Full spectral pulse oxymetry using the Chromation system

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Abstract
Full spectrum pulse oximetry represents a significant market opportunity for broadband and portable spectral sensors. Human hemoglobin has a number of variant forms which are sensitive indicators of several health parameters, including blood oxygenation, carbon monoxide exposure, sickle cell anemia status, and state of diabetic shock. Full spectrum measurement of the pulse oximetry signal has been challenging and previously required the fabrication of a range of custom LEDs at the isosbestic wavelengths of the hemoglobin variant forms. The Chromation sensor, with its compact size, high spectral resolution, and spectral range, can effectively measure and differentiate these signals, presenting a new opportunity for portable and wearable medical pulse oximeters, integration with consumer electronics such as smart watches, and incorporation in mobile devices.

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Introduction to pulse oxymetry

Pulse oximetry typically uses two wavelengths of light to determine the fraction of oxygenated hemoglobin in the blood. One measurement is taken at a wavelength corresponding to an isosbestic point of hemoglobin (the wavelength at which both oxy- and deoxyhemoglobin variants have the same absorptivity), and a second measurement is then taken at a wavelength where the absorption curves are well separated. By comparing the ratio of these two measurements the relative fraction of each variant can be determined and normalized for overall light intensity, skin pigmentation (which is relatively spectrally uniform), and total blood volume.

While two wavelength pulse oximetry is an inexpensive and routine technology, there are several complications to its broader application. Several additional variants of hemoglobin also exist including the sickle cell hemoglobin variant, methemoglobin, hemoglobin bonded to carbon monoxide, and fetal hemoglobin. Each of these forms has different absorption curves and cannot in general be measured using the same systems that measure blood oxygenation in normal patients.

Full spectral pulse oximetry systems

One solution to measuring a broader range of hemoglobin variants is to use additional wavelengths to identify the contribution of additional hemoglobin variants. The only multispectral pulse oximeter currently on the market is the Masimo Rainbow system, which is co-marketed with several partners (including GE and Philips healthcare). This system uses 7 LEDs to separately measure oxyhemoglobin, deoxyhemoglobin, methemoglobin, and carboxyhemoglobin. The sourcing challenges with this many separate light sources are formidable - in 2012 Masimo acquired Spire Semiconductor, the foundry performing their LED fabrication, to insure a steady supply of these LEDs.

The use of a white light source and spectrometer to identify multiple hemoglobin variants has been demonstrated by several groups.[1] This approach uses the spectral selectivity of the detector to map the spectral response of the system. Such an approach, which is well addressed by the Chromation spectrometer, allows for a simpler and more compact architecture using a single light source and a single detector.

Hemoglobin variants detectible using full spectrum pulse/ox

There are a number of hemoglobin variants that can be measured using full spectrum analysis, which are capable of providing information relevant to both clinicians and consumers. Figure 1 (a) shows the absorption spectra of several of these variants, demonstrating the benefit of a spectroscopic approach to measurement.

Carboxyhemoglobin: Carbon monoxide binds tightly to hemoglobin and decreases the oxygen carrying capacity of blood. Carboxyhemoglobin, the form of hemoglobin with carbon monoxide bound to it, has a distinct spectrum which can be identified through spectroscopic analysis.

Methemoglobin: Methemoglobin is a form of hemoglobin which leads to reduced oxygen carrying capacity. Acquired methemoglobinemia can be triggered by exposure to a number of drugs including several commonly used anesthetic agents and over the counter medications. The onset of methemoglobinemia requires discontinuation of the drug's use and in some cases supportive oxygen therapy. A recent study found a 4% incidence of non-inherited methemoglobinemia among non-infant patients at an acute general hospital. Methe-

Figure 1. (Left) The spectrum for deoxyhemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin. These curves offer multiple isosbestic points and also require measurement at points of mutual separation for effective measurement; multiple wavelengths are required to separate these variants. (Center) A consumer pulse oximetry product produced by Omron (Right) A typical medical-grade oximeter module, showing the Rainbow SET from Masimo.

moglobinemia is itself dangerous, and the modified spectrum also confounds traditional pulse oximetry indicating a high oxygen saturation independent of the actual value.

There are several other dyshemoglobins and natural hemoglobin variants which can be detected spectroscopically. Even in cases where there is no clinical impact to the identification of the variant, measurement of oxygenation can be challenging in these cases without the use of a full spectral analysis because of a shift in the useful isosbestic points. Use of a spectroscopic instrument to analyze these cases significantly expands the applicability of this approach.

Use cases for pulse oximeters

Smartwatches: A smartwatch can incorporate a full spectrum measurement system using the Chromation spectrometer. This will allow for superior measurement of traditional oxygenation and heart rate, as well as other hemoglobin state parameters (e.g. exposure to carbon monoxide).

Mobile device: Use of a finger pad with an LED and spectrometer on a mobile device can allow for a spot check of the state of health, measurement of heartbeat, and determination of the degree of oxygenation. The flagship Samsung phones (Galaxy S5 and later models as well as the Note 4 and later models) ship with this type of sensor.

Medical devices: Both consumer and professional pulse oximetry systems can benefit from a move to full spectrum analysis. Using more effective wavelengths allows for the separate identification of a broader range of hemoglobins and unlocks functionality for patients with less common issues such as CO poisoning events or inherited/ acquired dyshemoglobin variants such as .

Size of the market opportunity

The market for this technology includes a range of both medical and consumer applications. In 2017 standalone pulse oximeters represented a $1.5B market. Smart watches and health bands currently have annual sales of $16B on sales of about 15 million units per year. Samsing's flagship phones with integral pulse oximetry represent sales of approximately 80M units per year. Chromation's technology has significant opportunity for integration in both professional and consumer health products such as smart watches.

There are additional high value and high volume opportunities for such monitoring systems. One example is CO poisoning measurement devices for first responders, which can be implemented using the Chromation spectrometer. Carbon monoxide poisoning is the top cause of fatal poisoning in the US, with about 6000 deaths and 50,000 hospitalizations per year. NFPA 1584 requires assessment of firefighters for carbon monoxide exposure upon a possible exposure, and specifically recommends the use of carbon monoxide sensitive pulse oximetry. There is a demand for systems that can be deployed in EMS units for use on suspected poisoning victims as well as for wearable systems that can be used by first responders. There are more than 1 million active duty firefighters and 600,000 police officers in the United States, leading to a potentially significant new market.

We have been in serious discussions with Flex and their Lab IX investment arm to investigate this and several related concepts. Flex manufactures 75% of wearable devices worldwide. Chromation has been in discussion with Osram's sensor division, which makes one of the most popular smartwatch pulse oximeter LED/detector hybrid units. We have also met with the Apple sensors group, which is responsible for iPhone and Apple Watch components as well as Samsung's components sourcing organization.

References

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[2] Kwame Baah et al. Perceived acceptability of colour matching for changing substrate white point. In *Color Imaging: Displaying, Processing, Hardcopy, and Applications*, page 86520Q, 2013.