epidermal BFC does not yield stable power levels. The extraction of biochemical "fuels" and electrical power from the wearer's epidermis represents a major advance within the fast-growing field of epidermal electronics. The new epidermal bioenergy paradigm thus holds considerable promise as a viable autonomous power source for wearable electronics.

Experimental details are available in the Supporting Information.

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