Bandage for Continuous Monitoring of Wound Healing

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Abstract — Chronic wounds are fraught with unpredictable and suboptimal healing processes, culminating in a physical, financial, and emotional burden to patients. Because chronic wounds are a pervasive global health issue, documented indicators of poor wound healing already exist, specifically for antigen and oxygen concentrations. Thus, instantaneous data acquisition of oxygen levels and antigen production can provide key insight into the fluctuating progression of healing. In a Smart Bandage, an immunologically sensitive field-effect transistor (IMFET) and Clark electrode oxygen sensor monitor the biomarkers of antigen production and oxygen levels, respectively; operational amplifiers used in conjunction with comparators process the biomarkers; and a 555 timer generates an actionable signal when the biomarker concentrations reach the threshold value. Design considerations include specifications such as the use of anti-inflammatory material, high device sensitivity, and wearability. In the future, issues such as fluid leakage, infection, scalability and the effects of temperature on the oximeter will need to be addressed with rounds of iterative design. Essentially, a wearable integrated system like the Smart Bandage which would enable continuous monitoring of wound healing, is a widely relevant bioinstrumentation device for applications in therapeutics and research.

Index terms — IMFET, Clark electrode, oxygen sensor, wearable.

I. INTRODUCTION

Chronic wounds are a major global health issue. Chronic wounds fail to proceed through the reparative process in a timely manner, ambiguously defined as greater than between thirty days and three months[1]. Additional shared features include any combination of prolonged/excessive inflammation, persistent infection, and formation of drug-resistant microbial biofilms. In the optimal course, wound healing consists of coagulation, inflammation, proliferation and wound remodelling. Healing often detains in one or more phases in chronic wounds. Stagnation in the inflammatory phase and an impaired proliferative phase are the common causes of the problem[2]. The usual signs of issue in acute wounds may be modified in chronic wounds to more subtle indicators[3], hindering diagnosis and treatment, and ultimately prolonging patient suffering.

A stark total of 6.5 million Americans suffer from chronic wounds[4]. Treatment often utilizes advanced and costly therapies, including growth factors, negative pressure wound therapy, and engineered skin, conclusively costing 2% to 3% of total healthcare expenditure in developed countries. In the United States, this amounts to an excess of 25 billion US dollars annually[4]. Thus, due to the associated financial, physical and emotional stress, the treatment and monitoring of chronic wounds represents an area of unmet clinical need. Due to the pervasive nature of chronic wounds, several wound biomarkers have been identified in the literature. The scope of

II. METHODS: FET, IMFET MECHANICS

A field-effect transistor (FET) controls the voltage between a gate and source, modulating the electric field to control current flow from drain to source (Fig. 1). Multiple design advantages, and how they pertain to the decision to utilize FET in the Smart Bandage, should be noted. Abnormal healing processes have small differences compared to normal healing, and the FET accounts for this with high sensitivity. Moreover, the low-cost, compact-size and low power consumption of FET increases its wearability and accessibility to the broader populace.

An immunologically sensitive field-effect transistor (IMFET) utilizes immobilized antibodies on an ion-permeable membrane as its gate to detect target antigen concentrations (Fig. 2). In brief, the IMFET changes its current flow with the variable conductance, as calculated (Fig. 3). Multiple IMFETs, each operating at the experimentally derived range, can be used in conjunction The IMFET represents an optimal choice for the Smart Bandage as it incorporates multiple caveats to increase specificity; in order to be sensed, the absorbing species on the membrane must possess a net charge, and untargeted antigens will not be detected. The increased sensitivity of the IMFET, consequently, increases the validity of the Smart Bandage.
Looking at the IMFET circuit of Figure 7, $R_{\text{effective}} = R_1 \cdot R_3 \div R_2$, and converts the current from the IMFET into a voltage. With the “Resistive T”, we are able to create a high impedance using smaller resistor values.

III. METHODS: OXYGEN SENSOR

A Clark electrode uses a platinum cathode and silver anode to react with oxygen in a small, confined space containing potassium chloride, embedded in the bandage’s polydimethylsiloxane (PDMS) membrane. The thickness of the PDMS membrane between the skin and electrode complex is 25μm, thin enough to allow a relatively timely reading as the oxygen concentration level inside synchronizes with the wound oxygen level, while still remaining thick enough to prevent fluid leakage. The membrane is designed to be insensitive to other molecules such as CO₂. A power supply of 600mV is applied between two electrodes, and a current output is collected and amplified to feed the 555 timer.

![Fig. 3: Clark Electrode Oximeter](image)

The mechanism of the Clark electrode allows it to generate a current in a linear relationship not with the concentration of oxygen in its surrounding liquid, but rather with the partial pressure of oxygen (pO₂) in the environment. The reduction of oxygen in the platinum (Pt) cathode and silver (Ag) anode can be expressed as the following:

\[
O_2 + 4H^+ + 4e^- = 2H_2O \quad (1)
\]

\[
Ag + Cl^- \rightarrow AgCl + e^- \quad (2)
\]

It is experimentally determined from previous studies⁸ that a 600mV voltage drop between the two electrodes provides the desired linearity that leads to the relationship between output current $I_{\text{out}}$ and [pO₂]. This can be represented by the following relationship, where $n$ is the number of electrons; $F$ is Faraday’s constant; and $S$ is the sensitivity of the electrodes determined from the diameter of the electrode $d$, thickness and diffusion coefficient $D_m$ of the membrane⁹, and the charge $nF$ accumulated between the electrodes.

\[
I_{\text{out}} = S [pO₂] \quad (3)
\]

\[
S = nF D_m \quad (4)
\]

With the defined parameters - electrode diameter of 25μm, voltage drop of 600mV and PDMS membrane thickness of 25μm - previous literature⁸ has experimentally determined the device sensitivity to be approximately 20pA/mmHg, and 99% of the current response can be achieved in 25s at 37°C ⁸.

In human tissues, a healthy level of [pO₂] is no less than 30-40 mmHg. Unhealthy tissues experiencing hypoxia have a level of 10-20mmHg⁸. Hence, any current output lower than 400pA, based on (3), will mark the threshold value for a depravity of oxygen in the wound tissue. As a result, since most 555 timers require a voltage input at 0-1 V magnitude, an amplification of 1.25*10⁶ is required using Operational Amplifiers (Fig. 4).

IV. METHODS: COMPARATORS and 555 Timer

Comparators serve to provide a binary output by comparing the two inputs. If the positive terminal input is greater than that of the negative terminal input, the positive terminal output is returned. If the positive terminal input is less than that of the negative terminal input, the negative terminal output is returned. For our circuits in Figures 6 and 7, the output is either +0.5V or 0.0V.

An astable 555 Timer works to generate a periodic square wave when a certain voltage threshold is reached. Provided that the frequency of the square RF wave is 402 MHz for the Clark electrode and 405 MHz for the IMFET, the circuit component values can be determined using a design specification for the duty cycle (5,6). Duty cycle is the ratio of time the circuit is on versus off, and was made to be 50% with the addition of a diode—a semiconductor that allows current to flow in a singular direction—to pins 2 and 7 of the 555 timers.

![Fig. 4: Gain Amplification, G=1.25*10⁶](image)

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V. RESULTS

The final Smart Bandage circuit design (Figs. 6 and 7, corresponding circuit elements Table 1) incorporates signals from both the Clark electrode and IMFET, monitoring oxygen
and antigen production respectively, with the comparators and astable 555 timers. The Clark electrode signal, RF signal 1, produces a 402 MHz square wave, and the IMFET signal, RF signal 2, produces a 405 MHz square wave, both of which are within the MedRadio frequency band for diagnostic medical devices\[^{11}\]. By creating circuits that generate two different frequencies, we allow for greater specificity in the design: the physician or nurse is able to identify whether oxygen or IL-6 levels are aberrant in the patient’s wound based on what frequency the wireless receiver senses.

**Table 1. Circuit Component Values for Figs. 6 and 7**

<table>
<thead>
<tr>
<th>Circuit Components</th>
<th>Value</th>
<th>Circuit Components</th>
<th>Value</th>
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<tbody>
<tr>
<td>(resistor) R_A</td>
<td>50 MΩ</td>
<td>R_1</td>
<td>60 Ω</td>
</tr>
<tr>
<td>R_B</td>
<td>1 kΩ</td>
<td>R_2</td>
<td>100 Ω</td>
</tr>
<tr>
<td>R_C</td>
<td>25 kΩ</td>
<td>R_3</td>
<td>178 Ω</td>
</tr>
<tr>
<td>R_D</td>
<td>30 Ω</td>
<td>R_4</td>
<td>178 Ω</td>
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<tr>
<td>R_E</td>
<td>20 Ω</td>
<td>R_5</td>
<td>86 Ω</td>
</tr>
<tr>
<td>R_F</td>
<td>4000 Ω</td>
<td>R_6</td>
<td>86 Ω</td>
</tr>
<tr>
<td>R_G</td>
<td>1000 Ω</td>
<td>(capacitor) C_0</td>
<td>10 pF</td>
</tr>
<tr>
<td>R_H</td>
<td>2 Ω</td>
<td>C_1</td>
<td>10 pF</td>
</tr>
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Using an alternating current source with amplitude of 400pA and offset of 400pA at frequency of 0.1Hz in the Multisim simulation software, a voltage output of the comparator to serve as the input of the 555 timer was developed (Fig 8).

**Fig. 8: Output Voltage from Oximeter, which models the variable voltage the Clark electrode may produce from the wound bed environment**

The model (Fig. 9) for the Smart Bandage utilizes inlets to allow for cross-communication between the electronic components and wound bed.
VI. DISCUSSION

While the design outlined in this study certainly holds incredible potential, there are limitations associated with the Smart Bandage. The accuracy of the device will require finetuning be hindered by some aspects of the oximeter. The oximeter is temperature sensitive, which may be of particular interest as infected or otherwise compromised wounds often have elevated temperatures\[9\]. The oximeter utilizes oxygen, which may have the unintended consequence of misreading the oxygen levels of the applied area. However, certain design considerations may address these concerns. If the device vibrates continuously, its overall accuracy would increase due to the constant agitation. A small area of wound contact will limit the oximeter’s intake of oxygen from affecting oxygen readings, also addressing any unintended changes acquired from the fact that deprivations of oxygen are unevenly distributed far from the center of the wound. An internal calibration system can ensure the final output display of oxygen concentration correlates for the oximeter’s intake of oxygen and inaccuracies caused by distance from the wound center.

These uncertainties will be further exacerbated by the large output voltage gain applied on the oximeter current. Although a thin membrane can ensure the device temperature is identical to the wound surface temperature, not all wound surface temperatures will be around 37\(^{\circ}\)C; the thickness of the newly generated protective tissue, as well as the depth and location of the wound can affect the results. As such, it must be stipulated the current iteration of the Smart Bandage will function optimally on fresh, open wounds.

Future research is needed to develop a mature product. Effectively amplifying the sensor output and determining the accuracy of the sensors are the two important factors in terms of the device accuracy. Moreover, it is as important to determine whether the device will negatively impact wound healing, and the associated severity as a function of time will need to be determined. A potential research direction is to test whether adding anti-inflammatory substances in PDMS membrane will promote healing. The incorporation of multiple biomarkers with the use of OR logic gates connected to the IMFET 555 timer would further increase the information potential of the Smart Bandage. The use of colored LEDs for each sensor could further increase ease of interpretation for healthcare professionals. To reduce the power consumption of the device, we could also use TLC555 timers, which operate with less power than the standard 555 timers.

The Smart Bandage can revolutionize the monitoring of wound healing in therapeutics and research. In terms of therapeutics, while the general observation of chronic wounds will most certainly hold potential, the device’s convenience and applicability particularly aligns with the needs of non-communicative patients. Unconscious, pediatric and neonatal, and otherwise non-communicative patients will have their needs attended to in a timely manner with the Smart Bandage. Additionally, remote care can be provided with the wireless remote wound monitoring device. In terms of research, the Smart Bandage can aid in the pursuit of comprehensive drug testing and toxicological evaluation, as methods for evaluating how various treatments might expedite or harm the healing process in preclinical and clinical situations.

Overall, the real-time data acquisition of oxygen levels and antibody production provided by the Smart Bandage creates a multiple-parameter, wearable point-of-care system that will allow for the monitoring of the dynamic wound healing processes in therapeutic and research pursuits.

VII. REFERENCES


Fig. 10: The Smart Bandage can have various wound-healing properties added.