Flexible Microfluidics-Integrated Organic Transistor as Biofeedback for Advanced Wound Healing

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1 Abstract

This paper will discuss how incorporating a biofeedback sensor into an electrical stimulation bandage used on chronic ulcers will improve the healing process. Current wound healing devices, and specifically wearable ones, are an open loop system that incorporates electrical stimulation with hopes of a positive result, but creating a closed loop system would improve results, especially on chronic ulcers. The human skin is the largest organ in the body that is dynamic and naturally absorbs Na^+ ions and secrets Cl^- ions when a wound occurs, making the area under the skin positively charged. The flexible microfluidics-integrated organic transistor use printers to generate an array making it possible to create a real-time biofeedback sensor that can be integrated with a wound healing device. Sodium and potassium ions (Na^+ and K^+) are important electrolytes in biological processes, including control of the hydration status, nerve and muscle impulse transmission, osmotic pressure balance and pH regulation. By monitoring the electrolyte imbalance and the hydration status caused by a wound, electrical simulation can be adjusted as needed to heal the wound site. The Organic Electrochemical Transistors (OECTs) with a Poly(imide) (PI) polymer microfluidic membrane would be able to monitor the hydration level at the wound bed and the rate of Cl^- ionic movement as an external electrical signal is applied. By monitoring the hydration level and Cl^- ion movement would improve the wound healing rate for chronic ulcers. [1-3]

Keywords: microfluidics, biofeedback, wound healing

2 Introduction

The main layers of the human skin include the epidermis, dermis, and the subcutaneous layer. The stratum corneum is the upper most layer of the epidermis which consists of dead cells that function as a barrier to protect underlying tissue from infection, dehydration, chemicals and mechanical stress. When the skin experiences a cut or ulcer, there is a potential gradient established that alters the electrical current flow signaling the body that a repair is needed. The human body enters the stages of wound healing which are inflammation, proliferation, and maturation or remodeling. The first phase is inflammation where homeostasis begins; blood vessels constrict and seal themselves off as the platelets create substances that form a clot and stop the bleeding. The second phase is proliferation where new tissue is made up of a mixture of extracellular matrix and collagen that allows for the development of a new network of blood vessels to replace the damaged ones. Maturation or remodeling is the final stage in wound healing where the scab falls off and collagenous fibers become more organized.

Current wound healing devices are larger in size and do not provide an effective biofeedback system to aid in the healing process. The design being discussed would be able to be easily attached to the wound area and use biofeedback to stimulate cellular regeneration at an expedited rate. Research has shown the voltages used range from 3 volts to 200 volts and the drive currents range from 0.2 µA to 11 mA with monophasic and biphasic waveforms provide the best electric flow around the wound bed. The device was designed to operate a drive current from 0 to 800 µA and a boost circuit was designed to get voltage high enough to provide positive results. Using the information from research, a model was generated using Comsol Multi-Physics to observe how electrical stimulation may effect a wounded skin region. Through correspondence with the Federal Drug Administration stated, a wound management devices comes under Title 21, Code of Federal Regulations, Part 878.4780, (21CFR, Part 878.4780), which is considered a regulatory status class II

3 Device Design

3.1 Electronics Portion

The device contains five sub-circuits, as shown in Figure 1, that include the safety cutoff, digital control, power and charging, driver, and voltage boost. The device will be powered by replaceable 3.6 V battery that will allow for compact and portable size. There will be a biphasic drive that will sense and control the output current, the safety circuit. The programmable controller will be designed to receive the current values from the sensing resistor through on-board Analog to Digital Converters (ADCs). The current limits specified by the program in the controller sends digital control through serial interface to adjust the resistance values

in digital potentiometer. The biofeedback sensor will monitor the rate of healing at the wound bed and relay that information to the microcontroller, which in turn will make necessary output adjustments for optimal outcomes.

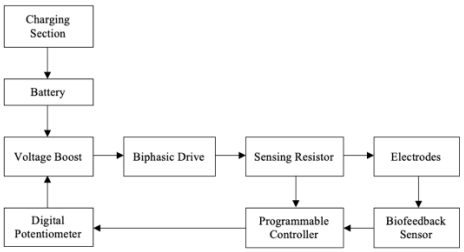

Figure 1: Electrical Block Diagram

3.2 Microfluidics Biofeedback Sensor

The Organic electrochemical transistors (OECT) have changed the efficiency of biofeedback devices in the medical field. (OECT) use a thin layer of organic semiconductor is deposited on the channel area between the source and drain electrodes and exposed to an electrolyte with the gate electrode, Figure 2. They are highly sensitive transducers with inherent amplification capability that can convert biochemical signals into electrical signals. These transistors can be used in sensors that can measure lactate, glucose, dopamine, UA, and bacteria levels. The development of high-performance OECT biosensors are employed to aid in medical treatments, including wound healing. UA sensors incorporating OECT have been shown to have detection limits of approximately $1x10^8$ M, which is approximately three times the magnitude better than conventional electrodes. When an injury is caused by trauma alarmins are released; uric acid(UA) is considered a major alarmin by dying cells and they are categorized as Damage Associated Molecular Patterns(DAMP). The UA stimulates the dendritic cells to start the inflammation phase, the beginning of the wound healing process. Studies were performed by Patschan et al. on mice with a kidney injury induced by ischemia, which is a wound resulting from an inadequate amount of blood flow, where in a period of 30 minutes the UA concentration was elevated and returned to normal within 1 hour when healing started. [4,5]

The flexible microfluidics-integrated organic transistor use printers to generate an array making it possible to create a real-time biofeedback sensor that can be integrated with a wound healing device. Sodium and potassium ions (Na^+ and K^+) are important electrolytes in biological processes, including control of the hydration status, nerve and muscle impulse transmission, osmotic pressure balance and pH regulation. By monitoring the electrolyte imbalance caused by a wound, electrical simulation can be adjusted as needed to heal the wound site. The use of a n-type organic field effect transistor where the Gate is at the edge of the wound, the Source at the center and the Drain used as the feedback. There is a voltage gradient between the edge of the wound bed and the inner regions that would activate the transistor and allow current to flow. As the wound heals, the gradient will change, which will change the Drain current used for feedback to the microcontroller. A custom fit bandage can be printed that incorporates a microfluidic-integrated organic transistor array to allow for optimum performance. The bandage will include the electrical pads that delivers the voltage, current and pulses from the wound healing device along with feedback transistor that will monitor the healing process and provide feedback to the microcontroller on the wound healing device. The microcontroller would then adjust the driver voltage and currents to the wound site to prevent damaging the site with too much power. [4]

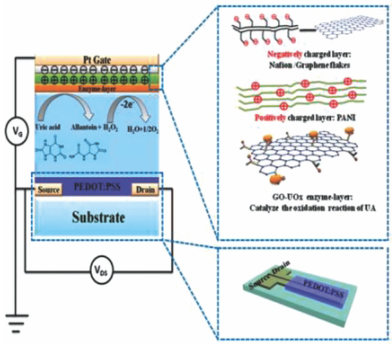

Figure 2: Flexible organic electrochemical transistors (OECTs)

4 Device Fabrication

4.1 Circuit Fabrication

All circuits were designed in Multisim and Ultiboard for the board layout, both National Instruments products. The completed designs were sent to Osh Park for board construction and Osh Stencil for solder stencil; components for the circuits were ordered from various online vendors. Sub-circuits were designed, constructed, and tested for function independently, then a completed circuit was generated, built and tested.

Figure 3: Completed Circuit

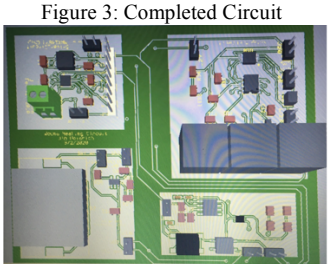

Figure 4: Ultiboard Rendering

4.2 Biofeedback Sensor Fabrication

Microfluidic test targets were created through means of traditional soft lithography [6] as seen in Figure 5. A) First, Silicon wafers are treated through a HF bath for 5-7 minutes to remove all organic particulate on the wafers surface. The wafers are then cleaned using an acetone, methanol, Di water rinse and Nitrogen gas drying. This is then put through a dehydration bake for 5 minutes at 100°C to remove any remaining liquid. B) The wafers are coated in SU-8 photoresist through means of spin coating. In this case the spin recipe was set to yield feature size 60µm deep. Following this, the wafers are put through a soft bake. C&D) The photomask containing the test target design, is then placed over the wafer and "etched" by means of UV light, or photolithography, etching the channels. E) The wafer is then post baked for 20 minutes and then developed using SU-8 developer for 15 minutes. Fully developed wafers can then be treated for 1 hour with hexamethyldisilazane (HDMS) (Sigma Aldrich, Saint Louis, MO, USA). F) Patterned water are then be coated with PDMS created using a 10:1 mix ratio (Sylgard 184, Dow Corning). G) After 1 hour of curing under 110°C and a 508 mm Hg vacuum, the PDMS is then torn from the silicon and plasma bonded using a plasma cleaner PDC-32G (Harrick Plasma, Ithaca, NY, USA) to the substrate or in this case quartz, glass, and/or a PDMS layer. A mixture of dye and glycerin are passively pumped through the device using a vacuum chamber of 558.8 mmHg. The devices are then sealed by dripping a small amount of uncured PDMS over each inlet hole and allowing for it to cure

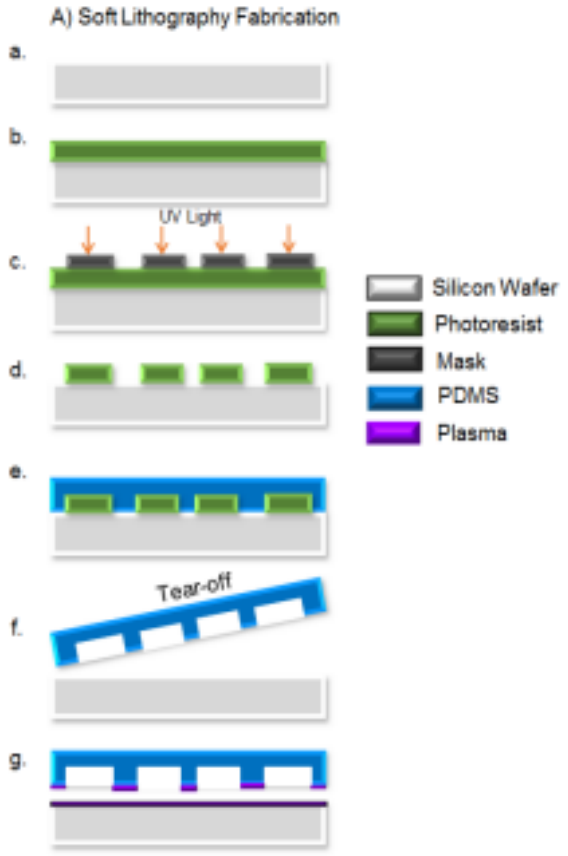

Figure 5: Microfluidic soft lithography fabrication method.

5 Results

5.1 Comsol Modeling

Comsol Multi-Physics simulation software was used to model the concept prior to construction, reference Figure 6, 7, and 8 below.

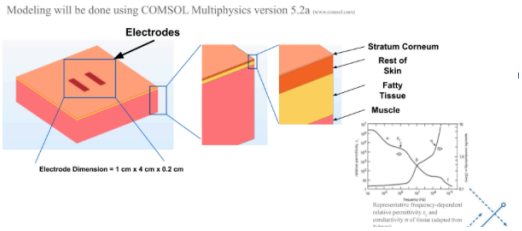

Figure 6: Comsol Computational Modeling

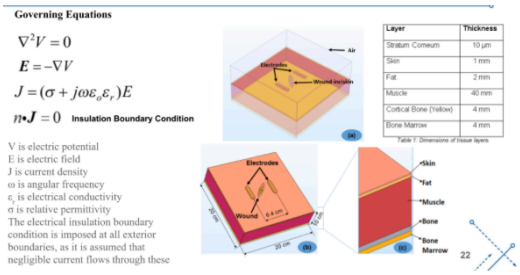

Figure 7: Comsol Preliminary Analysis

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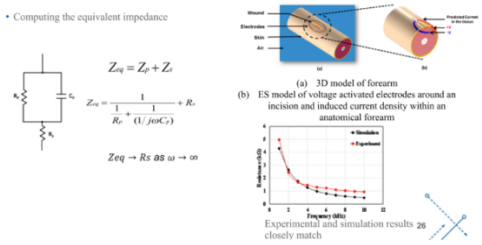

Figure 8: Equivalent Impedance of human tissue

5.2 Circuits Results

The safety cutoff, digital control, power and charging, driver, and voltage boost circuits were constructed and tested individually to ensure functionality, all performed as required. A combined circuit was constructed and an Arduino microcontroller was programmed; there were some issues stemming from human error associated with the construction, but the overall design should work as expected with better manufacturing processes.

5.3 Biofeedback Sensor

At this time, the construction date for this portion has been on hold due to extenuating circumstances starting with the pandemic.

6 Conclusions

This paper talks about the wound healing process in human skin and the need to address chronic wounds. The electronics and control circuits were shown to function as designed and will be able to deliver the necessary voltage, current, and pulses to the wound bed region to aid in the healing process. The Comsol model shows that in theory the concept discussed in this paper is feasible in the chronic wound healing process. When the addition of the biofeedback sensor is able to be completed, the device will perform as expected.

7 References

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