Research and Technology
- Pulse Oximetry: Where it came from and where it is going -

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1. Introduction
To gain perspective on the past, present, and future of pulse oximetry, it is valuable to look at the development of other major noninvasive monitoring technologies over the past 500 years.

Referring to Figure 1, the first thing that one notices is that there are fairly few total devices, roughly one new parameter every 30 years. (The author apologizes for any major monitoring technologies that were inadvertently excluded.) Perhaps more surprising is that the rate of generation of new monitors has not increased over the past 200 years, even though humanity’s rate of overall technological progress most certainly has!

This graphical timeline shows historically-significant dates in the development of the major non-invasive medical monitors. As an example, for the Electrocardiogram (EKG), Carlo Matteucci first recognized in 1842 that an electrical impulse accompanies each heart beat, but Willem Einthoven created the first accurate recording devices used as a clinical tool around 1895. The value of multiple chest leads (12-lead EKG) was not acknowledged until the early 1930s. Along the bottom is a single timeline indicating only the first introduction or discovery of a new monitoring technology. During the last 200 years, a new monitoring technology was introduced roughly every 30 years. Note: The authors should be contacted for further information on various assumptions that were made and on what event is signified by each data point. Monitors not considered in this timeline include Bilirubin, Anesthetic Agent, Gastric Tonometry, and Niroscopy. The data is compiled from multiple sources including References 1 through 9.

2. An (Exceedingly) Brief History of Pulse Oximetry
Pulse oximetry, arguably the last new major monitoring technology, was really an evolution, as was the case with all major monitoring modalities. In the early 1860s, Felix Hoppe-Seyler, a professor of applied chemistry in Tübingen, Germany, first used the term hemoglobin to describe the compound in blood that absorbed blue and green light. With the aid of a crude spectroscope, he also realized that the amount of light absorbed changed when the blood was mixed with oxygen. Early attempts to build oximeters were made in the 1930s and 40s by Matthes of Germany and Millikin of England, but it was Dr. Earl Wood of the Mayo Clinic who in the late 1940s introduced oximeters to a clinical setting. Unfortunately, these early instruments were unreliable, difficult to set up, and hard to calibrate. Hewlett-Packard introduced the first self-calibrating oximeter in the 1970s. The HP 47201A Oximeter used a sensor mounted on the ear with light delivered via a fiber optic cable and used a heating element to keep the tissue locally perfused with blood.

The modern "pulse" oximeter has its beginnings in the work of Takuo Aoyagi, an engineer working with Nihon Kohden Corporation in Tokyo, Japan. Aoyagi recognized that pulsatile signals measured at two different wavelengths could be accurately related to the oxygen levels of the arterial blood. This was a significant finding, because it reduced the number of wavelength bands necessary for accurate measurement of oxygen saturation from the eight used in the HP instrument down to two, and it also eliminated the requirement to know the intensity of light that was entering the tissue-under-test. Aoyagi and his team announced the first modern pulse oximeter in March 1974, the OLV-5100. Aoyagi's device used a tungsten light source and two narrow band filters to generate the required two channels of nearly monochromatic light. Unfortunately, these filters also blocked the vast majority of the initial light intensity, leaving precious little light for the measurement of oxygen saturation.

The pulse oximeter as we know it today was created with the advent of light-emitting diodes (LEDs). LEDs generated an enormous amount of narrowband light power. This was exactly the type of light required to vastly improve the signal quality of oximetry instruments. During the late 1970s, Scott Wilbur and his team at Biox Technology in Boulder, Colorado began development of a pulse oximeter that used a sensor with LEDs and a photodiode mounted at the tissue site. In 1981 Biox introduced the pulse oximeter in its first truly commercially-viable form.

3. Pulse Oximetry Today

Current pulse oximeters are impressive instruments. They can make accurate readings on tissue over a wide range of optical densities caused by large differences in tissue thickness at the sensor site and varying levels of skin pigmentation. Pulse oximetry can measure oxygen saturation from the thinnest of earlobes to the thickest and most darkly pigmented infant's foot. The dynamic range of a typical pulse oximeter is more than 100,000 to 1. Many of today's pulse oximeters are accurate in clinical situations that include electromagnetic noise from electrosurgical equipment, a high degree of patient motion, and/or an extremely wide range of tissue perfusion levels. Yet regardless of how capable the instrumentation has become, we still focus on its shortcomings. One of the authors recently witnessed two instruments in clinical use, side-by-side on a quiescent patient (with no cross contamination of the sensor light sources), reading more than 40% apart in oxygen saturation. This demonstrates that there is still plenty of room for improvement in the measurement capabilities of pulse oximetry.
There are also benefits to be gained from additional measurements that a pulse oximeter can yield. One additional parameter that is now available on at least a few commercial oximeters is "perfusion index" (PI). This is a simple measure of the pathlength change that has occurred in the tissue-under-test (for example, the finger) over the cardiac cycle. When this parameter was first recognized as being something that a pulse oximeter could measure, it was difficult to imagine a value to the measurement because it is affected by so many different physiological and environmental variables, including systemic vascular resistance, volume status, blood pressure, and ambient temperature. But as time continues to pass since its introduction, more applications for PI are found. The most obvious use for perfusion index is as an aid in sensor placement. It provides a means to quantify the validity of a given sensor site and, where desired, to maximize measurement accuracy. PI has also provided a simple and easy to use means to test for sufficient collateral blood flow in the ulnar artery to allow for harvest of the radial artery for coronary artery bypass graft (CABG) surgery and for monitoring peripheral perfusion in critically ill patients. The authors are aware of other work where PI has been used for biofeedback training for Raynaud's Syndrome sufferers, as a measure of vasoconstriction, for determination of the viability of the tissues after bowel resection surgery, and for tracking vascular degeneration in the extremities of diabetic patients.

4. The Future of Pulse Oximetry

The future of pulse oximetry lies along two separate paths. The first is what the future holds for "pulse oximetry," meaning SpO₂ and PI measurements. The second is what the future holds for the science of photoplethysmography, the monitoring modality that pulse oximetry uses to make its measurements.

Pulse oximetry, as a technology, is still in its infancy with a great deal of room for improvement. Expect improvements in accuracy, precision, and resolution, a continued reduction in artifactual readings, ever-expanding sensor offerings, and considerable improvements in trending and data analysis. Also look for expanding diagnostic potential in the analysis of pulse oximetry data. One example of this last element is the discovery that a detailed, high resolution, trend analysis of pulse oximetry data can identify upper airway instability. Another study used perfusion index (PI) to monitor the severity of illness in neonates. The infants were rated using the Score for Neonatal Acute Physiology (SNAP). If the SNAP was greater than 10, or there was severe neonatal morbidity, the illness was rated as high severity. The researchers found that a PI = 1.24 (on the study oximeter) had a 91.2% sensitivity and 93.7% specificity in predicting high illness severity.

In fact, the development of pulse oximetry is following a path not unlike that taken by previous monitoring technologies. As with any promising monitoring modality, as the underlying technology is better understood, develops further, and becomes more robust, the diagnostic capabilities of the resulting instruments increase. It would have been hard to imagine the detailed analytical capabilities of the 12-lead EKG and the ability to localize ischemia to a specific region of the heart or provide detailed information as to arrhythmias when the first tracings appeared from the first two-lead EKG systems used to continuously monitor the heart. Or that the first wrist sphygmograph would evolve into a device capable of
simultaneously monitoring the systolic, diastolic, and mean blood pressures. A recent paper expressed one author's belief on what the future holds for pulse oximetry:

"It is anticipated that, in the future, a new class of high fidelity interpretive oximeters will be developed to engage these emerging patterns thereby extending the functionality of pulse oximetry to provide a new generation of diagnostic devices."

The future of photoplethysmography holds the promise of several new noninvasive parameters. Virtually any chromophore, or light absorbing substance, in the "tissue window" has the potential to be measured non-invasively with pulse oximetry. The "tissue window" is that portion of the electromagnetic spectrum over which light can pass through tissue to a measurable extent. It corresponds to a region that is roughly between 630 nanometers (nm) and 1350nm. Referring to Figure 2, note that at wavelengths shorter than about 630nm, hemoglobin becomes a "brick wall" filter that essentially blocks almost any light from getting through the tissue.

![Figure 2: Optical Absorption Curves for Oxyhemoglobin and Reduced Hemoglobin](image)

This graph shows the absorption coefficients for the various species of hemoglobin assuming a concentration of 15g/dL for each specie of hemoglobin. The visible spectrum shown at the top of the graph shows the spectral position of the various colors from ultraviolet at 400nm out to the infrared starting at about 750nm. Also shown is the "tissue window" (the region...
above about 625nm), below which almost all light is blocked by the absorption of hemoglobin. The data is compiled from multiple sources including References 17 through 21.

You already know this, in one sense. Anyone who as a child played with a flashlight in the dark knows that when you shine white light into your hand, only red light comes out. This is because all other colors of the visible spectrum, namely those below 630nm, are blocked by the blood.

This is an unfortunate difficulty for in vivo measurements, because the extinction curves are quite spectrally "active" in the 535nm to 670nm region. This explains why CO-oximeters use this spectral region to measure oxyhemoglobin (O$_2$Hb), carboxyhemoglobin (COHb), methemoglobin (metHb), reduced hemoglobin (RHb), sulfhemoglobin (SHb), and fetal hemoglobin (HbF). These instruments can work in a region of high extinction (or absorption) levels because they are in vitro devices. Being an in vitro device means that they can work with lysed blood, which eliminates the problems of measuring the absorption of light in a highly light scattering medium such as that created by the presence of whole blood cells, and that they can utilize pathlengths that are extremely small (approximately ½ mm). In vitro blood analyzers, in contrast to pulse oximeters, also make their measurements across only simple blood samples, without the intervening tissue that can contain skin, bone, venous blood, and fingernails. In vivo measurements are considerably more problematic.

On the other end of the tissue window, water becomes a "brick wall" filter above about 1350nm (see Figure 3). Thus the tissue window places certain constraints on the spectral range for in vivo measurements.
This graph shows the absorption curves for the various species of hemoglobin, assuming a concentration of 15g/dL for each specie, as well as the absorption curves for water. The upper and lower extents of the tissue window are also shown ranging from approximately 625nm out to about 1300nm. The data is compiled from multiple sources including References 17 through 21.

Nonetheless, there is a collection of important chromophores that have at least some absorption in the spectral range of the tissue window. Almost all species of hemoglobin, including O$_2$Hb, RHb, COHb, metHb, sulfHb, and HbF show measurable absorptions over this portion of the spectra, although COHb is fairly transparent compared to the rest. This opens up the possibility of measurement of these species of hemoglobin. Additionally, given that water may also be measurable, the continuous, real-time, and noninvasive measurement of total hemoglobin or hematocrit may also be feasible.

Some other chromophores that show up in this region include several dyes used for diagnostic and therapeutic purposes, including indocyanine green, methylene blue, and indigo carmine. It has already been demonstrated that photoplethysmography can be used to measure cardiac output through the use of indocyanine green and photoplethysmography via the dye dilution technique.

It is important to recognize that the inherent limitations imposed on noninvasive
measurements by the tissue window will continue to be eliminated over time. As electronics and optics technologies improve, the ability to detect and analyze smaller signals will expand the spectral range over which photoplethysmography can operate. This will ultimately increase the number of blood analytes that this monitoring modality can process and the accuracy with which the measurements can be made.

5. References


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The values for H₂O were generated from data from:


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