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14. ABSTRACT Pain is a subjective experience that is reflected in both behavioral and physiologic responses. It is inherently difficult to objectively assess and/or quantify [1, 2], yet appropriate treatment and management of pain is predicated on adequate assessment. Whenever possible, the existence and intensity of pain are measured by the patient's self-report [2, 3]. Patients who cannot reliably self-report their pain, due to underlying medical conditions or concurrent treatments, are at significantly higher risk for inadequately managed pain [1]. For example patients in the intensive care unit, older adults with dementia, patients with major cognitive or communicative impairments, infants, and patients under general anesthesia may not be able to reliably self-report [1, 4-7]. For them, other strategies must be used to assess pain. Consistently, multi-dimensional approaches to pain assessment have proven superior to metrics focused on a single variable [1, 4]. No single clinical indicator is sufficient to assess pain. Therefore, it is critical to combine behavioral pain assessment with physiological monitoring, and to interpret behaviors in a patient specific context [2].					
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Executive Summary

Pain is a subjective experience that is reflected in both behavioral and physiologic responses. It is inherently difficult to objectively assess and/or quantify [1, 2], yet appropriate treatment and management of pain is predicated on adequate assessment. Whenever possible, the existence and intensity of pain are measured by the patient's self-report [2, 3]. Patients who cannot reliably self-report their pain, due to underlying medical conditions or concurrent treatments, are at significantly higher risk for inadequately managed pain [1]. For example patients in the intensive care unit, older adults with dementia, patients with major cognitive or communicative impairments, infants, and patients under general anesthesia may not be able to reliably self-report [1, 4-7]. For them, other strategies must be used to assess pain. Consistently, multi-dimensional approaches to pain assessment have proven superior to metrics focused on a single variable [1, 4]. No single clinical indicator is sufficient to assess pain. Therefore, it is critical to combine behavioral pain assessment with physiological monitoring, and to interpret behaviors in a patient specific context [2].

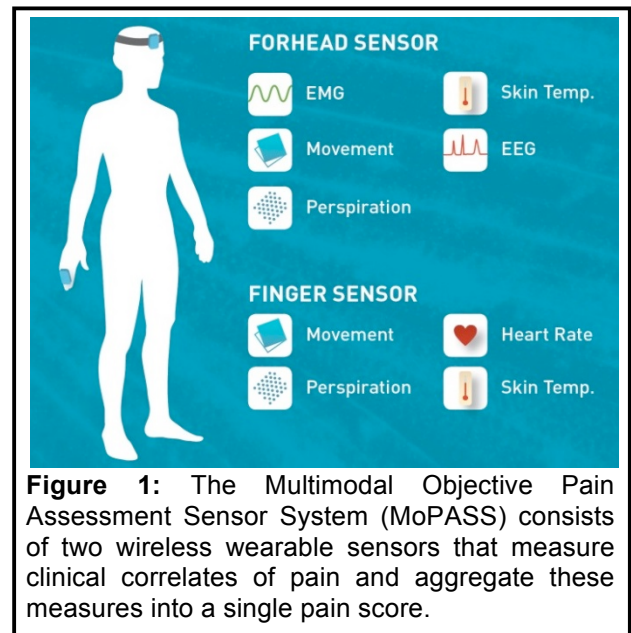


Figure 1: The Multimodal Objective Pain Assessment Sensor System (MoPASS) consists of two wireless wearable sensors that measure clinical correlates of pain and aggregate these measures into a single pain score.

There are several important benefits to our versatile and multimodal approach:

- 1) Multimodal - machine learning algorithms include behavioral and physiologic indicators
- 2) Versatility - the forehead or finger sensor can be removed due to patient specific issues
- 3) Specificity - the contribution of pain indicators to the pain severity score can be adjusted for different populations (e.g., movement may be irrelevant for intentionally sedated patients)
- 4) Fieldability - low-cost, lightweight system can easily be deployed in a field hospital or clinic
- 5) Continuous - wearable low-power sensors enable long-term continuous monitoring

During Phase I of this project, we designed and prototyped a Multimodal Objective Pain Assessment Sensor System (MoPASS, Figure 1). MoPASS is a wearable and low power system for rapid pain assessment and continuous long-term monitoring. The system will implement a multimodal pain assessment algorithm that will be developed using machine learning techniques based on the results of clinical studies conducted during Phase II (see *Phase II Work Plan*). To monitor these parameters, we designed and prototyped a system of two lightweight, comfortable, wireless, wearable sensors, worn on the forehead and finger, which relay real-time signals to the MoPASS software developed in Phase I.

The prototype Forehead Sensor consists of a functional unit which records and transmits two lead EEG (Figure 2). During Phase I we identified NeuroSky (San Jose, CA) as our preferred vendor for EEG hardware component

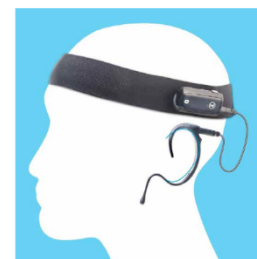


Figure 2: The EEG component of the Forehead Sensor (courtesy of NeuroSky, San Jose, CA)

because their chipsets provide access to algorithmically optimized data. These pass-band filtered signals will be used directly in our MoPASS algorithms. The prototype that we developed during Phase I is capable of streaming at 512 Hz in real-time via Bluetooth to a nearby computer running MoPASS software. Clinical studies in Phase II will examine these parameters in response to acute pain.

The prototype Finger Sensor records and transmits tri-axial acceleration, temperature, and GSR (Figure 3). During Phase I, we identified Shimmer (Dublin, Ireland) as our preferred vendor for GSR because it is a validated device, it has Bluetooth capabilities, and we have had previous positive experiences with Shimmer sensors. This firmware uses a command response communication protocol to successfully communicate with the MoPASS software. The firmware we developed allows the MoPASS software to dynamically control and query sensor status, start and stop data streaming, and configure the sampling rate and gain. Signals are acquired at 100 Hz.



Figure 3: The movement, GSR, and temperature component of the Forehead Sensor (courtesy of Shimmer, Dublin, Ireland).

The design specifications for the Finger Sensor were to measure tri-axial acceleration, skin conductance, heart-rate, and skin temperature. During development we decided to include blood oxygen saturation (i.e., pulse-ox) because optics was our preferred method of recording heart-rate and using this sensing modality pulse-ox was readily available without any cost or user comfort implications. We developed a prototype of the Finger Sensor by combining a wireless pulse oximeter with the previously discussed Shimmer GSR sensor (Figure 4). Signals are acquired at 100 Hz.

The prototype of the Finger Sensor that we have developed extends to the wrist (Figure 4); however, in Phase II we will design and manufacture a custom sensor to make all relevant measurements directly from a single sensor on the finger.

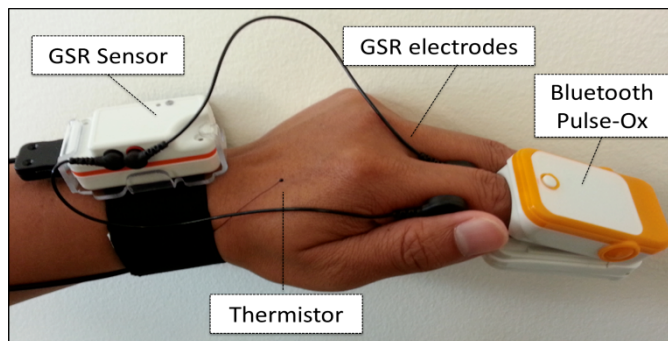


Figure 4: The prototype of the Finger Sensor that was developed during Phase I. During Phase II the components on the wrist will be eliminated and all measurements will be made by a single customized sensor worn on the finger.

The off-the-shelf hardware used in Phase I does not have an acceptable form-factor for a commercialized device. In Phase II, we will design and manufacture a single forehead sensor that is capable of making all measurements (GSR, EEG, and acceleration).

The MoPASS software that we developed during Phase I uses the Bluecove library, which implements the Java Bluetooth standard JS-82. Bluecove was developed by Intel and is now widely used in Java Bluetooth applications. It supports multiple Bluetooth communication protocols, including RFCOMM, which is used by the MoPASS devices. Using the MoPASS software we are able to query the status of each MoPASS sensor, control the sampling status in real time, parse incoming data streams, plot time-series data, and export data in Matlab or

ASCII delimited text formats. We have also implemented an extensible sensor data parsing component in the MoPASS software. This allows a flexible architecture for incorporating or removing specific sensors in the future without changing the software architecture.

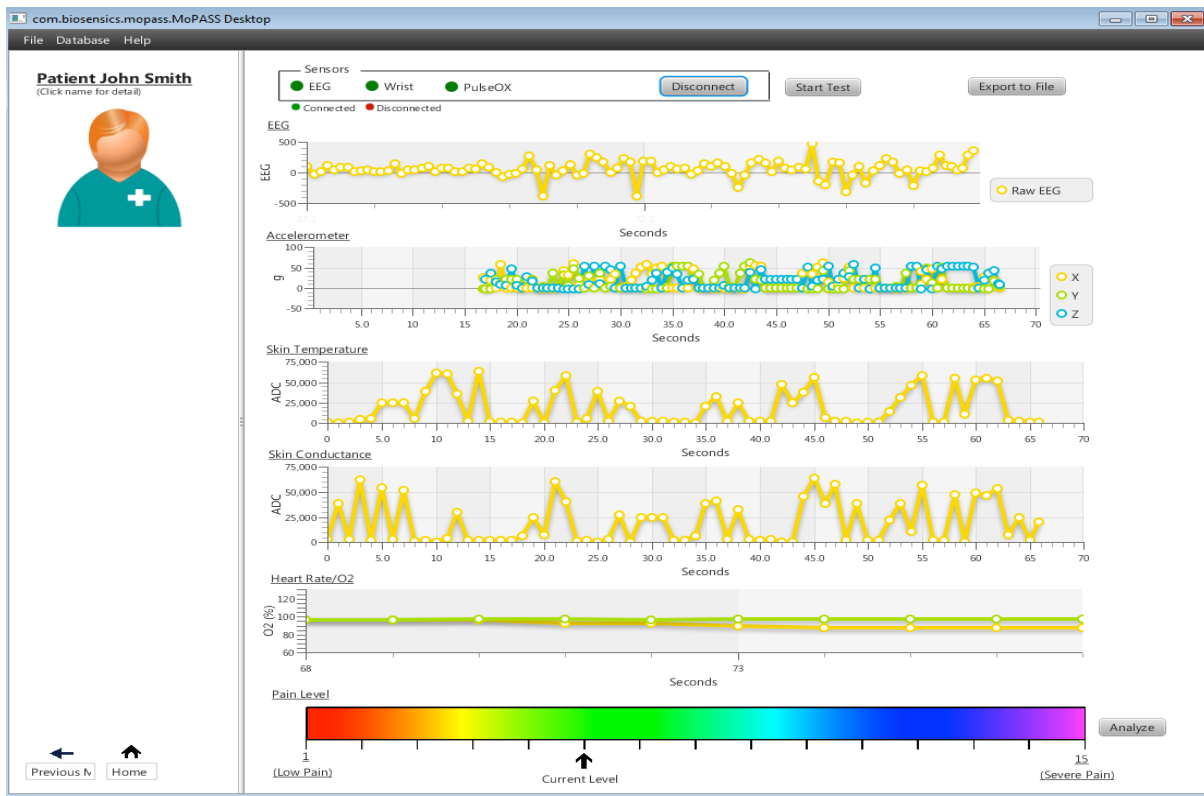


Figure 5: MoPASS software for wirelessly acquiring real-time signals from the Forehead and Finger Sensors. Algorithms developed based on these trials in Phase II will be used to modulate the pain intensity score shown at the bottom of the screen.

Thus, the key outcomes of our Phase I work were:

- System design including pain metrics and appropriate wearable sensing modalities
- A functional beta-prototype consisting of two wearable sensors and software
- Clinical trial design and selection of a clinical site for trials to be conducted in Phase II

First Phase I Outcome: Identification of Pain Measures & MoPASS Sensing Modalities

Consistently, multi-dimensional approaches to pain assessment have proven superior to metrics focused on a single variable [1, 4]. No single clinical indicator is sufficient to assess pain. Behaviors do not specifically reflect pain intensity; rather they indicate distress, which could be physiologic or emotional in nature [8]. Physiological parameters can change in response to many factors other than pain, and the absence of changes in these signals does not indicate the absence of pain [2].

Several tools have been developed to aggregate observational ratings of behavioral parameters and physiologic measures into one pain assessment score [1, 4, 9-11]. These tools are superior to unimodal methods [4] but are subjective in nature and require regular repeat assessment by care providers. Automated multimodal pain assessment has great potential for improving the quality of pain management care. Recently, Worley et al. demonstrated that a multimodal assessment tool could detect noxious heel lance and touch stimuli in infants with 100% sensitivity and specificity [12]. This assessment tool incorporated videography, EEG, EMG, and electrocardiograms (ECG), along with measures of total hemoglobin concentration, respiration rate, and oxygen saturation. This provided an important demonstration of the efficacy of objective multimodal pain assessment. However, the system developed by Worley et al. was not designed for continuous monitoring of clinical pain. In particular, analysis was performed offline and subjective analysis of videography was used to assess behavior.

Based on interviews with experts in clinical pain management, discussions with project consultants from the Departments of Anesthesiology and Surgery at the University of Arizona, and emerging trends in the scientific literature, we identified two behavioral and four physiological parameters that are correlated with acute pain (Table 1). Therefore, it is critical to combine behavioral pain assessment with physiological monitoring, and to interpret behaviors in a patient specific context [2]. The behavioral and physiological variables that are monitored by our wearable sensor system are listed in Table 1 and discussed in detail in subsequent sections.

Table 1: Pain indicators measured by MoPASS

	Parameter	Sensor Unit	Sensor Modality
Behavioral	Facial Expression (grimace, clenching)	Forehead	Electromyography
	Movement (restlessness, guarding)	Forehead and Finger	Accelerometry
Physiological	Perspiration	Forehead and Finger	Skin Conductance
	Heart Rate	Finger	Optical
	Skin Temperature	Forehead and Finger	Thermocouple
	Pain related electrocortical activity	Forehead	Electroencephalography

Behavioral Indicators:

The primary behavioral categories used to help identify pain are facial expression (such as grimacing, frowning, and wincing) and body movement (such as restlessness and guarding) [1, 2, 4, 5, 13]. To quantify **facial expression** we use surface electromyography (EMG) in the forehead sensor node to record electrical potentials on the forehead and temples. Bandpass filtering and blind-source separation techniques can be used to isolate muscle activity (e.g., from the occipitofrontalis, zygomaticus, or temporalis) and then the activity time-course can be used to distinguish normal muscle activity (e.g., blinking or chewing) from facial tension (e.g., grimace, wincing, frowning). We have previously used similar techniques to separate neck muscle activity from electrocortical activity during human locomotion [14-17]. **Restlessness** can

be quantified with inertial sensors on the forehead and hand using algorithms that are modified from those we currently use to quantify physical activity and gait in our commercially available wearable inertial sensor systems (LEGSys™ and PAMSys™). Our target patients are non-communicative and often non-ambulatory; nevertheless, restlessness (i.e., persistent movements and adjustments in the bed or chair) are an important behavioral pain indicator.

Physiological Indicators:

Several physiological indicators have been used to assess of pain. Increases in heart rate, perspiration, and skin temperature (as well as increased variability in these parameters) may all be indicative of pain [18-21]. MoPASS measures **heart-rate** using optical sensors in the finger sensor unit, and **perspiration** on the finger and the forehead based on skin conductance. Finally, MoPASS measures **skin temperature** on both the forehead and finger using thermocouple based skin contact temperature sensors.

Cortical Representation of Pain:

Advances in neuroimaging are rapidly elucidating the cortical pain network, which includes structures in the sensorimotor, insular, anterior cingulate, and prefrontal cortex [22-27] (Figure 7). Many neuroimaging techniques have evaluated brain responses to controlled acute pain (see [25] for a review). The only noninvasive, wearable, and fieldable method for monitoring brain responses to pain is electroencephalography (EEG). EEG measures electrical potentials on the scalp generated by synchronous firing of cortical neurons. EEG signals that are time-locked to a short duration pain stimulus (i.e., event-related potentials) have been widely studied [28]. While informative, these techniques are not generally useful for assessment of clinical pain [25, 28]. A few studies have demonstrated that changes in continuous EEG spectral content correlate with self-reported pain scores [25, 29-31]. These studies hold great promise for clinical pain assessment. Most recently, Nir et al. demonstrated that increases in peak alpha frequency (8-12 Hz) on the bilateral temporal scalp during tonic noxious temperature exposure were correlated with self-reported pain score. When combined with other behavioral and physiological indicators of pain, continuous EEG monitoring may provide an invaluable tool for pain assessment in the non-communicative patient.

MoPASS measures electrocortical activity using surface electrodes in the forehead sensor unit. Based on the location of these surface electrodes we are able to record electrocortical activity from the medial and dorsolateral prefrontal cortex, which are critical regions in the cortical pain network [22-27]. MoPASS software enables the collection and storage of raw EEG data as well as alpha-band (8-12 Hz) and beta-band (12-30 Hz) spectral power. Further, patient specific baseline values can be recorded and stored in MoPASS software for later comparison to spectral parameters during periods of acute pain. These fluctuations from baseline will serve as input to our multimodal pain assessment algorithm that will be developed based on the clinical trials conducted during Phase II.

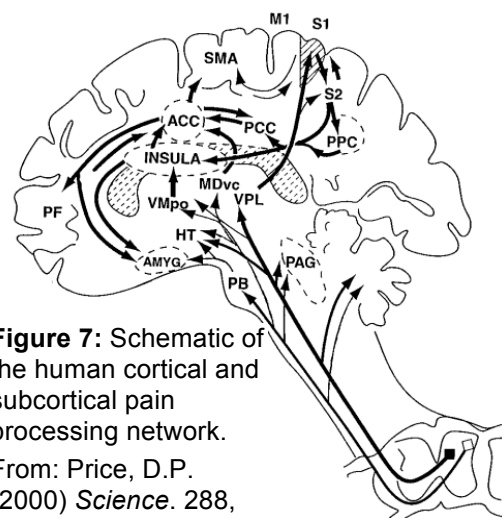


Figure 7: Schematic of the human cortical and subcortical pain processing network.

From: Price, D.P. (2000) *Science*. 288, 1769.

Second Phase I Outcome: Development of Functional Prototype of MoPASS

The majority of our efforts during Phase I were related to the development of a functional prototype MoPASS system. The design objectives of this system, which included hardware and software, were to wirelessly record and display synchronized real-time data from the forehead and finger sensors, including EEG, skin temperature, movement (i.e., acceleration), heart rate, and skin conductance. The prototype system we developed in Phase I is fully functional and ready to be used immediately in clinical studies. Phase II engineering efforts will be devoted to form-factor optimization and design for manufacturing. During Phase II, off-the-shelf components used in Phase I will be replaced with custom manufactured hardware. To see video of the MoPASS system being used to record and display data in real-time visit www.biosensics.com/mopass/ and enter the password DHP12-015.

The following Gantt chart was used during the six months of Phase I development. The remainder of this section will go into more detail about each stage of the development process.

Table 2: Gantt Chart of Phase I development stages

Months	1	2	3	4	5	6
Development of prototype sensor units						
Hardware design and firmware development						
MoPASS PC Software						
Validation of prototype system						
Report preparation and Phase II proposal						

Stage 1: Development of Prototype Sensor Units

Task 1: Identification of MoPASS Sensors

A design matrix (Table 3) was used to identify the final sensors that would make up the MoPASS integrated system.

Table 3: Design matrix used to finalize sensors used in MoPASS system

	SENSOR MODALITY OPTIONS													
	MOVEMENT	EEG	BLOOD OXYGEN SATURATION & PULSE	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN	SKIN
	BioSensics PAMSys	NeuroSky	Emotiv EEG NeuroHeadset	Interaxon Muse	NellCor	Bluetooth Finger Pulse Oximetry	Spacelabs Pulse Oximeter	Shimmer Research	Equival GSR	GE MA Series	Thermistor	Smith Medical	Temperature Probe	PA SPORT
Data quality	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Wearability	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N
Cost	Y	N	N	N	N	Y	N	Y	N	Y	Y	Y	Y	Y
Ease of Integration	Y	Y	N	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Compactness	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	N	N

In selecting the final sensors, we were most interested in the quality of the data and how easily and comfortably the sensor could be worn. Other factors that influenced our selection were low cost, ease of integration with our existing capabilities and a sensor that was relatively small in size. A 'Y' denotes that the sensor met a specific criteria whereas an 'N' denotes that the sensor failed to meet the criteria.



We elected to use our own PAMSys for recording movement. PAMSys was proven to work well as a product for body motion analysis as a platform for long-term physical activity monitoring. In addition, PAMSys is capable of taking external analog and digital signals from other sensors in MoPASS system (e.g. GSR and thermistor). Thus, choosing PAMSys makes integration of these sensor readings easy and reliable. Lastly, PAMSys is equipped with Zigbee and Bluetooth wireless capability, which makes it easy to offload data wirelessly to nearby base station (i.e. laptop running MoPASS

GUI).



We elected to use Mind Band (NeuroSky, San Jose CA) for recording EEG. NeuroSky is the global leader in low-cost dry-electrode EEG technology. Their ThinkGear EEG module is used in more than 1 million consumer EEG devices. This level of broad adaptation gives us high confidence in their technology. Unlike many wireless EEG providers, NeuroSky offers a comprehensive SDK and access to both raw data and algorithmically optimized data. Specifically, the NeuroSky chipsets perform A/D conversion, signal amplification, off-head detection, EMG noise filtering, 50/60 Hz line noise filtering, and pass-band filtering (delta, theta, low/high alpha, low/high beta, and gamma). These pass-band filtered signals will be used directly in our MoPASS algorithms. Specifically, alpha- and beta-band signals from electrode locations above the medial and dorsolateral prefrontal cortex will serve as input to our multimodal pain assessment algorithms; these are critical regions in the cortical pain network. Finally, the patented NeuroSky eSense signal processing toolbox has great potential to assist in the development of our MoPASS algorithms. Specifically eSense has built in eye-blink detection and can quantify level of attention. Eye-blink detection will be used in the behavioral indicators portion of our multi-modal algorithm and level of attention may prove to be beneficial as a neuro-cognitive indicator (clinical testing in Phase II will evaluate the efficacy of this approach). For all of these reasons NeuroSky was the obvious best supplier of EEG hardware for the MoPASS System. We have already discussed this project with development engineers at NeuroSky and have executed a Developer Agreement.



We elected to use a Bluetooth Finger Pulse Oximeter for recording blood oxygen saturation and pulse. This pulse oximeter was chosen because it met all five of our selection criterion. The Bluetooth functionality makes it easy for us to integrate the sensor with our capabilities and control the quality of the data received. In comparison to the other sensors, we preferred this sensors' size and method of attaching it to the user. Lastly, this was the cheapest sensor in comparison to the alternatives. For these reasons, this sensor will be used in the final integration of the MoPASS system.



We elected to use Shimmer GSR sensor, a validated biomedical-oriented research application, for recording skin conductance. Shimmer GSR sensor interfaces with PAMSys through an existing daughter circuit board

designed and is manufactured to mate directly with PAMSys motion sensor board. This reduces engineering time for integrating GSR sensor reading into MoPASS integrated system. In addition, Shimmer GSR sensor has a pre-designed case that encloses the daughter card and the PAMSys sensor, which protects the circuit boards and provides good usability and wearability. Lastly, the Shimmer GSR sensor circuit is configurable. For example, it supports four digitally controlled measurement ranges which developers use to ensure accurate measurements and it allows gain selection to be hard-coded or manually selected.



We elected to use a GE MA Series Thermistor for recording skin temperature. This thermistor was chosen because it met all five of our selection criterion. The main reason we chose this thermistor over the others is because it is a medical grade product meant to be worn and collect data. Thus, our wearability and quality of data criterions were met. In addition, this thermistor's compact size was more attractive than the alternatives. Lastly, the low cost and easy-to-integrate capabilities ultimately led us to select this sensor for the final integration of the MoPASS system.

Task 2: Sensor Hardware Development

The aforementioned sensors were used in the hardware development of the wrist unit for the MoPASS system, as shown in Figure 8.

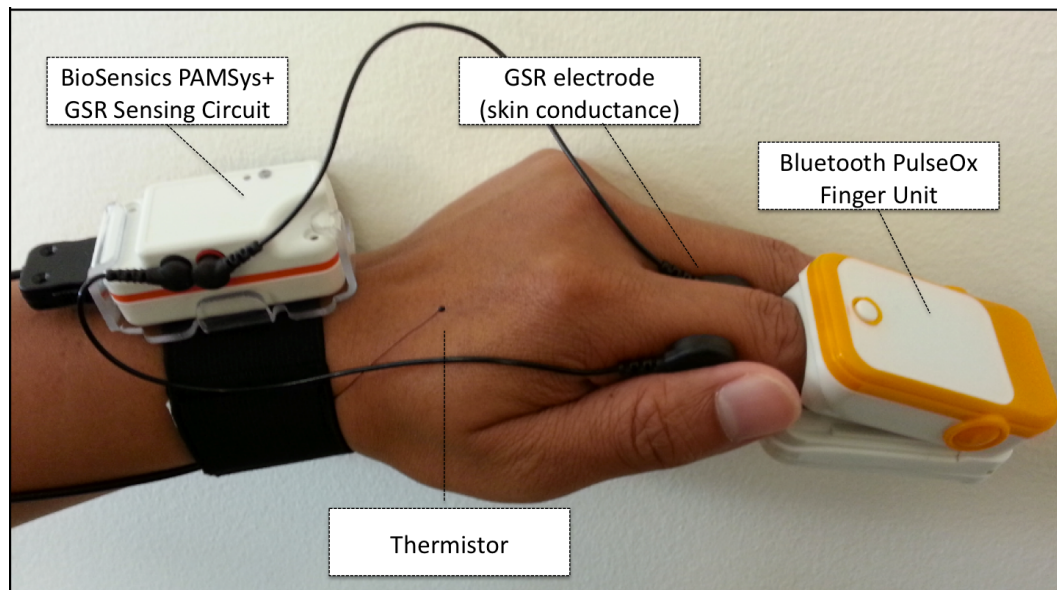


Figure 8: MoPASS Wrist Unit for real-time measurement and streaming of movement, skin conductance, skin temperature, heart rate, SpO₂ readings over Bluetooth wireless connections to the monitoring station.

The wrist unit is equipped with a 3-axis accelerometer for measuring hand movement, a thermistor for measuring skin temperature, a GSR sensor for measuring skin conductance, a pulse oximeter for measuring heart rate and blood oxygen saturation level (SpO₂). The main data communication unit is BioSensics' PAMSys device, designed for physical activity

monitoring. In addition to 3-axis accelerometer, PAMSys is equipped with 2GB flash data storage, Zigbee and Bluetooth wireless data transceiver, USB docking capability for device charging and fast data off-loading/backup. Thermistor, GSR, and accelerometer sensor readings are acquired through the analog-to-digital-converter (ADC) ports on PAMSys' main processor (a MSP430 micro-controller from Texas Instrument) with 12-bit resolution. The sampling rate is configurable through firmware settings and is currently set to be 100Hz.

Stage 2: Hardware Design and Firmware Development

Task 1: Design of MoPASS System Architecture

We defined MoPASS system to be consisted of a MoPASS Desktop Application, the Forehead/Head Unit, and the Wrist Unit, as shown in Figure 9. The Forehead Unit records 3-channel EEG, skin temperature, and head movements. The Wrist Unit measures heart rate, SpO2, skin temperature, skin conductance, and hand movements. Through Bluetooth, a MoPASS Desktop Application receives, parses, and analyzes the collected samples from Forehead Unit and Finger Unit. Using data from multiple wearable sensors, MoPASS derives a single score for automatic and rapid assessment of pain intensity and delivers the objective pain assessments to clinicians. We detail each component of the system in the following sections.

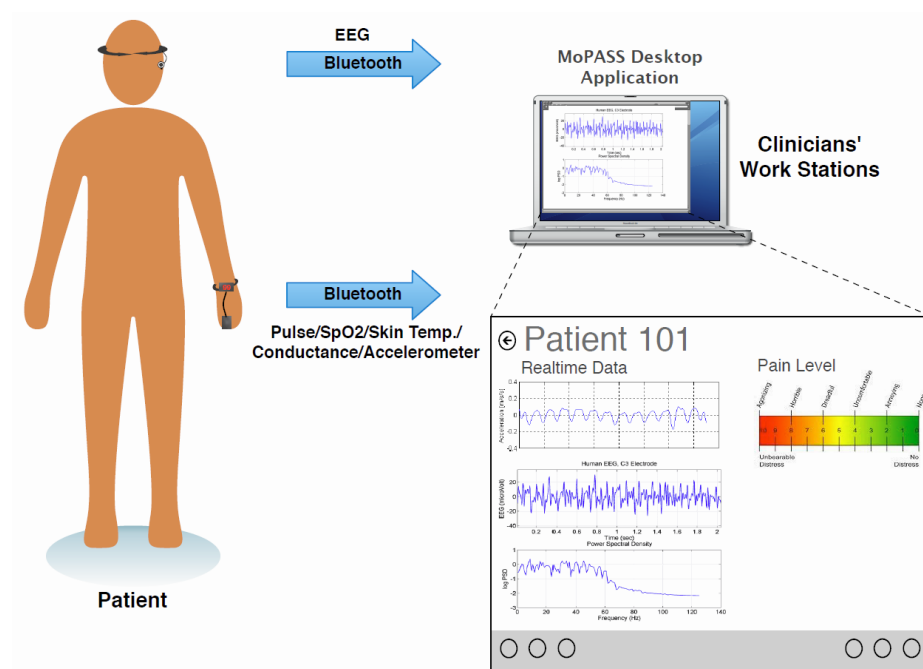


Figure 9: Overall architecture of MoPASS system. Forehead Unit and Finger Unit both contain multiple sensors, sample them, and communicate with preliminary MoPASS Desktop Application software in real-time over Bluetooth wireless links.

Task 2: MoPASS Sensor Platform Development

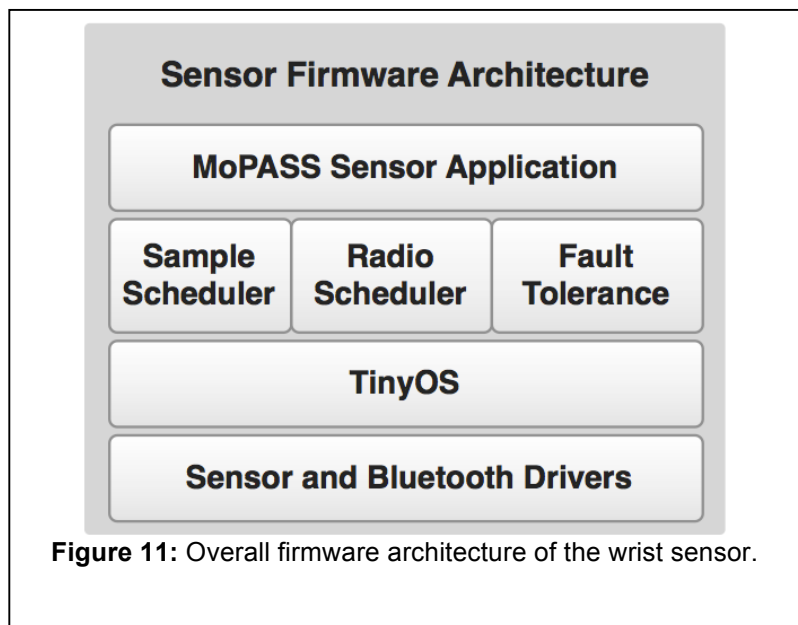
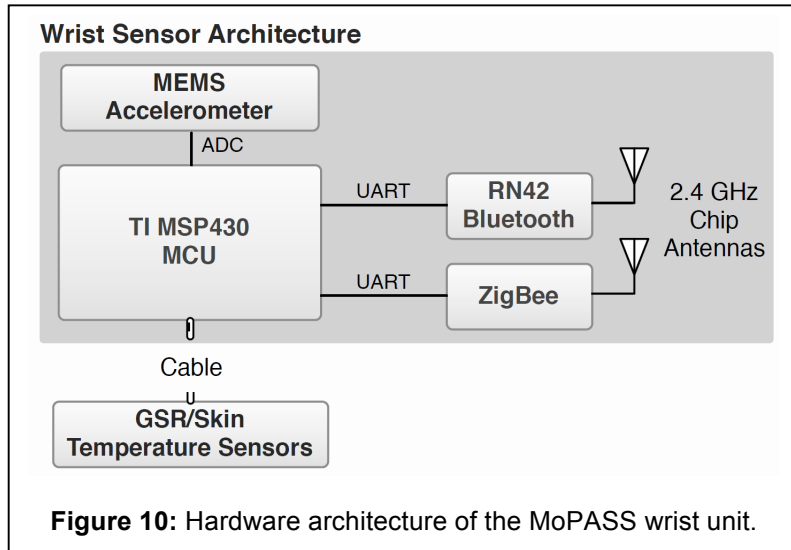
We developed wireless head sensor unit and wrist sensor unit that are used to measure movement, EEG, pulse, blood oxygen saturation (SpO₂), skin temperature, and perspiration of subjects. The data collected by these sensors will be used to extract various pain parameters and to estimate the objective pain level. The tasks required for developing the the sensor units include development of a sensor firmware for data collection and wireless data communication. The sensors

are required to be small and lightweight, capable of automatic wireless data transmission without any attention from the user.

In order to provide real-time measurement of the required pain assessment parameters, the forehead sensor hardware includes EEG electrodes, analog electronic interfaces, a low power processor for signal processing, and a Bluetooth transceiver. The finger sensor unit includes a tri-axial accelerometer and an external fingertip sensor (connected through a removable daughter board) to measure pulse and SpO₂. For real-time processing and transmission of sampled signals, we include a 2.4GHz Bluetooth transceiver with an embedded micro-controller in the sensor. As shown in Figure 10, the sensor units include a Bluetooth transceiver with an embedded micro-controller for real-time data transmission and processing of sampled signals.

For control and wireless communication capabilities, we have selected Bluetooth (IEEE 802.15.1) to support real-time data transmission.

Figure 11 shows the firmware architecture that will be used to operate the wrist sensor unit. We chose TinyOS to be the operating system for our firmware. TinyOS provides critical networking services such as media access control (MAC) protocol as well as wireless time synchronization (e.g. FTSP). The MoPASS sensor firmware application schedules sampling timing and stores the collected sample in a local buffer. The radio scheduler then sends the data from the buffer in the First-In-First-Out (FIFO) order. In addition, the firmware architecture includes a fault tolerance layer to handle hardware malfunction (e.g. sensor failure or wireless transmission failure). This layer



reports unexpected behaviors to MoPASS Desktop Application so that users are notified about potential system failures and can take actions to reboot or replace malfunctioning sensor units.

Task 3: Streaming Firmware

We developed streaming firmware for PAMSys to collect real-time data from the wrist unit. The PAMSys has accelerometer sensors sampling at 40Hz, which can be configured to be up to 1000Hz. The firmware reads accelerometer data through three ADC channels, and saves it into an internal buffer to be transferred to our desktop software.

We have completed the development and integration of sensing and wireless data streaming features from PAMSys-based wrist unit, finger-worn pulse oximeter, and NeuroSky EEG MindBand. PAMSys firmware drives on measurements of 3-axis acceleration of the subject's hand, skin temperature, and skin conductance. We have developed the firmware driver that samples the above sensors at up to 100Hz. The sampling rate will be made configurable from the MoPASS Desktop Application Software. PAMSys firmware also implements Bluetooth communication with the laptop computer running MoPASS Desktop Application Software.

Bluetooth Finger Pulse Oximeter implements a Bluetooth communication protocol based on Radio Frequency Communication (RFCOMM). We were able to read the data stream from the sensor from any PC/Macs/Tablet computers with a Bluetooth transceiver. The Bluetooth Finger Pulse Oximeter sends optical measurements in a 7-byte message format at 100Hz. Also, the Bluetooth Finger Pulse Oximeter measures Pulse and SpO₂ information and sends the collected data at 115200 bps to the on-board Bluetooth transceiver. In a single message, the pulse oximeter sends the subject's SpO₂, heart rate, and plethysmogram data (each sample of which is 6 bits), as well as sensor connectivity and status (each of which is 1 bit).

NeuroSky EEG MindBand also transmits data through Bluetooth. MindBand measures and transmits EEG alpha, beta, gamma, theta, and delta waves, as well as connectivity and battery status. The NeuroSky EEG MindBand firmware samples data in 512Hz.

For the wrist sensor unit to communicate with the MoPASS Desktop Application (MoPASS GUI), we designed and implemented a simple command-response communication protocol for MoPASS. The protocol is implemented both in the firmware of the wrist sensor unit as well as in the MoPASS GUI software. We describe the protocol in detail below.

After powering up, the wrist sensor unit enters into idle mode and waits for incoming commands from the MoPASS GUI. The following commands are supported:

- Status Inquiry (STATUS_INQ)
- Current Sensor Reading (SAMP)
- Start Streaming (START_STREAM)
- Stop Streaming (STOP_STREAM)
- Set Sampling Rate (SET_SAMPRATE)

Status Inquiry (STATUS_INQ) command allows the MoPASS GUI to receive the following information from the wrist sensor unit: physical sensor status (i.e. report status of accelerometer, thermistor, and skin conductance sensor), battery level, sampling ranges, and sampling rate. The MoPASS GUI always transmits this command when the wrist sensor is first connected to the PC. Current Sensor Reading (SAMP) command will trigger sampling of one

data point from each sensor type from the wrist sensor unit and transmission of the measured values back to the PC to the MoPASS GUI over Bluetooth wireless connection. The Start Streaming command (START_STREAM) starts the continuous sampling and data streaming from the wrist sensor unit to the PC at the predefined sampling rate, set to 100Hz by default. The Stop Streaming command (STOP_STREAM) stops the data streaming and set the wrist sensor unit back to the idle mode. The Set Sampling Rate command (SET_SAMPRATE) configures the wrist sensor unit to sample at one of the following supported frequencies: 10Hz, 50Hz, 100Hz, 125Hz, 200Hz, and 250Hz. The above commands allow the MoPASS GUI to dynamically control and query sensor status, start/stop data streaming, and configure sampling rate.

Stage 3: MoPASS PC Software

Task 1: MoPASS Desktop Application Design and Development

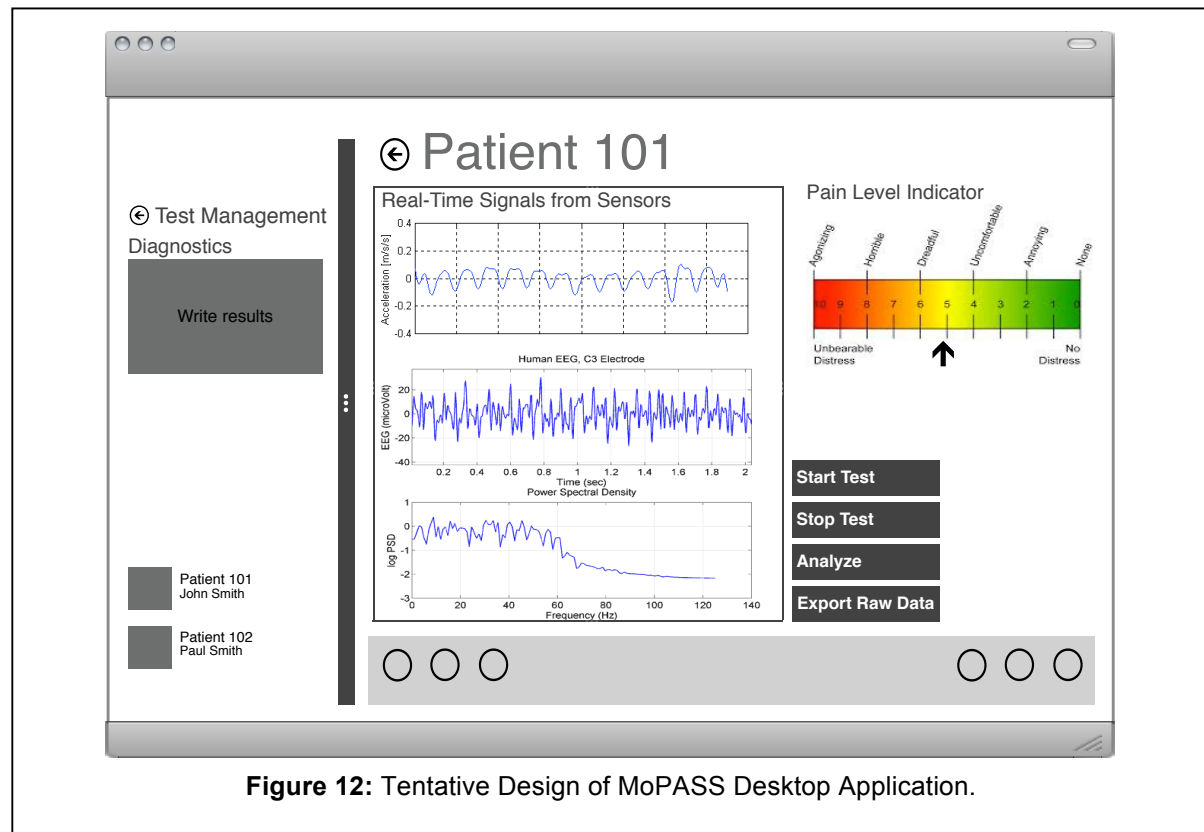


Figure 12: Tentative Design of MoPASS Desktop Application.

MoPASS Desktop Application will be able to perform multi-modal pain assessment based on the collected data from head and wrist sensor units. MoPASS desktop application shows a series of real-time sensor data, a pain indicator, as well as panels to manage data from multiple patients. Figure 12 illustrate the preliminary version MoPASS graphical user interface (MoPASS GUI). MoPASS GUI will provide features that allow clinicians to export raw data, export analyzed data, save and print the analyzed results. MoPASS Desktop Application is developed in Java programming language and will be cross-platform. At this stage we plan is to support Microsoft Windows and MacOS platforms. MoPASS Desktop Application is designed to run on desktop and laptop computers. However, with minimal effort, we can extend its usage to mobile platforms, such as Android or Apple iPad tablet computers.

Task 2: Mockup GUI



Figure 13: Development version of the Desktop MoPASS GUI.

This screenshot shows our development version of the Desktop GUI. As we mentioned in the previous section, our desktop software shows corresponding signals: EEG, Accelerometer, Skin temperature, Skin conductance, Pulse, Oxygen Rate. The desktop program is developed by the following MVC (Model-View-Controller) model in JavaFX, as JavaFX is known to be a well-designed framework for MVC. Right under the menu bar, we show sensors and their connectivity. Users can click the button next to them to connect and disconnect. Once all sensors are connected, hitting on the 'Start' button initiates real-time data streaming and collection. Users can stop tests at any time by hitting on the 'Stop Test' button. All the collected data can be exported to a file (e.g., Comma Separated Value file). At the bottom, we show a pain level indicator by using a color bar: leftmost corresponding to the lowest pain level and rightmost, the highest. The 'Analyze' button next to the bar can give users pain level at any point in experiments.

Task 3: Desktop Application Software Development

To connect and stream data from the sensors, users first need to find their sensors. Our Desktop software provides an interface to find those sensors and save needed information. The following figures show screenshots of this feature.

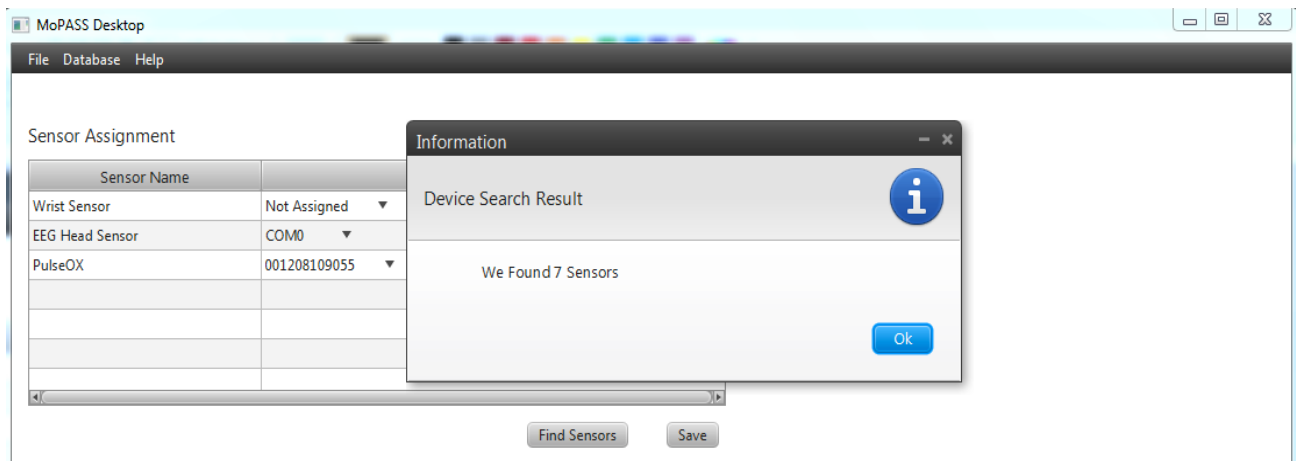


Figure 14: Screenshot showing how to find and connect sensors.

As Figure 14 shows, by clicking on the “Find Sensors” button, users can find their sensors and by clicking on the “Save” button, they can save the discovered sensors’ information to a file. Therefore, users do not need to repeat finding sensors afterwards, unless they change their sensors.

Although the listed devices use Bluetooth for communication, some vendors do not allow developers to access directly through Bluetooth. Rather, they allow developers to access data through RS-232 serial communication protocol. The protocol was originally developed for communicating with peripheral devices through serial cables. As the serial protocol is prevalent in popular operating systems, Bluetooth drivers in OS emulate the serial communication. Therefore, developers, after identifying which serial ports their devices operating on, can read and write data through the serial ports. For example, “COM0” stands for a serial port used to communicate with EEG Head Sensors. In summary, Wrist Sensors and EEG sensors work in serial protocol whereas Bluetooth Finger Pulse Oximeter works in direct Bluetooth communication.

To connect Bluetooth Finger Pulse Oximeter, we use Bluecove as the underlying communication library, implementing Java Bluetooth standard JS-82 [13]. Originally developed by Intel Corporation, Bluecove is now widely used in Java Bluetooth application and supports multiple Bluetooth communication protocols, including RFCOMM (the one that our devices’ Bluetooth use).

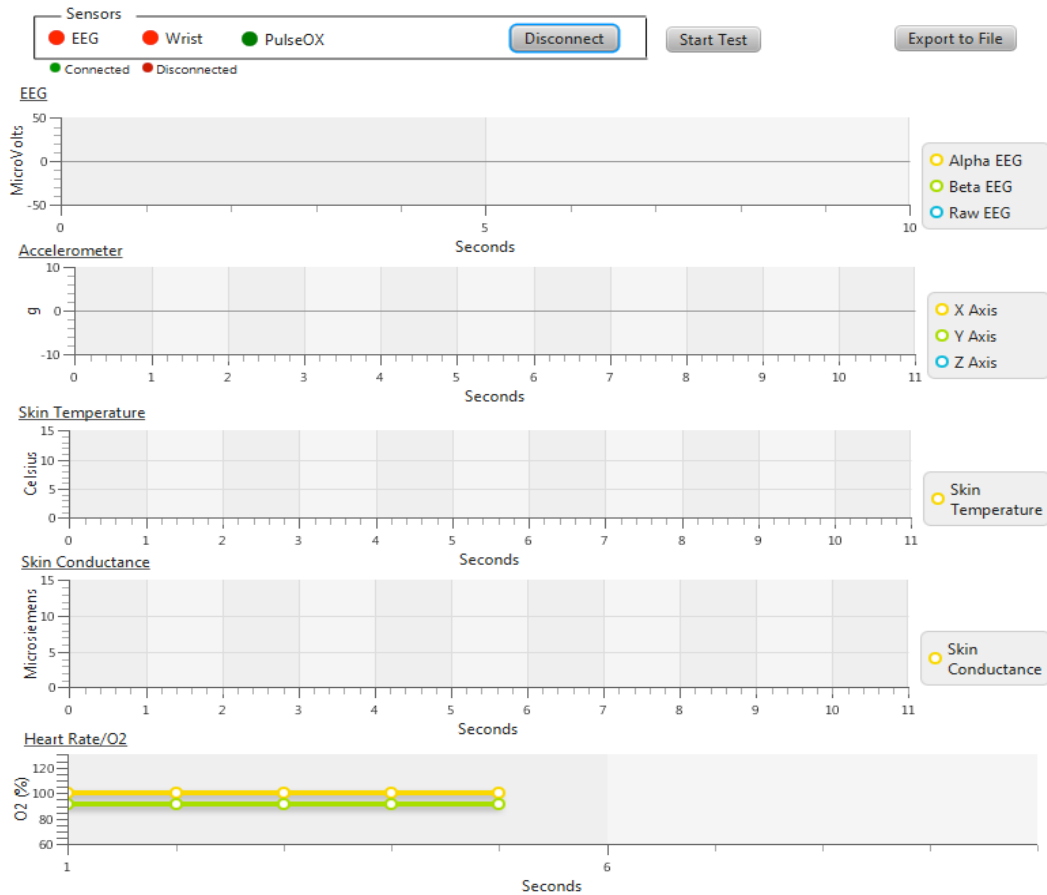


Figure 15: Real-time plotting in development version of Desktop GUI

Moreover, the GUI displays connectivity information by using colors on a diagram. As shown in the figure, only the sensors connected to the GUI present its colors in green (Pulse Oximeter Finger sensor), whereas disconnected devices show their colors in red (top of the figure). Also, as presented in the figure, the sensors not connected to our desktop program do not visualize any data. We finished visualizing Pulse Oximeter Finger sensor and NeuroSky EEG MindBand.

We developed the MoPASS GUI and have included the communication module that implements both a) the protocol described in Task 1 and b) the proprietary communication protocol supported by NeuroSky's MindBand. After this module is completed, we were then able to query the status and to control the sampling status of both sensor units in real time using the MoPASS GUI. We also implemented an extensible sensor data parsing component in the MoPASS GUI. This allows a flexible architecture for incorporating or removing specific sensors in the future without changing the architecture of the MoPASS GUI software. Specifically, the MoPASS GUI can successfully start, receive, parse, and plot, as time series data, of the following sensor data in real time:

- EEG (from MindBand)
- Wrist Movement (3D acceleration)
- Skin temperature
- Skin Conductance

- Pulse
- SpO₂

The collected data can be exported into Excel and MATLAB readable format for off-line analysis. Thus, we've successfully implemented real-time data streaming and data visualization for all the components that make up the MoPASS system.

Stage 4: Validation of Prototype System

We successfully validated the sensor data received from the wrist and head sensor unit of the MoPASS prototype. This validation involved the collection and analysis of real-time multi-modal sensor signals from the Bluetooth Finger Pulse Oximeter, the thermistor, the GSR sensor, the MindBand sensor and PAMSys. We were able to obtain correct pulse, SpO₂, temperature, skin conductance, as well as hand movement data. Figure 16 shows all the sensor components of the MoPASS prototype.

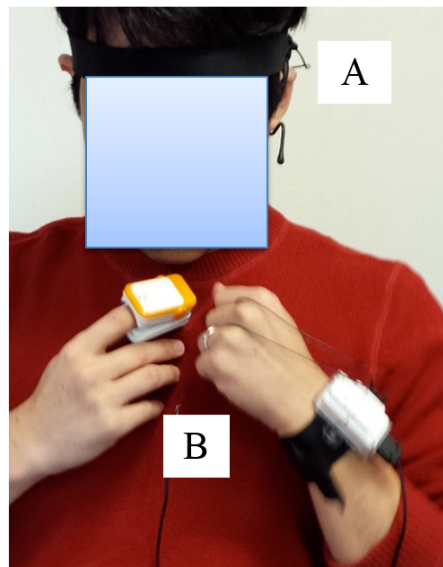


Figure 16: MoPASS prototype system consisting of (A) the head unit and (B) the wrist unit. More specifically, the head unit comprises of the NeuroSky MindBand sensor and the wrist unit comprises of the PulseOx finger unit, the GSR electrode, the thermistor and the BioSensics PAMSys+ GSR sensing circuit.

Figure 17 is a screenshot of the MoPASS Desktop Application for real-time measurement and streaming from both the wrist and head components of the MoPASS system. The top graph shows the real-time EEG measurements from the MindBand during a normal days-worth of activity. The remaining graphs depict measurements from the wrist unit. The second graph is specifically gathering real-time movement measurements. The third and fourth graph are depicting skin temperature and conductance, respectively. Lastly, the fourth graph is gathering real-time, accurate heart rate measures. We have successfully collected real-time signals for the wrist and head components, validating the MoPASS prototype system as a whole. In Phase

II of this project, we will build on the MoPASS GUI as a foundation for running the algorithm for multi-modal pain detection and assessment.

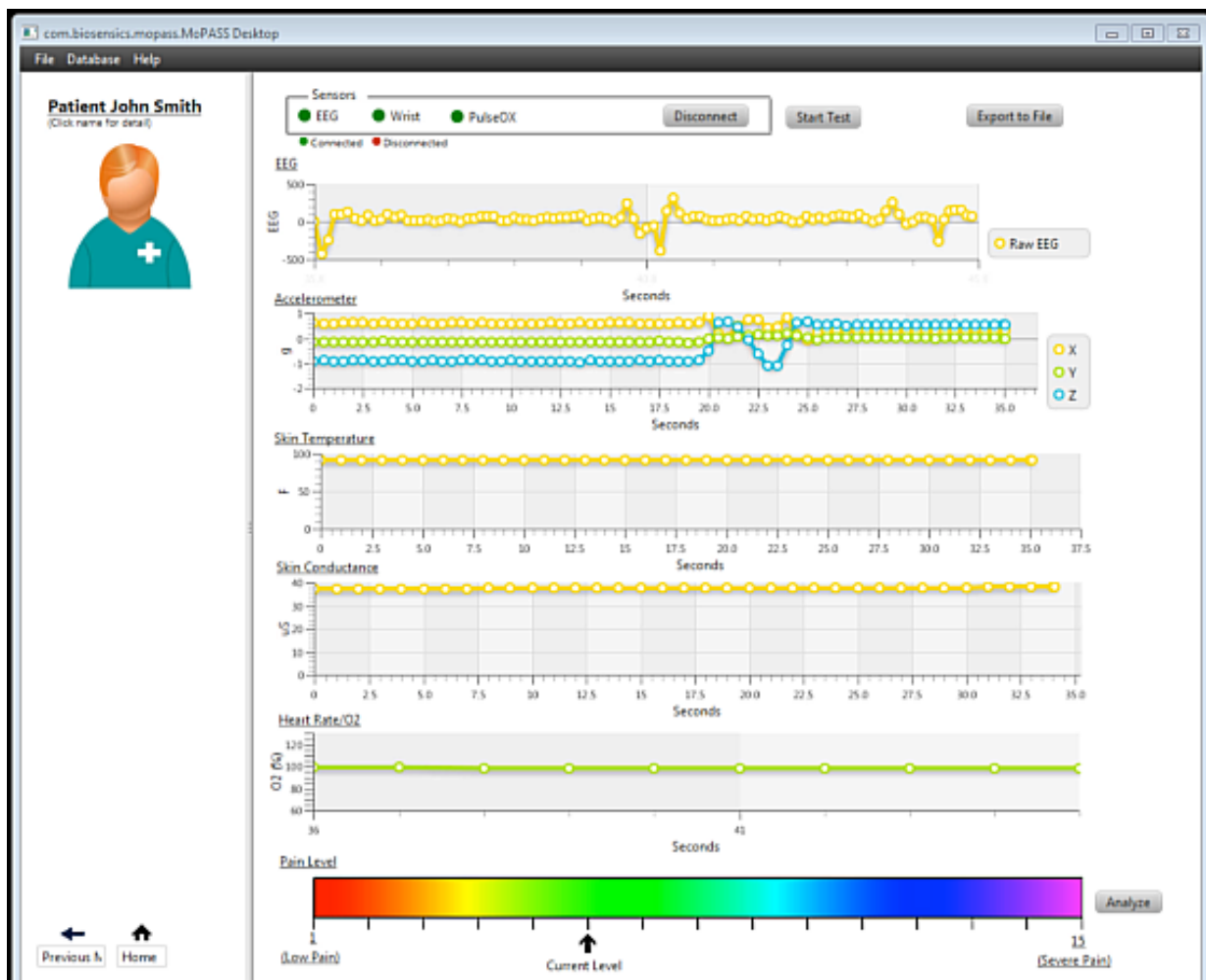


Figure 17: MoPASS Desktop Application for real-time measurement and streaming from both the wrist and head components of the MoPASS system.

Third Phase I Outcome: Clinical Study Design

The third outcome of Phase I was the design of clinical studies to be carried out in Phase II and the identification of an appropriate clinical site and clinical investigators. These studies are described in detail in the Phase II work plan. In brief, we have identified an excellent clinical research team at the University of Arizona who will partner with us in these efforts, and we have identified a research plan involving long-term monitoring of patients in the medicine ICU. This is the ideal environment for the clinical studies for several reasons: 1) patients are often in the ICU for an extended period of time allowing us the opportunity to acquire clear baseline signals and then evaluate changes in response to painful procedures or medications, 2) patients in the medicine ICU often undergo painful procedures (e.g., central line, chest tube, spinal tap) and it is critical to monitor this pain, 3) many of these patient will be intubated, providing a portion of the sample population that is non-communicative, and 4) the first civilian commercialization target for MoPASS will be as a device intended for use in the ICU.

Phase II Technical Objectives

There are three objectives and associated deliverables of this Phase II project:

1. Clinical Studies

Objective: Conduct a clinical study using hardware developed during Phase I to collect MoPASS data and gold-standard clinical assessments of pain in the medicine ICU, and use this data to develop an algorithm to combine indicators of pain into a single pain score.

Deliverables: There are three deliverables related to this objective: 1) the MoPASS pain intensity algorithm, 2) a filed U.S. Patent Application covering the specific approach to multi-modal pain assessment that is discovered during these trials, and 3) a publication in a peer-review scientific journal demonstrating the statistical significance of the correlation between the MoPASS pain intensity score and the gold-standard clinical assessments of pain.

2. Sensor Improvements

Objective: Improve the finger and forehead sensors by designing for manufacturability and improving the form-factor compared to the system developed in Phase I.

Deliverables: A manufacturing plan including a complete bill-of-materials, vendor selection, cost-estimates, and tooling, as well as a first batch of 20 manufactured units.

3. MoPASS Computer for Clinical Use

Objective: Develop a Windows-based MoPASS software platform that runs on a ruggedized mobile personal computer and allows only the MoPASS software to run on the device.

Deliverables: A ruggedized mobile computer that boots-up directly into the MoPASS software, pairs automatically with MoPASS sensors in range, continuously displays and logs a patients' pain intensity score, and can be configured to optionally deliver an auditory alert and/or SMS format alert in the event that the pain score exceeds a clinician set threshold.

Conclusion

Based on the significant work that we have completed during Phase I we are in an excellent position to meet these objectives. Specifically, we are ready to begin the clinical study at the outset of Phase II (following IRB approval). This will allow us to pursue Phase II engineering developments in parallel with Phase II clinical studies. By the completion of Phase II we will have a finalized device that is ready to be used in a comprehensive clinical trial during Phase III in anticipation of an eventual FDA submission for approval as a Class II Medical Device.

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