Dove: Shoulder-Based Opioid Overdose Detection and Reversal Device

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ABSTRACT

Naloxone is a life-saving drug capable of reversing a fatal opioid overdose. Although this drug has existed for over 50 years, opioid overdose-related deaths have consistently risen and surpassed 120,000 globally in 2021. Opioids induce respiratory depression by activating μ-opioid receptors at specific sites in the central nervous system. This results in overdose deaths caused by slow and shallow breathing, also known as opioid-induced respiratory depression. 1.6 million individuals suffer from opioid use disorder annually, making them at high risk of overdose, primarily due to the increasing prevalence of Fentanyl. Over 52% of these deaths occur when the individual is alone. Immediate response to an overdose by delivering naloxone can save the individual's life. To solve this problem, we developed a closed-loop sensor-driven auto-injector that can determine a fatal overdose and inject naloxone. 76% of this population is willing to wear such a device on the shoulder, a canonical injection site. This paper presents the DOVE, a shoulder-based opioid overdose detection and reversal device. It noninvasively measures the subject's motion state and changes in blood oxygen levels (SpO_2) along with the respiration state. These biomarkers are measured from the shoulder using an optical sensor and accelerometer to determine if a fatal overdose occurred. We evaluated our DOVE device against an FDA-cleared commercial pulse oximeter by inducing apneic events as they have very similar SpO_2 trends to an overdose. Results show that SpO_2 can be measured on the shoulder across different skin tones with an accuracy of 96.8% and a high Pearson correlation of 0.766 ($p < 0.0001$).

KEYWORDS

Opioid Overdose, Optical Spectroscopy, Wearable Device

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1 INTRODUCTION

Opioid Use Disorder (OUD) is a chronic brain disease which impacts over 16 million people worldwide as of 2021 [9]. The economic burden on the U.S caused by OUD and fatal opioid overdose during 2017 totaled close to $1 trillion [20]. In 2020 150 million opioids were prescribed in the U.S [6]. Although, the rate of opioid prescriptions has decreased over the last decade, overdose deaths have increased by 38% between 2019 and 2020 [7]. Naloxone is an opioid receptor antagonist which blocks the effect of opioids, thereby reversing an overdose. Opioids affect the region of the brain that controls an individual's respiratory system. This leads to respiratory depression during a fatal opioid overdose, meaning the affected individual stops breathing [49]. Delivering naloxone immediately reverses the effects of opioid drugs, restoring normal breathing within two to three minutes [58, 29]. The current commercially available methods for delivering naloxone to reverse an opioid overdose require a trained bystander to administer a intranasal nasal spray or intramuscular injection. Furthermore, more than half of opioid overdose deaths occur when the individual is alone [44]. In our previous work, we found that 76% of OUD patients were willing to wear a device which can both sense an opioid overdose and inject naloxone if the device is concealable and on the shoulder [28].

This paper takes a patient-centric approach in developing a device to detect a fatal overdose along with the ability to inject nalaxone to reverse it. We focus on non-invasively detecting SpO_2, state of respiration, and body motion. We combine these biomarkers to estimate if the individual is experiencing a fatal overdose which in turn triggers the injection mechanism. We look at both state of respiration and SpO_2 to decrease false positives when estimating an overdose. This is vital in maximizing patient adherence due to their aversion towards receiving naloxone [32]. Finally, our

drug-delivery prototype allows us to deliver naloxone through subcutaneous/intramuscular injections, forming a closed-loop system.

We address the following research questions:

RQ1: How do we accurately monitor patient vitals including SpO_2, state of respiration, and state of consciousness, on a non-canonical sensing site: the shoulder?
RQ2: How can we normalize the optical sensors specific to each user's skin tone and human physiology?
RQ3: How can we create a wearable device that can provide life saving interventions for opiod overdose?

The traditional opioid overdose reversal tools that exist commercially require a trained bystander to recognize an overdose and administer naloxone. Opioid overdose detection tools are already being developed [39, 63, 48, 10]. Detection and overdose-response closed-loop devices using a single biomarker are also being researched to reverse an overdose when a subject is alone [8, 26, 13]. Enabling researchers, clinicians, scientists, and even the general public with a more comprehensive wearable overdose prevention device will increase the amount of meaningful data collected as well as lead to novel clinical applications. Compared to prior work, our ability to detect both SpO_2 and respiration rate on an injectable site enables us to develop a modular, closed-loop device that patients are willing to wear.

Our contributions are summarized as follows:

(1) A shoulder-based sensor capable of creating longitudinal datasets of the subject's motion levels, SpO_2, and respiration state non-invasively.
(2) An algorithm to normalize optical-sensor measurements based on the subject's skin tone and human physiology.
(3) An sensor-triggered injector prototype capable of delivering naloxone into the subcutaneous/intramuscular region.

The remainder of our paper is structured as follows: Section 2 summarizes the work related to this paper. Section 3 introduces the DOVE hardware, including the components used, its form factors, and the underlying theory that supports its operation. Section 4 describes the system architecture and normalization process. Section 5 evaluates the hardware prototype and our algorithm. We conclude the paper with a discussion on future work in Section 6.

2 RELATED WORK

We introduce spectroscopy and discuss its use in health care monitoring. We then discuss wearable optical sensing of respiration rate, and blood oxygenation using pulse oximetry on a noncanonical site. Finally, we examine existing implementations of wearables focused on the detection and reversal of opioid overdoses.

2.1 Optical Spectroscopy

Spectroscopy is the study of spectra produced when electromagnetic radiation and matter interact. It is an important technique that is applied in multiple sectors, such as medical radiology, forensic science, and agriculture. Common types of spectroscopy include atomic spectroscopy [30], ultraviolet and visible spectroscopy [61], infrared spectroscopy [60], Raman spectroscopy [60], and nuclear magnetic resonance [25]. This can be further classified into absorption and emission spectroscopy. Photoplethysmography (PPG) is an application of spectroscopy commonly used in several health-monitoring wearable devices such as smartwatches, pulse oximeters, and performance trackers.

Optical wearable sensors allow for the continuous monitoring of various biomarkers. The basis of wearable optical sensing involves a light source to introduce light of different wavelengths into the body through the skin and a photodiode to capture changes in the light [41]. Although optical spectrometers have become a part of our everyday life in health tracking, their monitoring functionalities have been limited to canonical sites such as the fingertip or earlobe due to lower intersubject variability and higher perfusion rates. For example, smartwatches leverage PPG sensors on the wrist whereas pulse oximeters on the finger can detect pulse rate, blood oxygen levels, atrial fibrillation, body temperature, and blood pressure [55, 46]. Even forehead reflectance pulse oximetry has gained market acceptance as a replacement for other traditional sites in the event of compromised circulation [56, 38].

2.2 Non-canonical Spectral/Optical Sensing

Beyond the canonical sites for spectra and optical sensing listed above, research has begun exploring non-canonical sites as viable locations for optical sensors [31, 51, 35]. These sites provide researchers with new opportunities when developing devices that leverage optical-sensing capabilities. These devices are capable of not only monitoring biomarkers, but also providing treatment at the noncanonical sites. For example, the arm provides a location where recovery drugs can be injected into the deltoid [14, 16]. A device could be placed here which is capable of sensing motion, SpO_2, and respiration rate on the arm [31] and injecting naloxone, the reversal drug if the biomarkers indicate an overdose.

Due to high blood perfusion, canonical sites for PPG detection in a medical setting are on the finger and ear lobes. Analysis of PPG signal quality on other sites, such as the chest, arm, toe, wrist, and forehead, has shown lower signal strengths. It is more complex to estimate the biomarkers on these sites compared to the finger. However, studies have shown the feasibility of detecting SpO_2 on the chest [51] and calf [31] with reasonable accuracy compared to the finger. The forearm is also capable of detecting respiration and pulse rates [40], as is the forehead which outperforms the finger when motion is introduced [35]. The Moxy and PortaMon [37] are commercial examples of Near-infrared spectroscopy-derived muscle oxygen saturation (SmO2) monitors [19]. They are used to determine muscle oxygenation levels during workouts and exercises noninvasively on any muscle. These works motivate our choice of a non-canonical site, the shoulder, for development of our device.

2.3 Wearable Overdose Treatment Devices

The opiod epidemic is a growing problem in the U.S [20]. Over 47,000 deaths resulted from opiod overdoses in 2017 [59]. As respiratory depression is common during an overdose, bystanders are relied upon to administer life saving interventions [50], including delivery of naloxone, a medicine that rapidly reverses an opioid overdose, and calling emergency medical services. In many cases, however, overdoses occur when the person is alone [44]. Wearable devices solve this problem by making life-saving interventions available to the person in this case.

Few overdose detection and reversal devices have been previously researched. Respiratory depression is typically used as the sign of an overdose. Once detected, these devices employ various drug delivery solutions. Respiratory depression is estimated using noninvasive measurement of oxygenated and deoxygenated hemoglobin through the skin, accelerometric values of chest movement, mobile sonar technology, and electrocardiography (ECG). The goal is to build a device that detects the overdose and then administers a life-saving intervention such as the delivery of a medication. Even in research outside of drug overdose, closed-loop sensor-driven auto-injectors have been an elusive objective. For example, this can be seen in continuous glucose monitors interfacing with insulin pumps which have only achieved a hybrid closed-loop system status [53].

Chan et al. focuses on monitor breathing cessation caused during an opioid overdose [8]. They use multiple accelerometers on the abdomen to reliably track diminished respiratory motion. If the device detects cessation of breathing over 15 seconds, it triggers the injection mechanism, a commercial subcutaneous injector preloaded with naloxone. Their device was validated on 25 participants at a supervised injection facility to accurately track respiration in a real-world opioid use environment. Their off-the-shelf injector mechanism was validated on 20 participants in a hospital setting showing naloxone being delivered as expected.

Dhowan et al. explores the usage of minimally-invasive implantable high-density polyethylene-based naloxone delivery capsule that can release the drug when heated by a radio-frequency magnetic field externally adhered on the arm [13]. The capsule is placed percutaneously via a trocar or a biopsy needle in an outpatient setting. The patient's electrocardiogram (ECG) is monitored on their chest to determine respiration rate and cessation of breathing as a biomarker for an opioid overdose to trigger the magnetic field that heats the drug capsule, thereby releasing naloxone. Respiration rate that was used in the previous examples as a biomarker for overdose detection can also be monitored wirelessly using smartphones implementing sonar [39].

Unlike the previous examples, Imtiaz et al. monitor SpO_2 values on the arm and determine a fatal overdose when the subject shows signs of hypoxia [26]. The individual is classified as hypoxic if their SpO_2 levels drop below 90% [5, 3, 43], triggering the injection mechanism actuated by compressed gas. In this injection mechanism, Nalmefene is administered instead of the conventional naloxone. This is due to its longer half-life and effects against newer, high-affinity, long-acting, synthetic opioids [57, 23, 17].

Different from the above discussed approaches, the DOVE device approaches the closed-loop injector system with a patient-centric design. It senses SpO_2, respiration state and motion levels noninvasively from the shoulder which is a canonical injection site. The size and form factor of the device increases patients' willingness to wear such a device. The ability to combine respiration state and SpO_2 allows us to detect a fatal overdose, thereby decreasing false positives and increasing patient adherence. Finally, our normalization mechanism allows for calibration of the optical sensors specific to each user's skin tone and human physiology.

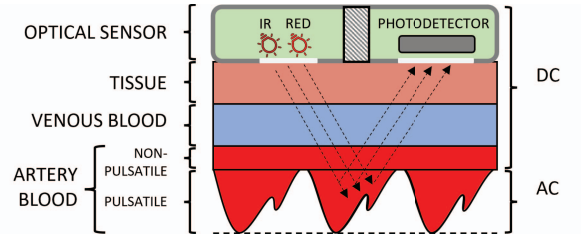


Figure 1: Principle of photoplethysmography.

3 DEVICE DESIGN

In this section, we discuss the hardware that makes up the DOVE. We first examine the theory of operation and its applications in determining a fatal opioid overdose. Then, we describe the 3D printed form factor created to house our device and comfortably fit the curvature of the shoulder. Finally, we discuss the off-the-shelf components and circuitry used to create our device.

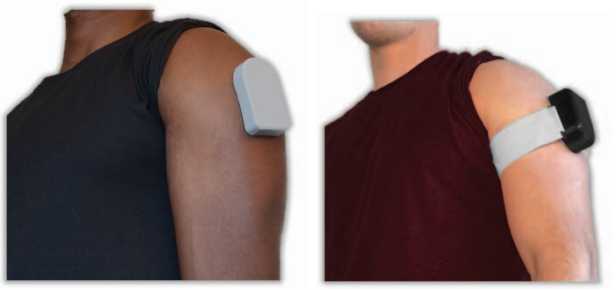
3.1 Theory of Operation

PPG is an optical technique for detecting changes in blood volume within the tissue bed [2]. A PPG waveform is generated by illuminating the skin and measuring changes in light base on absorption or reflectance. It is a low-cost, non-invasive sensor that collect readings on the skin's surface. PPG technology has been used in many commercially available medical devices for measuring oxygen saturation, respiration rate, heart rate, blood pressure, and cardiac output, assessing autonomic function, and detecting peripheral vascular disease [2]. The PPG signal or waveform consists of a pulse ('AC') waveform and a slowly varying ('DC') baseline waveform as shown in Fig. 1. The pulsatile waveform is caused by changes in the blood volume with each heartbeat. This is superimposed on the slowly varying ('DC') baseline with various lower frequency components attributed to respiration, sympathetic nervous system activity, and thermo-regulation [2].

Traditionally, pulse oximetry is done by emitting light at various frequencies and measuring the amount transmitted or reflected by peripheral tissues. Transmission-based pulse oximetry places the photodetector on the opposite side of the finger from the light source. Reflectance-based oximetry places the sensor and light source on the same side of the detection site. Studies have shown both transmission and reflection-based devices can provide accurate oxygen saturation measurements [36]. Peripheral oxygen saturation SpO_2 readings on the finger are within 2% of the more accurate and invasive arterial oxygen saturation (SaO_2) from arterial blood gas analysis [42]. Due to it high accuracy SpO_2 is used to determine hypoxemic events caused by a fatal opioid overdose.

3.2 Form Factor

The DOVE is 70mm x 40mm x 18mm, which is 1.6 times the size of the Omnipod®, a commercially available insulin pump. The DOVE is a slightly larger device as it houses both the injector and sensor. It also requires a rechargeable battery, unlike the Omnipod, a one-time-use device that lasts three days. The DOVE consists of 3D-printed parts and a few additional easy-to-find components. The base of the device is designed considering the deltoid's curvature. The curved base ensures that the sensor and injector have



(a) Adhesive (b) Strap

Figure 2: DOVE form factors.

maximum contact with the skin. The current form factors use an arm-band strap or bio-compatible double-sided medical adhesive from 3M [1] to fasten the device onto the shoulder as seen in Fig. 2. The curved base on the device allows for a better fit and longer adhesive lifespan. The adhesive allows for a clean fixture, decreasing the device's movement and constant pressure against the skin. Although longer-lasting adhesives are available in the market, the recharge requirements of the device require constant removal and replacement of patches. We've chosen biocompatible adhesives that last three to five days to improve the ease of fastening and removing the device. The strap mechanism can be reused multiple times and removed when not in use. While the strap mechanism makes it easier to wear, it lacks contact stability against the shoulder. The device placement and fastening ability vary based on positioning and tightness of the strap on the shoulder.

3.3 Components

The DOVE consists of two primary mechanisms, the sensor and the injector. The sensor ensemble uses an accelerometer and an optical sensor. The accelerometer is used to determine the individual's state of motion. The optical sensor collects raw PPG data using reflectance pulse oximetry. The injector delivers the reversal drug subcutaneously. The sensor and injector components are controlled by a microcontroller and powered by a battery. To house these electronics, a custom-printed circuit board (40mm x 45mm x1.6mm) was developed to ensure a small footprint to fit into our form factor. Figure 3 shows the component-level diagram for our device.

Accelerometer: A 6-axis Inertial Measurement Unit is used to measures 3D accelerometry and gyroscopic data relative to the force of gravity. The LSM6DS3 sensor consists of an accelerometer and gyroscope that is used to detect whether an individual is in motion or motionless. The accelerometer is also used to determine respiration rate by monitoring their shoulder motion during inhalation and exhalation. Only the accelerometer component is used as the gyroscope consumes ten times higher battery usage [54]. The LSM6DS3 sensor consumes 24μA when continuously collecting motion data at 13Hz. During a fatal opioid overdose, the individual is motionless and shows a lack of response when alerted. This also allows us to duty-cycle the device, optimizing battery consumption to enable the optical sensors only when needed.

Optical sensor: The MAXREFDES117S sensor from Maxim Integrated is used for SpO_2 estimation due to its high Signal-to-Noise

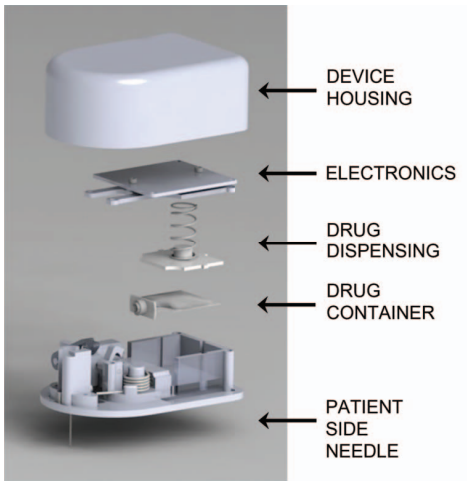


Figure 3: The DOVE injector mechanism.

Ratio, size, and low power consumption. Reflectance pulse oximetry is implemented in this scenario as light cannot fully travel through the deltoid to show an optical response on the other side [15]. The light sources and sensor are placed side by side as seen in Fig. 1 for reflection-based measurements, which gives more flexibility for on-body locations of measurement [38, 11]. It consists of the heart rate/SpO_2 sensor (MAX30102), an efficient, low-power step-down converter (MAX1921) that allows a 2V to 5.5V supply at the power input and ensures 1.8V power supply to the sensor, and an accurate level translator (MAX14595) for I2C communication. The entire design typically operates at less than 5.5mW and is 12.7mm x 12.7mm in size. The MAX30102 uses red and infrared light-emitting diodes of wavelengths 660nm and 880nm to illuminate the deltoid and measure the light reflected using a photodetector. The output of the sensor is in the form of analog-to-digital Conversion counts with 18-bit precision. The raw red and infrared PPG samples are sent to the microcontroller over a four-second window to estimate SpO_2 after filtering the noise from the signal.

Injector: The injector is used to deliver naloxone either subcutaneously or intramuscular when an overdose is detected. The injector mechanisms consists of three subcomponents: a drug storage unit, a patient-side drug delivery needle which injects and retracts when overdosing, and the drug-delivery trigger. The drug storage unit consists of a mini-bag (35mm x 35mm) which can store up to 2mL of any drug. It is made of Polytrifluorochloroethylene (PCTFE) or Cyclic Olefin Copolymer (COC) flexible film which allows it to be thin, free shape, unbreakable and, known to be patient safe. The patient-side needle consists of a 15mm long 19 gauge needle stored in a retracted state behind a sanitary sheath. The injection and retraction mechanism is controlled by a micro-metal gear motor constrained by a limit switch. The patient-side needle is connected to the drug-delivery trigger by a tube. The drug-delivery trigger consists of a latch holding a spring-loaded secondary needle that is used to puncture the mini-bag. During the injection process, the motor torques the lever clockwise, pushing the patient side needle downwards, which triggers the drug-delivery mechanism.

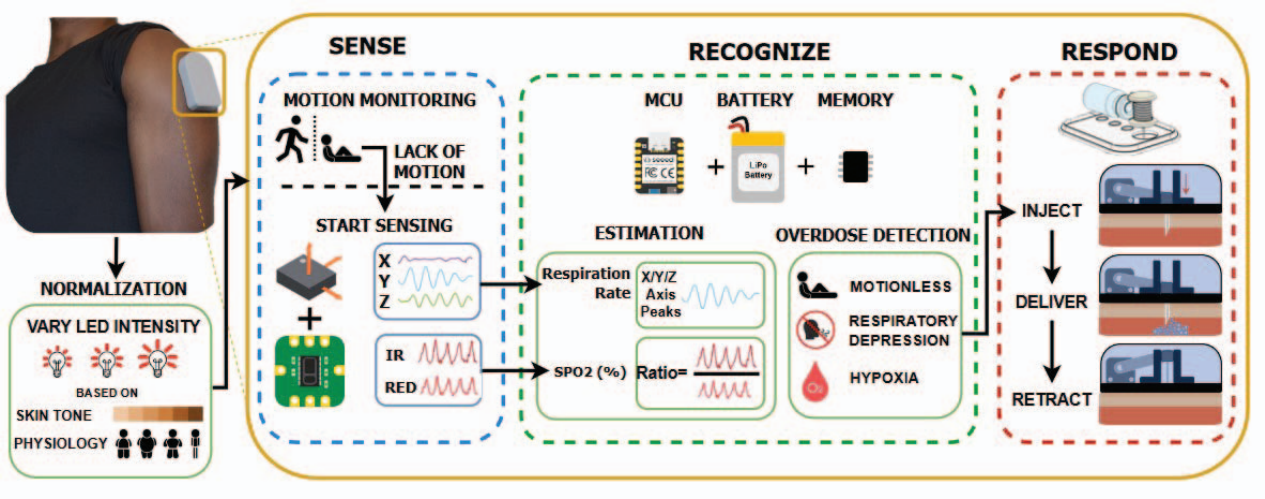


Figure 4: The DOVE system architecture.

As the needle moves downward, penetrating the user's skin, the spring-loaded needle facing the mini-bag is released. The secondary needle punctures the mini-bag forcing the drug to travel through the secondary needle into the patient via the sterile tubing and patient-side needle. Once the drug is delivered, the patient-side needle is retracted.

The Seeeduino XIAO BLE Sense was chosen to control the sensor and injector due to its high processing power, ultra-low power mode, and size. The Seeeduino has an ARM Cortex-M4 processor with Bluetooth 5.0 capability, battery management, and an accelerometer. This allows us to power the device using a 3.7V lithium polymer rechargeable battery with a 400 mAh capacity, giving us approximately twenty hours of battery life at peak usage. The PCB also has a 32MB external flash memory to store raw PPG and accelerometry data locally, making the device portable for real-world studies.

4 SYSTEM ARCHITECTURE

The DOVE system is a real-time opioid overdose prevention support system which evaluates biomarkers and injects Naloxone into patients at risk of dying from an overdose. It uses motion and PPG techniques to identify a fatal opioid overdose. DOVE consists of three major components: a sensor ensemble, an opioid overdose estimation algorithm, and an injection system. The sensor ensemble consists of an optical sensor and accelerometer to collect raw PPG data and motion readings non-invasively. The overdose estimation algorithm calculates heart rate, SpO_2, and motion state, which is used in combination to determine a fatal overdose. The injection system is triggered when the SpO_2 readings show signs of respiratory depression and the user does not respond to the alert. It triggers the device to inject Naloxone subcutaneously to reverse the overdose. Figure 4 provides an overview of the DOVE system.

4.1 Normalization and Duty Cycling

The PPG signal quality is affected by several factors such as skin tone, environmental light, applied pressure change against the device, human physiology, and blood perfusion. To maximize accuracy and decrease the impact of these factors, each LED's brightness is normalized precisely to the wearer and to the environment. This initial normalization process occurs automatically each time the user fastens the device. It takes approximately two to five seconds to normalize both LEDs each time the user removes and wears the device. The normalization process is necessary to mitigate over and under-saturation on the detector side.

The normalization process adjusts the light intensity until a targeted reading is obtained at the photodetector. We calibrate each LED's brightness on the photodetector to maximize the perfusion index. The optical sensor has an 18-bit resolution giving us a maximum value of 262,143 counts. The targeted range is set between 200,000 to 260,000 counts. The iterative calibration process is performed by adjusting the current to the LED using the 8-bit LED driver on the optical sensor that adjusts the light intensity until it reaches our targeted value. This adjusts the LED with a resolution of 0–255, approximately 0–50mA. Altering LED intensities does not affect SpO_2 accuracy at values above 85% [12]. At each iteration i, we calculate the error between the targeted reading r_t and the current reading r_i. A proportional controller calculates the adjustment required for each LED to achieve the desired count value in which the gain K_p is the ratio of output response to the error signal. During each iteration, we calculate the intensity I as

$$I_{i+1} = K_p(r_t - r_i). \tag{1}$$

Once the new intensity value is calculated, we update the LED and repeat the process until the targeted reading is reached. The value of K_p determines the rate at which the controller converges. Using $K_p = 0.01$ converges the fastest with an average of 4.8 steps and a duration of 2.4 seconds. In general, this iterative process is completed between two to fifteen iterations (or between three to five seconds). The intensity normalization for the red LED based on different skin tones is shown in Fig. 5. Overall, we found that skin tones with higher melanin content require higher LED intensity value due to light absorption.

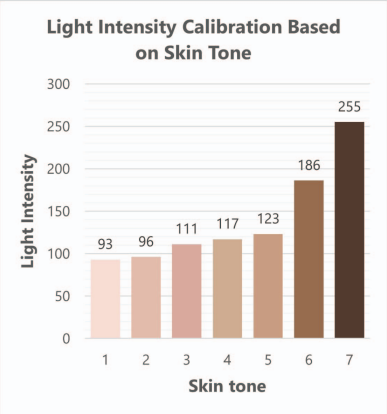


Figure 5: Impact of skin tone on LED calibration values.

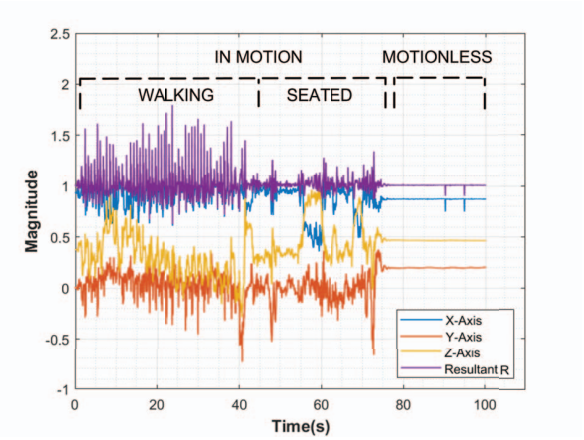


Figure 6: Monitoring motion using accelerometer values.

A 400 mAh LiPo battery powers the Seeeduino microcontroller, optical sensor, accelerometer, and DC motor. The device can last up to twenty hours at maximum battery consumption, which can be optimized by using the optical sensors only when the wearer is motionless. The Seeeduino consumes 5μA when used in ultra-low power mode. The low power mode, combined with the LSM6DS3 accelerometer, monitors the individual's motion levels and wakes the MCU when needed to collect optical data from the sensor, thereby increases battery life by up to 72 hours of continuous monitoring. The LiPo battery, along with the battery management system on the Seeeduino, allows us to recharge the device for reusability, unlike similar devices like the Omnipod®.

4.2 Vital Signs Monitoring

The DOVE continuously monitors the individual's vital signs by sampling longitudinal data to determine their motion state, responsiveness to stimuli, respiration rate, and blood oxygenation. First, we determine the motion levels of the individual to understand if they are in motion or motionless and optimize battery usage accordingly. Second, after denoising the signals we convert raw PPG waveform data into SpO_2, and 3-axis accelerometry data into respiration data. Finally, we identify if an overdose has occurred based on the calculated biomarker values.

Determining motionlessness of the individual is critical as body limpness is a key indicator of an overdose [49]. Furthermore, motion estimation is necessary for battery optimization. Motion is also used as a response to stimuli caused by the overdose alert mechanism. The LSM6DS3 6-axis IMU sensor uses an onboard accelerometer at 24Hz during low power mode and 104 Hz if the subject becomes motionless. The raw accelerometer reading contains a 3-axis vector $\{x, y, z\}$ that is used to determine the vectorial sum R_{Motion} (discussed in Section 4.3).

Accelerometry is also used to determine the individual's respiration rate since respiratory depression and apneaic events are other symptom of a fatal overdose [49]. American Academy of Sleep Medicine states that apneas can last for ten or more seconds [4]. A ten-second threshold is too low in terms of apnea detection within the OUD population [8]. This could result in higher false positives, thereby decreasing patient adherence. Opioid-induced apneas are simulated by not breathing for fifteen seconds [8]. Respiration rate is determined by monitoring the motion caused during inhalation and exhalation. Similar to determining the subject's motion state we analyze the 3-axis vector $\{x, y, z\}$ data individually to determine their respiration state. The respiration state is broken down into breathing normally versus depressed breathing.

Pulse oximetry is used to monitor oxygenation SpO_2 levels to determine the presence of hypoxemia [27]. Hypoxemia caused by respiratory depression, when combined with motionlessness, indicates an opioid overdose. In a clinical setting, hypoxemia is defined as $SpO_2\% < 88$. Optical sensors are commonly used to continuously monitor an individual's heart rate and SpO_2. We use the MAX30102 optical sensor placed on the deltoid to record red and infrared light reflected by peripheral tissues. The sensor's housing ensures maximum contact against the skin and is held in place by a biocompatable adhesive. The photodetector on the sensor samples the reflected light at 400Hz with an 18-bit. The LEDs are set to 411μs pulse width as the deltoid has more tissue layers compared to the finger. A sampling average window of 16 is used to denoise the ADC counts. It averages sixteen samples into a single sample. The raw ADC count values for both wavelengths are recorded at 25Hz after the sampling average is applied. SpO_2 is continuously monitored when the subject is determined motionless.

4.3 Data Processing

The raw values recorded by the accelerometer and optical sensors are denoised and filtered, and then used to calculate motion, respiration rate, and SpO_2 levels. Accelerometry data is processed first as motion data critical to optimizing battery usage. Depending on the motion state, the optical sensors are activated to monitor respiration rate, and SpO_2. The 3-axis vector from the accelerometer is used to determine the individual's posture and motion state. The sampled data is smoothed using a moving-average filter over one second and motion state is determined using the vectorial sum as

$$R_{\text{motion}} = \sqrt{x^2 + y^2 + z^2}, \tag{2}$$

which is visualized in Fig. 6. Motion can be classified into in-motion and motionless states which are determined by monitoring the

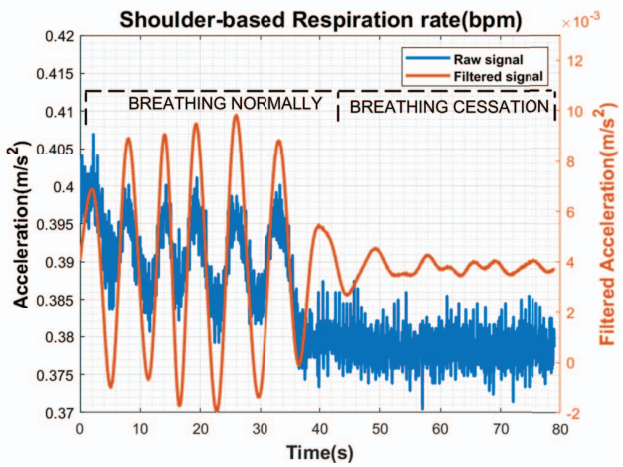


Figure 7: Detecting respiratory rates.

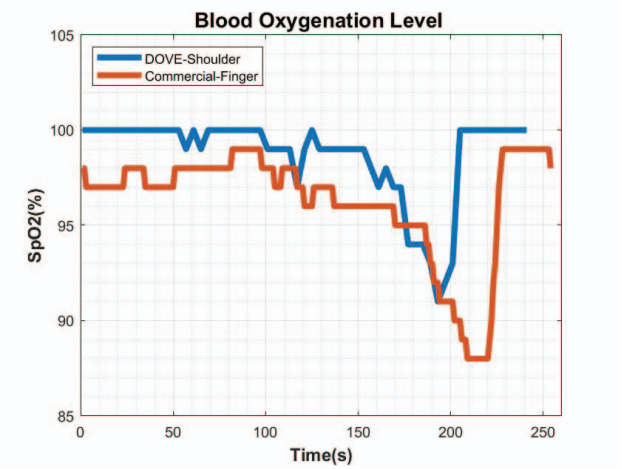


Figure 8: Blood oxygenation levels calculated by DOVE compared to a commercial pulse oximeter.

standard deviation of R_{motion} over ten seconds using a threshold for motionlessness based on lab testing. The individual is determined as responsive if the R_{motion} values exceed the set threshold. If R_{motion} is less than the threshold for more than ten seconds, the optical sensors are activated to monitor the SpO_2 readings.

Respiration rate is calculated from the accelerometry signals based on the periodic movement of the deltoid caused by breathing. Fifteen-seconds epochs are monitored to determine if the individual exhibits breathing cessation. We can detect respiratory patterns when the individual is sitting, sleeping, or in a passed-out state leaning on the sensor, as shown in Fig. 7. The 3-axis vector data is analyzed, and the axis with maximum peak-to-peak periodic motion is chosen. The signal is then filtered of high-frequency noise greater than 0.5Hz using a 4th-order Chebyshev Type II filter [34]. A peak detection algorithm is then used to estimate the respiration rate as breaths per minute. During breathing cessation, all three accelerometry axes lack inhalation peaks. Lack of respiration over fifteen seconds in combination with the SpO_2 levels dropping are indicators of a fatal opioid overdose.

SpO_2 is estimated from raw analog-digital conversion (ADC) counts generated by the photodetector interacting with the reflected red and infrared light. The raw values are filtered using a Chebyshev Type II band-pass filter removing removing frequencies lesser than 0.75Hz and greater than 3Hz. Four-sec epochs are taken for each SpO_2 estimation consisting of 100 raw ADC counts. Next, baseline drift is corrected by detrending the windowed signal. Once the raw ADC counts are preprocessed, SpO_2 is calculated by comparing the AC and DC components of both wavelengths as shown in Fig. 1 to calculate the ratio

$$R_{SpO_2} = \frac{\frac{AC_{red}}{DC_{red}}}{\frac{AC_{ir}}{DC_{ir}}}, \tag{3}$$

which is then used to estimate SpO_2 by using the calibration coefficients $\{a, b, c\}$ provided by the sensor manufacturer as per

$$SpO_2 = aR^2_{SpO_2} + bR_{SpO_2} + c. \tag{4}$$

The calibration coefficients are calculated by the sensor manufacturer by comparing the $RSpO_2$ values against SaO_2 in a hypoxia lab [21]. These coefficients are determined for a particular sensor model and location on the body. Testing the device on the shoulder will require a separate calibration step to determine these coefficients. The current shoulder based SpO_2 estimation uses calibration coefficients calculated for the finger. This results in an amplitude offset as seen in Fig. 8.

4.4 Overdose Detection

An opioid overdose can be determined by observing symptoms such as paleness in the face, clammy skin, body limpness, vomiting, lack of response, and slow respiration and/or heart rate [49]. In a hospital setting, blood oxygen levels are monitored as the patient experiences respiratory depression leading to drops in SpO_2. The DOVE determines a fatal overdose by combining symptoms such as body limpness, breathing cessation, and a drop in SpO_2. Lack of motion over fifteen seconds from the subject triggers the optical sensor and respiration rate monitoring. SpO_2 levels dropping below 88% and breathing cessation over fifteen seconds are used to determine a fatal overdose. In the event of optical signal loss due to low perfusion or motion noise to determine SpO_2, we use respiration rate as a backup for the injector actuation mechanism. Respiration is used as a additional metric as OUD patients can experience isolated apneic events without experiencing an overdose leading to higher false positive rates [8].

If the sensing algorithm determines an opioid overdose, we alert the subject using a vibrating mini-motor disc to decrease false positives. A lack of timely response from the user to deactivate the alert mechanism will trigger the injector. A micro-metal motor pushes the patient-side needle into the subject's subcutaneous/intramuscular layer while simultaneously releasing the latch of a spring-loaded drug delivery system. The drug container is punctured by the drug-delivery apparatus, and 1mg/mL of naloxone is transported from the mini-bag into the subject's subcutaneous/intramuscular layer as a single dose bolus as seen in Fig. 4.

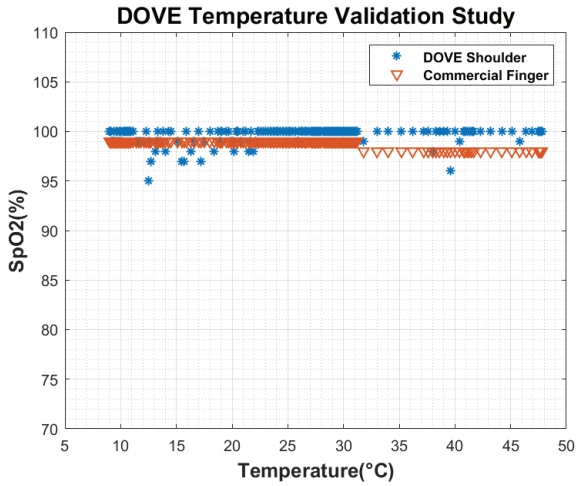


Figure 9: Measured SpO_2 values as function of temperature.

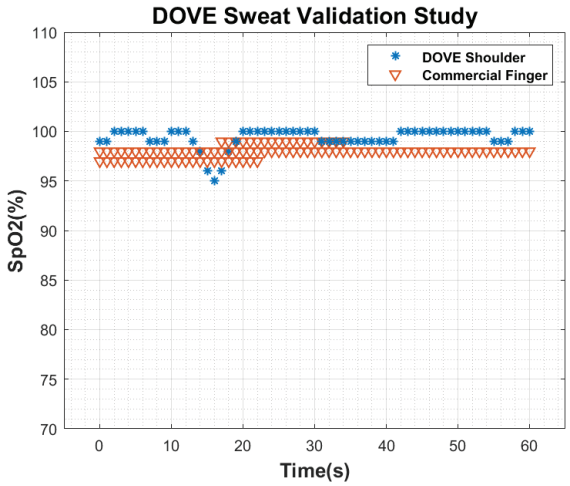


Figure 10: Validating performance in the presence of sweat.

5 EVALUATION

We begin by evaluating the DOVE's sensing mechanism, including its response to temperature and sweat as it is a wearable device and will encounter these in real-world use. Then, we examine its power requirements. Next, we compare the optical sensor against commercial FDA cleared pulse oximeters. Lastly, we explore the results of our injection mechanism on benchtop muscle models.

5.1 Exposure to Varying Temperatures

It is important that a wearable device withstand environmental conditions that humans experience. Temperature can affect sensor readings even when not outside of the normal operating range [52, 33]. To understand the effect of temperature on our device, we evaluated the sensor's response to hot and cold temperatures. The device is aimed to be worn before opioid usage to prevent a possible overdose. There are approximately 80,000 individuals suffering from OUD that do not have stable housing [62, 22]. This requires the device to accurately detect blood oxygen levels at varied outdoor temperatures. Naloxone can be stored between $5^{\circ}C$ and $40^{\circ}C$ [18]. We evaluate our device against a commercial pulse oximeter between $9^{\circ}C$ and $45^{\circ}C$. These temperatures were selected as they are on the edges of normal environmental conditions [47].

Figure 9 shows that the DOVE was able to detecting SpO_2 levels similar to a commercial FDA cleared pulse oximeter on the finger with a mean absolute error of 1.08%. It also has root mean square error (RMSE) of 1.23 which is <3.5 as per the FDA guidelines for reflective pulse oximetry [21].

5.2 Exposure to Fluids

In addition to temperature, fluids can also impact the sensors. The DOVE can be worn over multiple days using a biocompatable adhesive. Depending on the subject's environment the skin over the deltoid could begin sweating. Certain opioids can result in excessive sweating [24] and during an overdose the subject's skin becomes clammy [49]. To ensure optical sensor performance we evaluated the DOVE SpO_2 readings on the shoulder against a commercial pulse oximeter on the finger while simulating sweat on the deltoid by applying a drop of water between the optical sensor and skin. We repeated the test three times. As shown in Fig. 10, the DOVE is capable of accurately detecting SpO_2 levels within 2% of a finger-based pulse oximeter. The DOVE has a 1.97 RMSE which is within the FDA guidelines mentioned earlier.

5.3 Power Consumption

A digital multimeter was used to measure the power drawn by the device when all LEDs are at max intensity, the photodiode is sampled at 25Hz, and our 6-axis accelerometer is running. This is the max power draw from our device. With these settings, the DOVE consumes 15.5mA of current. This gives us approximately twenty six hours of battery life with a 400 mAh lithium-ion battery. This is more than sufficient for a normal research study. Longer studies are possible with a higher capacity battery. The optical sensor is the most power-hungry part of our device. In practice, our system could sample optical data less frequently based on accelerometry data. A sleep functionality will turn off the optical sensors when the subject is in motion. The device consumes 2mA when running only the accelerometer for motion detection. This increases the battery life to approximately seventy two hours.

5.4 Sensor Validation

To validate the MAX30101 optical sensor, an N=1 study was performed against a ground truth FDA-cleared pulse oximeter, and the trials performed are shown in Fig. 11. Here we decrease the subject's SpO_2 levels by inducing hypoxia through recycled breathing of carbon dioxide (CO_2). To induce hypoxia the subject breathes into a paper bag for three to four minutes. The test is repeated ten times. The ground truth finger pulse oximeter readings are plotted alongside the ones acquired via the MAX30101 sensor. For the most part, the MAX30101 readings follow the same pattern as the ground truth device which increases confidence in moving forward with this device. We did see more error at lower SpO_2 levels due to motion caused by labored breathing.

Compared to the ground-truth sensor, the DOVE sensor showed 0.766 Pearson correlation ($p < 0.0001$) and mean absolute error

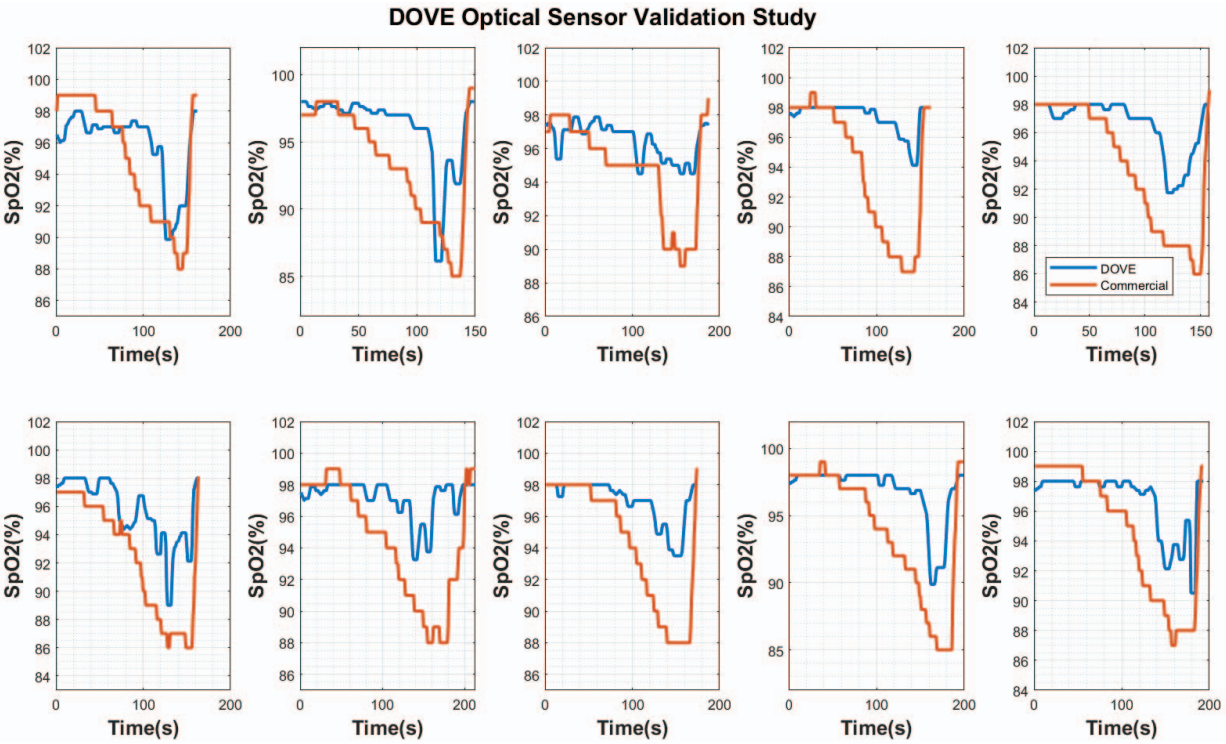


Figure 11: Ten trials of the sensor validation study.

of 4.91% during hypoxic events. However, the limitations of our shoulder-based pulse oximeter device are evident. We understand this device lacks the precision and accuracy of the commercial pulse oximeter. A few factors that affect accuracy are temporal distortion caused between physiological delays between the finger and shoulder, varied SpO_2 processing times, motion noise on the shoulder, and usage of calibration coefficients derived for the finger on the shoulder. However, this iteration of the sensor allows the user to conveniently wear it around the shoulder and detect drops in SpO_2. Additionally, sensing granularity and accuracy can be improved with hardware calibration and signal processing methodologies which will be discussed in Section 6. The goal of the device was to use off-the-shelf components to create a shoulder specific pulse oximeter. The current version of DOVE has a 3.8 RMSE score after removing physiological delays between commercial pulse oximeter and DOVE. This is above the 3.5 RMSE requirement by the FDA's guidelines for reflective pulse oximetry. Although the FDA guidelines are based on SaO_2 comparison, it is a good comparison metric against commercial SpO_2 detection devices.

5.5 Injector Performance and Reliability

The injector mechanism is used to deliver 1mg/mL of naloxone when a fatal overdose is detected. The device must reach a needle depth of 5-8mm to inject subcutaneous/intramuscular [45]. The device can inject in both subcutaneous or intramuscular region as the efficacy of naloxone is the same [29, 58]. The injector is tested for trigger reliability, injection depth, and injection speed in a fake

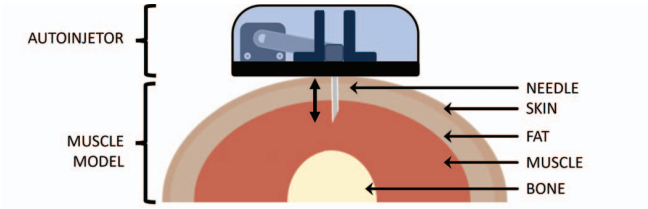


Figure 12: Injection testing on a muscle model.

benchtop muscle model which consists of skin, fat, muscle, and bone simulating an average deltoid. The set up is shown in Fig. 12.

A study consisting of N=100 injections was performed while replacing the patient needle per 10 injections to avoid resistance caused by needle degradation. A targeted injection depth of 8mm was chosen. The 15mm 19-Gauge needle consistently reached an injection depth averaging 7.48mm and 7.8mm with and without the muscle model respectively. Although the desired injection depth was not reached, the administration of naloxone within 5-8mm is safe and equally as effective [45]. The injection depth with the muscle model showed high precision with a 3.67% coefficient of variation score which is within the subcutaneous/intramuscular region depending on the subject's body mass index [45]. The micro-metal motor actuation showed 100% reliability in terms of injecting the model while triggering the drug-delivery apparatus when an overdose signal is generated. Finally, the device reached optimum injection depth in 300ms while testing on the model and 250ms

when testing without the model. The resistance caused by the layers of tissue increased injection time by 50ms.

6 DISCUSSION AND FUTURE WORK

We have demonstrated DOVE, a device for shoulder based pulse oximetry. It enables real-time, non-invasive, and continuous monitoring of motion, blood oxygen, and respiration rate. We acknowledge that the DOVE device is low fidelity compared to commercial pulse oximeters measuring on the finger, but it allows for detection of biomarkers on a non-canonical sensing site which is a canonical injection site. We envision the DOVE device being used for research purposes to develop other closed-loop injector systems. Adding Bluetooth functionality to the device allows for smartphone integration that can call emergency medical services or friends and family to your location.

6.1 Device Improvement

While our device provides the ability to detect drops in SpO_2 it lacks reliability due to the noisy physiological sensing site, the lack of motion artifact removal, and using a sensor calibrated for the finger. An analysis of the effects of the angle and distance between the PD and LEDs is needed to determine optimum spacing specific to the deltoid to the maximize perfusion index [51]. The perfusion index is directly related to the signal quality which affects accurate SpO_2 estimation. Finally, determining calibration coefficients for the sensor specific to the shoulder. This will be done in a hypoxia lab that focuses on pulse oximeter calibration.

The size and form factor can be improved through customization and miniaturization of parts. The size of the device can be reduced by switching out the Seeeduino XIAO BLE Sense microcontroller and Maxim Integrated optical sensor with a custom printed circuit board. The injector mechanism can be further shrunk by using smaller components produced by high resolution 3D printers. Using a smaller motor will also decrease size by 10%. Finally, the current power consumption rate allows for twenty six hours of continuous optical sensor usage. The battery life currently lasts approximately sixty four hours when power cycling the device using accelerometers at 2mA. This can be further reduced by operating the microcontroller and accelerometer at ultra-low power mode.

Overall, our current device has potential improvements that will improve accuracy and reliability in the optical sensing of biomarkers in the body. Furthermore, size reduction, custom sensors, and improving device specifications, such as battery usage, will greatly improve the performance and usability of the device.

6.2 Algorithm Improvement

Our algorithm estimates SpO_2 from raw red and IR ADC counts from the optical sensor. We have demonstrated good overall performance, which can be further improved along two facets: (1) during the normalization process, we can vary pulse width and frequency of the LED along with light intensity to maximize the perfusion index of the sensor while optimizing power consumption; and (2) denoising can be made more robust by further developing the filtering process and adding motion artifact removal.

The current respiration monitoring algorithm detects if the user is breathing normally or experiencing respiratory depression using accelerometers. A more granular detection mechanism can be implemented to detect respiration rate at breaths per minute. Respiration rate can also be extracted from PPG signals allowing us to fuse multiple biomarkers to increase reliability. Finally, improving on the motion detection algorithm will play a crucial role in battery optimization. The current process differentiates between in motion and motionless states. This can be further classified as whether the individual is motionless but active or incapacitated. This allows us to run device longer on low-power mode.

6.3 Real-World Deployment

The DOVE has been tested in a lab setting. To further improve our device, we plan to test it in the real world. DOVE will behave similarly to a wearable medical device, such as pulse oximeters, by locally collecting signals across multiple sensors that can be used to determine biomarkers such as heart rate, respiration rate, blood oxygen levels SpO_2, and motion. This will help run future studies on a wide variety of patients with varying human physiology, skin tones, and comorbidities. The device has a maximum battery life of approximately three days when duty-cycling. This will allow for longer at home user studies

The current form factor allows for easy fastening of the device and can be concealed under a shirt. The sensing mechanism of the device can first be tested in the real world on sleep apnea patients. This population shows biomarkers similar to an opioid overdose such as motionlessness and drops in SpO_2. The injection mechanism can be validated on animal models to ensure desired pharmacokinetics response is achieved.

7 CONCLUSION

In this paper, we present DOVE, a closed-loop wearable device capable of sensing biomarkers non-invasively and injecting the required drug. Using our custom PCB and off-the-shelf components, DOVE demonstrates sixty eight hours of battery life. We developed an algorithm to detect SpO_2 with a 3.8 RMSE of the shoulder in real-time to determine a fatal opioid overdose caused by respiratory depression. The SpO_2 detected by the device on the shoulder shows high correlation when compared to a commercial pulse ox. The device has also shown capability of determining the patient's motion and respiration state. Finally, the injector mechanism allows to subcutaneously/intramuscularly deliver any drug that can be stored in the minibag.

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