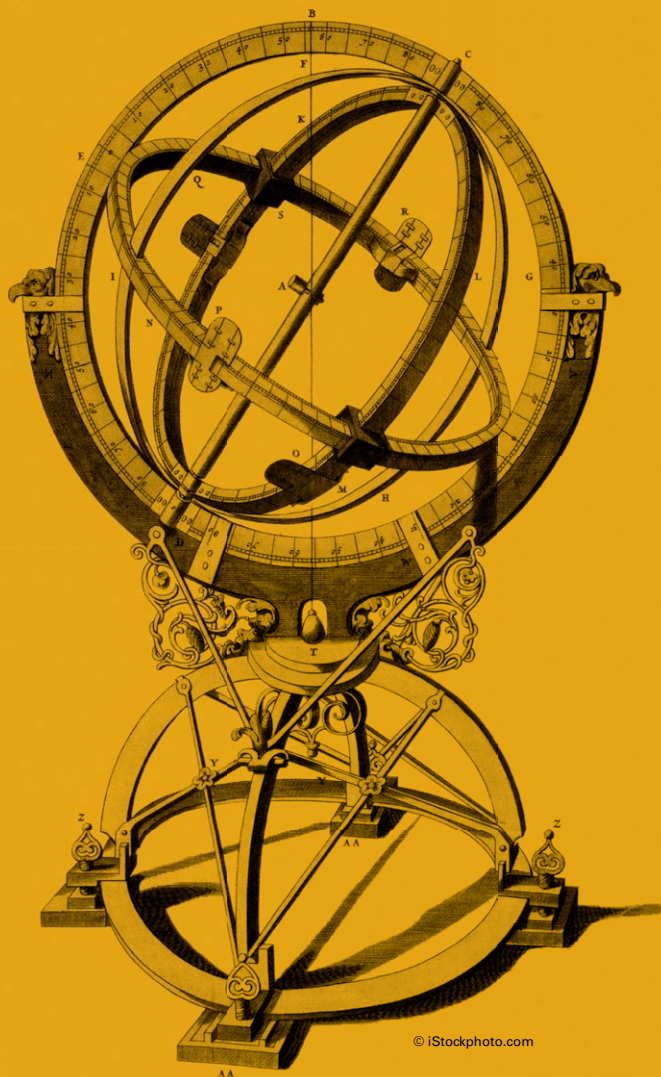


# The Measurement of Oxygen Saturation in Arterial and Venous Blood

Meir Nitzan and Haim Taitelbaum



Adequate oxygen supply to the body's tissues is required for normal body function. Values of oxygen concentration could be helpful in assessing heart and lung health, proper blood flow, and other blood-related issues. Many techniques have been developed for the assessment of oxygen supply, but most have not been widely accepted. One technique that is used effectively during surgical operations provides the surgeon a reading of respiratory efficiency from normal to dramatic deterioration. This article describes non-invasive optical measurement techniques to assess oxygen saturation in arterial and venous blood.

The most important of the techniques are based on the optical measurement of the percentage of oxygenated hemoglobin relative to the total hemoglobin in arterial or venous blood. This parameter is called oxygen saturation, and its value in the arteries is related to the adequacy of the respiratory system. The value of oxygen saturation in the veins is related to the amount of blood flow to the tissue. Both arterial and venous oxygen saturation have clinical and physiological significance, but whereas arterial oxygen saturation is routinely measured and monitored in the clinical environment, the measurement of venous oxygen saturation has not yet reached the accuracy and convenience required for its clinical use.

## Arterial and Venous Oxygen Saturation

One of the main tasks of the blood is to provide an adequate supply of oxygen to the body's tissues. Blood with a high concentration of oxygen is conveyed from the left ventricle of the heart into the tissue of the body's various organs via a branched arterial system, and after transferring part of its oxygen to the body's tissue through the walls of the capillaries, blood returns back to the right side of the heart in the venous system. The transfer of oxygen in the blood is mainly performed by the hemoglobin molecules. Hemoglobin molecules combine with oxygen molecules in the lungs and release the oxygen molecules in the low-oxygen-concentration environment of the tissues. The hemoglobin molecules are accumulated in the red blood cells, and each hemoglobin molecule can combine with four oxygen molecules.

Oxygen saturation,  $SO_2$ , is the ratio of oxygenated hemoglobin concentration,  $[HbO_2]$ , to that of total hemoglobin,  $[HbO_2 + Hb]$  ( $Hb$  denotes deoxygenated hemoglobin). That is,

$$SO_2 = [HbO_2] / [HbO_2 + Hb] \quad (1)$$

The value of  $SO_2$  in the *arterial* blood,  $SO_{2a}$ , depends on the adequacy of the ventilation and respiratory function. Normal values of  $SO_{2a}$  are 95–99%. Assessment of  $SO_{2a}$  is mainly important for the evaluation of proper respiratory function, and it is routinely performed in the clinical environment by the technique of pulse oximetry, which will be described later.

Most of the hemoglobin in venous blood is still oxygenated. Normal values of the oxygen saturation in the peripheral venous blood, denoted by  $SvO_2$ , are 70–80%.  $SvO_2$  also has physiological and clinical significance, as lower blood flow to the tissue results in higher utilization of the oxygen in the

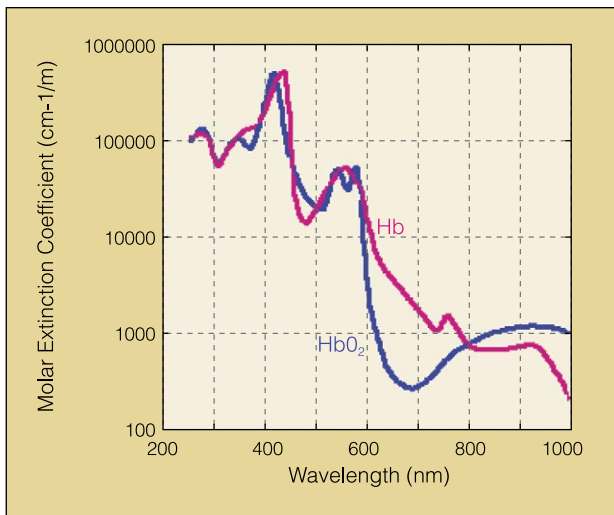


Fig. 1. The absorption spectra of the oxygenated and deoxygenated hemoglobin molecules. (©IEEE, figure by Dr. Scot Prahl, used with permission). [1]

blood and lower values of  $SvO_2$ . The assessment of  $SvO_2$  in the skin or muscle can provide information on the adequacy of local blood flow. Low values of skin blood flow can indicate the occurrence of shock or cardiac failure, in which blood flow is diverted from the peripheral circulation toward more vital organs. In contrast to the routine use of pulse oximetry for  $SaO_2$  measurement, no accepted method for the measurement of  $SvO_2$  is available at present.

### Optical Measurement of Arterial Oxygen Saturation

$HbO_2$  and  $Hb$  hemoglobin have different light absorption spectrums. This property enables the non-invasive assessment of  $SO_2$  in the blood. In the red and the infrared light regions, the absorption is relatively low and enables accurate measurement of light transmission. Figure 1 shows the absorption spectra of  $HbO_2$  and  $Hb$  molecules expressed by the extinction coefficient of  $HbO_2$  and  $Hb$  as a function of the light wavelength.

The extinction coefficient of hemoglobin is defined as the absorption constant of hemoglobin divided by the hemoglobin concentration. The relative concentration of  $HbO_2$  in the arteries, i.e., the arterial oxygen saturation defined in Equation (1), affects the value of the absorption constant of the blood under examination and consequently the transmission of light through the tissue. However, the absorption constant of the blood cannot be directly evaluated from the measurement of light transmission through tissue because of other factors that must be considered:

- ▶ light scattering, which increases the path-length of the light by an unknown factor (of about 5)
- ▶ the optical path-length changes between individuals and between different physiological situations even for the same individual

- ▶ the fact that light is also absorbed by the venous blood, so that measurements of total light transmission through the tissue cannot determine the  $SO_2$  in just the arterial blood.

### Arterialization

In order to isolate the contribution of the arterial blood to the light absorption, the absorption of light of several wavelengths through the ear-lobe was measured after heating the tissue to  $41^\circ\text{C}$ . This heating results in “arterialization” of the blood [2]. The blood flow increases to cool the tissue and is beyond the requirements for metabolism. In this test, the venous blood is also highly oxygenated. This technique was commercialized by Hewlett-Packard in 1970 but was not accepted by the clinical community because of its inconvenience.

### Pulse Oximetry

Pulse oximetry is a technique used to monitor the  $SaO_2$  of hemoglobin. At present, the usual technique to isolate light absorption by arterial blood is based on photoplethysmography (PPG). PPG is the measurement of light absorption changes due to cardiac induced blood volume changes [2], [3]. The PPG signal originates from the arterial blood volume increase during systole, so that the measurement of the PPG signal in several wavelengths—pulse oximetry—enables the assessment of the  $SaO_2$ .

Figure 2 illustrates a photoplethysmograph. The PPG probe consists of a light-emitting diode (LED) directed into finger tissue and a photodetector that measures the light transmitted through the tissue. Blood volume increases in the arteries during systole, which results in a decrease in light intensity through the tissue. Figure 3 shows a PPG signal. The maximal value of the PPG signal ( $BL$ ) is proportional to the light irradiance transmitted through the tissue at end-diastole, when the tissue blood volume is minimal. In general, the PPG signal is presented in inverted form (Figure 4) so that an increase in the PPG signal corresponds to an increase in arterial blood volume.

The theory of pulse oximetry is described in several textbooks and articles [3], [4]. In short, from the amplitude,  $AM$ , of the PPG signal and from the baseline,  $BL$ , of the pulse (see Figure 3) the relative maximal change of the PPG signal,  $AM/BL$ , is calculated.  $AM/BL$  does not depend on the intensity of the illuminating light. For each wavelength,  $AM/BL$  is proportional to three factors:

- ▶ maximal arterial blood volume increase during systole
- ▶ the extinction coefficient of that wavelength in that increment of blood
- ▶ the optical path-length in the tissue for that wavelength.

In order to create a parameter, which depends primarily on the extinction coefficient of the arterial blood (which depends on the oxygen saturation) and only depends slightly on the arterial blood volume increase at systole and on the optical path-

**One of the main tasks of the blood is to provide an adequate supply of oxygen to the body's tissues.**

length in the tissue, the light transmission is measured for two wavelengths  $\lambda_1$  and  $\lambda_2$ , and the ratio  $R$  is defined by

$$R = \frac{(AM/BL)_1}{(AM/BL)_2} \quad (2)$$

$R$  depends primarily on the ratio of the extinction coefficients for the two wavelengths, and this ratio depends on the arterial oxygen saturation  $SaO_2$  [3], [4]. By dividing the ratios in this fashion, we should, in principle, remove the dependence of the parameter on the blood volume increase through which the light is passing. The division of the ratios reduces the dependence on the optical path-length, but does not eliminate it totally. In order to achieve a larger difference in light transmittance between the two wavelengths, commercial pulse oximeters choose one of the wavelengths in the infrared region, and the other in the red region, where the difference in the extinction coefficient between oxygenated and deoxygenated blood is maximal. However, for this choice, the red light scattering constant differs significantly from that of the infrared light resulting in a non-negligible difference in optical path-lengths for the two wavelengths.  $R$ , the ratio of  $AM/BL$  for the two wavelengths, includes two factors: the ratio of the extinction coefficients for the two wavelengths and the ratio of the two path-lengths for the two wavelengths. The latter is not unity, so that  $SaO_2$  cannot be directly derived from  $R$ .

The actual relationship between  $R$  and  $SaO_2$  for each pulse oximeter sensor is determined by calibration [3]:  $R$  is measured in several people simultaneously with *in vitro*  $SaO_2$  measurements on extracted arterial blood. The *in vitro* measurements are performed using a co-oximeter, a device that measures oxygen saturation in samples of extracted blood through optical or chemical methods. For each person,  $R$  and  $SaO_2$  measurements are taken for several values of  $SaO_2$ . These different values of  $SaO_2$  are achieved by changing the partial pressure of oxygen in the air the subjects breathe. The table of the simultaneous measurements of  $R$  and  $SaO_2$  provides the required calibration for the derivation of  $SaO_2$ , the clinical parameter, from  $R$ , the measured parameter. It should be emphasized that the calibration is possible because arterial blood has the same value of oxygen saturation all over the arterial system, since oxygen is not diffused through the arterial wall.

The assumed reliability of the calibration is based on the assumption that the ratio between the path-lengths for the two wavelengths,  $\lambda_1$  and  $\lambda_2$ , does not change between different people and different physiological and clinical situations. The validity of this assumption is limited, and deviations from this assumption are probably the origin of the inherent inaccuracy of the pulse oximetry technique for the assessment of  $SaO_2$  in arterial blood.

Manufacturers of pulse oximeters for  $SaO_2$  measurement claim accuracies of 2%. That is, the standard deviation of the  $SaO_2$  measurement by pulse oximetry with respect to the "true value" of  $SaO_2$  found by performing an *in vitro* measurement by co-oximeter is 2%. A standard deviation of 2% means that for 5% of the examinations made, using PPG-based techniques, deviations higher than 4% (two standard deviations)

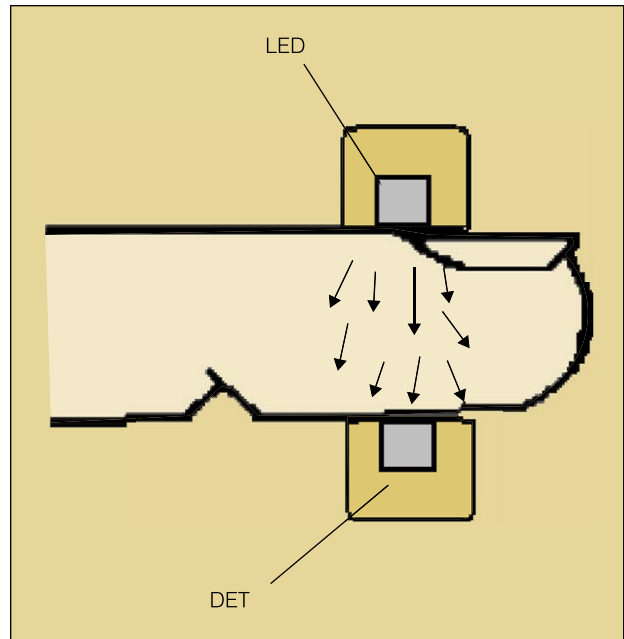


Fig. 2. Diagram of a photoplethysmograph. The light source (LED) emits light into the tissue, and the detector (DET) measures the transmitted light.

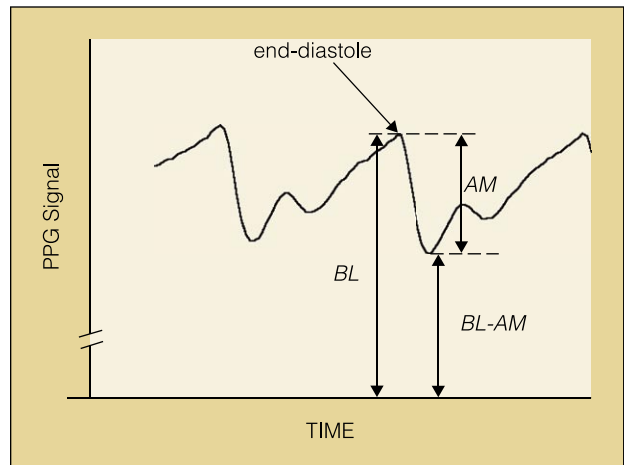


Fig. 3. A PPG signal over time. The baseline,  $BL$ , is the maximum of the pulse, and  $AM$  is the pulse amplitude.

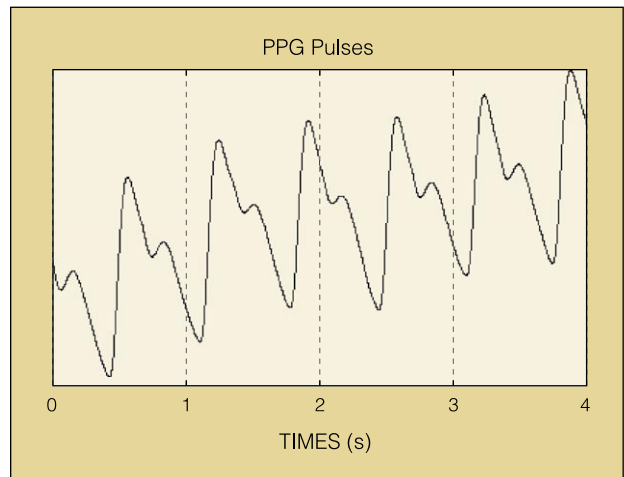


Fig. 4. The inverted PPG signal. The increase in the PPG signal corresponds to increase in tissue blood volume.

are expected. A deviation of 4% in a  $\text{SaO}_2$  measurement is acceptable for monitoring patients during surgical operation or in intensive care units, since the required clinical information is that no dramatic change in respiration or ventilation has occurred. However, a deviation of 4% in the  $\text{SaO}_2$  measurement is too high for the assessment of lung function in pulmonary function units, so that, in general, pulse oximetry is not used by pulmonologists for the determination of  $\text{SaO}_2$ .

### Pulse Oximetry with no Need for Calibration

The need for calibration can be avoided by using a pulse oximetry technique based on transmission measurements in two wavelengths that are close to each other so that the difference between their effective optical path-lengths is small. Then,  $R$ , the ratio of  $AM/BL$  for the two wavelengths, is equal to the ratio of the extinction coefficients for the two wavelengths [4]. Then, the relationship between the ratio  $R$ , the measured parameter, and the required clinical parameter, arterial oxygen saturation,  $\text{SaO}_2$ , can be derived by decomposing the extinction coefficient,  $\epsilon$ , into its two components; the extinction coefficients for oxygenated blood,  $\epsilon_o$ , and for deoxygenated blood,  $\epsilon_d$ :

$$\epsilon = \epsilon_o \text{SaO}_2 + \epsilon_d(1 - \text{SaO}_2) = \epsilon_d + \text{SaO}_2(\epsilon_o - \epsilon_d) \quad (3)$$

and after simple manipulation the following relationship between  $R$  and  $\text{SaO}_2$  can be obtained:

$$\text{SaO}_2 = \frac{\epsilon_{d1} - R\epsilon_{d2}}{R(\epsilon_{o2} - \epsilon_{d2}) + (\epsilon_{d1} - \epsilon_{o1})} \quad (4)$$

$\text{SaO}_2$  can be obtained without calibration by measuring  $R$  and substituting in the above equation the values of the extinction coefficients for oxygenated blood,  $\epsilon_o$ , and for deoxygenated blood,  $\epsilon_d$ , which are available in the literature.

### Optical Measurement of Venous Oxygen Saturation—Theory

Oxygen saturation in the peripheral venous blood,  $\text{SvO}_2$ , also has physiological and clinical significance, as described above, but in contrast to the routine use of pulse oximetry for  $\text{SaO}_2$  measurement in some clinical situations, no accepted method for the measurement of  $\text{SvO}_2$  is available. Similar to pulse oximetry, which utilizes the measurement of light transmission changes due to *arterial* blood volume changes, light transmission changes due to *venous* blood volume changes can also be measured by wrapping a pressure cuff around the arm and applying pressure greater than that of the venous blood pressure to the arm [4]. Using a pressure cuff in this way closes the veins but not the blood supplying arteries and results in venous blood accumulation. The measurement of the decrease in light transmission in two wavelengths due to the higher absorption in this accumulated venous blood could, in principle, enable the assessment of venous blood saturation in a method similar to pulse oximetry for the assessment of arterial blood saturation.

However, in pulse oximetry, the relationship between the measured  $R$  and  $\text{SaO}_2$  can be obtained by calibration, because  $\text{SaO}_2$  has the same value in the whole arterial system, whereas in  $\text{SvO}_2$  measurement calibration is not possible because blood extracted from big veins does not necessarily have the same value of oxygen saturation as that of the small veins at a specific skin site where the light transmission measurement is performed.

The technique that we suggested for the determination of  $\text{SaO}_2$  by measurement of light transmission in two wavelengths which were close to each other can also be applied for  $\text{SvO}_2$  measurement because it avoids the need for calibration.

In a way that is similar to the measurement of  $\text{SaO}_2$  by pulse oximetry,  $\text{SvO}_2$  can be derived from measurements of light transmission at two wavelengths before and after an increase in venous blood volume by a pressure cuff. When the venous blood volume increases, the light transmitted through the tissue changes from  $I_{max}$  to  $I_{min}$  and a ratio  $R_v$  is defined, where

$$R_v = \frac{\ln(I_{max}/I_{min})_1}{\ln(I_{max}/I_{min})_2} \quad (5)$$

From the value of  $R_v$  and the values of the extinction coefficients for oxygenated blood  $\epsilon_o$  and for deoxygenated blood  $\epsilon_d$ ,  $\text{SvO}_2$  can be obtained from an equation similar to Equation (4), with no need for calibration, by substituting  $R_v$  instead of  $R$ :

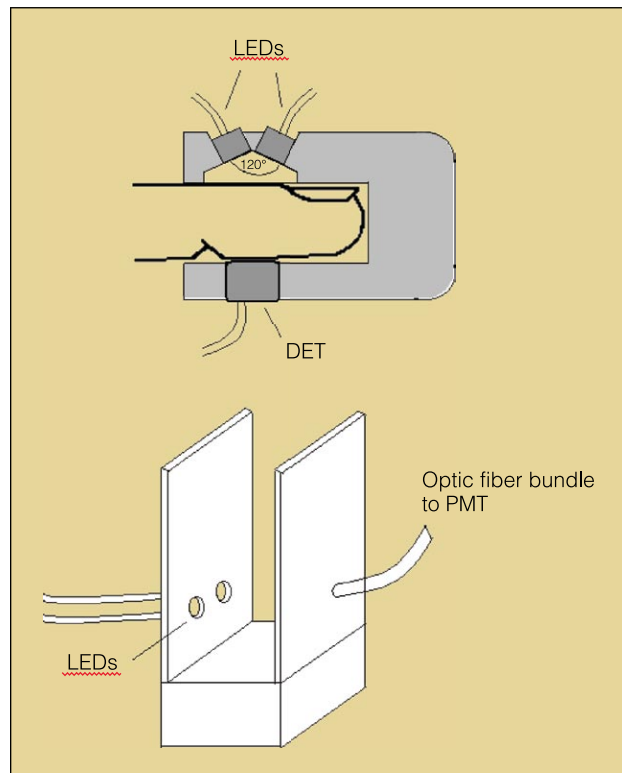


Fig. 5. (a) The two-wavelength PPG probe for a finger. (b) The device for the measurement of light transmission through the palm of the hand installed between the two plates. (©SPIE, *Journal of Biomedical Optics*, used with permission). [4]

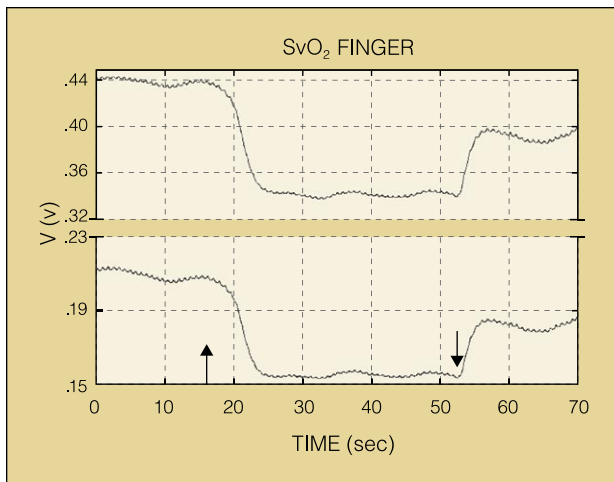


Fig. 6. The curves of light transmission (in volts at the photo detector output) through the fingertip for the two wavelengths 767 nm (upper curve in graph) and 811 nm. (©SPIE, *Journal of Biomedical Optics*, used with permission.) [5]

$$SvO_2 = \frac{\epsilon_{d1} - R_v \epsilon_{d2}}{R_v (\epsilon_{o2} - \epsilon_{d2}) + (\epsilon_{d1} - \epsilon_{o1})} \quad (6)$$

### Optical Measurement of Venous Oxygen Saturation—a Study

In a study we performed [4], we used two wavelengths in the infrared region, 767 nm and 811 nm, to measure SvO<sub>2</sub>. The light transmission probes for the finger and for the hand are shown schematically in Figure 5. Two LEDs were installed at 120° angles to each other for the finger probe. Using Equation (4), SaO<sub>2</sub> was derived from PPG measurements made at the two infrared wavelengths on the fingertip (Figure 5(a)). The photodetector in the finger probe was a p-i-n diode.

SvO<sub>2</sub> in the hand (Figure 5(b)) and in the fingertip were determined by measuring the light transmission in the two wavelengths through the palm of the hand or the fingertip, respectively, before and after the occlusion—the closing—of veins in the forearm of the same side of the body by means of a pressure cuff (exerting a pressure of 25 mmHg). The photodetector in the hand probe was a photomultiplier tube (PMT) (because of the low intensity of the transmitted light) attached to a fiber-optic bundle of 3 mm diameter.

SvO<sub>2</sub> was derived from the values of the light transmission before and after inducing an increase in venous blood volume. The increase in venous blood volume was achieved by applying external pressure of 25 mmHg on the forearm as described above. The values of the light transmission in the finger or in the hand before and after the pressure application were used for the evaluation of R<sub>v</sub> in the fingertip or in the hand, respectively. Then, Equation 6 was used for the derivation of SvO<sub>2</sub>.

Figure 6 presents the light transmission curves for 767 and 811 nm for SvO<sub>2</sub> in a finger. It shows the PPG pulses and low-frequency fluctuations (of 0.1 Hz). The decrease in the curves after about 15 s is due to higher light absorption in the venous blood volume increase induced by the venous occlusion. The two arrows indicate the period of venous occlusion.

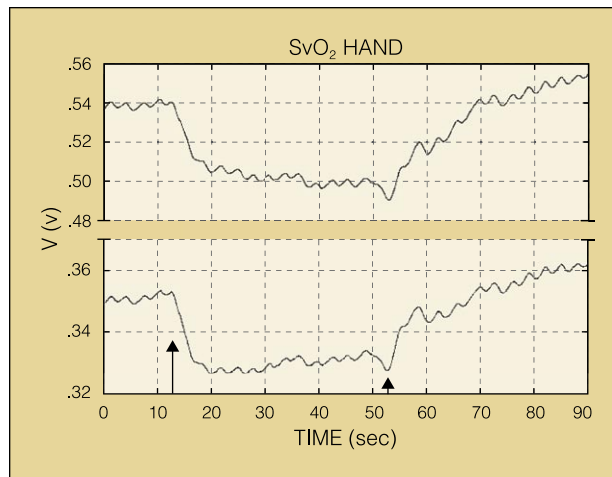


Fig. 7. The curves of light transmission (in volts at the photo detector output) through the palm of the hand for the two wavelengths 767 nm (upper curve in graph) and 811 nm. (©SPIE, *Journal of Biomedical Optics*, used with permission.) [4]

Figure 7 shows the hand curves of light transmission with blood volume oscillations at the respiratory rate. As for the finger curves, both 767-nm and 811-nm light transmission curves show a swift decrease due to venous blood accumulation after the venous occlusion.

The values of light transmission before and during the pressure application period were used for the assessment of R<sub>v</sub> and, consequently, of SvO<sub>2</sub>.

The mean value of SaO<sub>2</sub> was 95 ± 3%. The mean value of finger SvO<sub>2</sub> was 86 ± 4%, and of hand SvO<sub>2</sub> was 80 ± 8%. Figure 8 depicts the values of SaO<sub>2</sub>, finger SvO<sub>2</sub>, and hand SvO<sub>2</sub> for each of the subjects. The samples were numbered so that the value of SaO<sub>2</sub> increased from subject to subject. The value of SvO<sub>2</sub> is lower than SaO<sub>2</sub>. Because of the relatively large number of arterio-venous direct shunts (vessels in which blood from the arteries flows directly into the veins, and which are involved in body temperature regulation, but do not transfer oxygen to the tissue) in the fingertip, the value of SvO<sub>2</sub> in the fingertip is

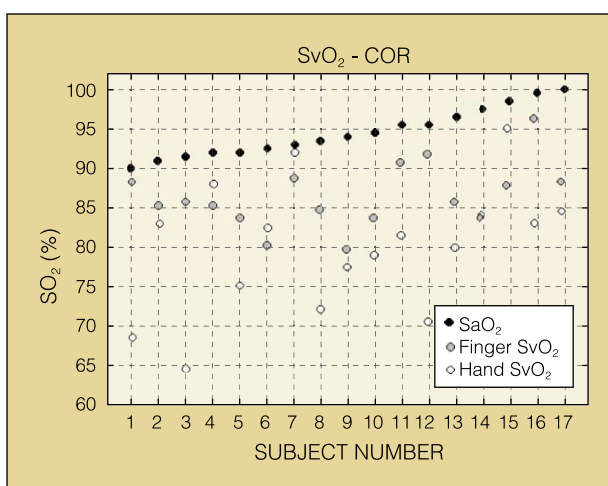


Fig. 8. The values of SaO<sub>2</sub>, fingertip SvO<sub>2</sub>, and hand SvO<sub>2</sub> for each of the subjects. SvO<sub>2</sub> is lower than SaO<sub>2</sub>. (©SPIE, *Journal of Biomedical Optics*, used with permission.) [4]

higher than the value of  $SvO_2$  in the hand. The value of 80% for the hand  $SvO_2$  is also higher than the typical value of tissue  $SvO_2$  in the body, which is about 70%, probably because the palm of the hand also contains some arterio-venous direct shunts.

### Near Infrared Spectroscopy Techniques for the Measurement of Venous Oxygen Saturation

Tissue near infrared spectroscopy (NIRS) is a non-invasive optical technique for the determination of the concentration of oxygenated and deoxygenated hemoglobin in tissue that includes both arterial and venous blood. From these measurements, oxygen saturation in total tissue blood, denoted by  $StO_2$ , can be derived, and in some cases venous blood oxygen saturation,  $SvO_2$ , can also be obtained. NIRS evaluates the concentrations of  $HbO_2$  and  $Hb$  in the tissue from the values of the absorption constant at several wavelengths derived from light transmission measurements at these wavelengths. Several techniques have been developed for the isolation of the absorption constant from the scattering effects [5], [6].

#### Time Resolved Spectroscopy

In this technique, infrared light pulses of duration less than 100 ps (picoseconds) are emitted into the tissue, and the temporal spread function of the transmitted light (with a typical power of a few picowatts) after traveling through several centimeters of tissue is measured and analyzed. The output pulse is measured with temporal resolution of better than 100 ps, which demands sophisticated equipment. Using an appropriate mathematical model for light transport in the tissue, the absorption and scattering constants can be derived from the dispersion curve.

#### Frequency-Domain Spectroscopy

In this technique, the illuminating infrared light in different wavelengths is modulated at radio frequency (typically 100 MHz), and the modulation and phase-shift in the transmitted light is measured. From the measured values of the modulation and phase-shift in the transmitted light, the absorption constant in the tissue can be derived using mathematical models with simplified boundary conditions.

#### Spatially Resolved Spectroscopy

In this technique, light transmission is measured as a function of the distance between the light-source and the detector for different wavelengths. By using an appropriate mathematical model, the dependence of light transmission on the distance between the light-source and the detector can be related to the absorption constant and scattering constant of the tissue, enabling the derivation of tissue concentration parameters and  $StO_2$ .

The NIRS techniques can be used for measurements of blood oxygenation in the total blood in tissue, which includes arteries, capillaries, and veins. It can also evaluate the concentrations of  $HbO_2$  and  $Hb$  or  $SvO_2$  in the venous blood by means of difference oximetry, which measures changes in light absorption of two wavelengths due to change in venous blood volume. Venous blood volume can be changed by applying external pressure and occluding the draining veins, by changing tissue level relative to the heart, or by deep breathing. In another kind of difference oximetry, changes in tissue oxygen consumption and in oxygen delivery to the tissue are induced by arterial occlusion (resulting in transient ischemia).

The reliability of these techniques depends on the extent of the suitability of the *homogeneous* mathematical model to the *heterogeneous* examined tissue. Tissue oxygenation parameters measured by NIRS techniques show low accuracy when the examinations are performed on living tissue, probably due to missing anatomical information regarding the distribution of tissue elements, mainly blood vessels. In particular, values of tissue blood oxygen saturation obtained by NIRS techniques in the arm and forearm were found to be lower than expected from known physiological data [5].

### Conclusion

The light path in biological tissue is complex and involves multiple scattering that results in higher light absorption due to prolongation of the optical path-length. The extent of light absorption depends on the wavelength of light, tissue characteristics, and the distribution of blood in the tissue through which it propagates. The determination of blood oxygen saturation in a given tissue sample cannot be derived directly from light transmission measurements through that tissue sample because of missing information regarding the scattering.

The available pulse oximeters for arterial oxygen saturation measurement use light in two wavelengths, in the red and infrared regions, and calibration is used to account for the difference in optical path-length between them. The accuracy of the commercial pulse oximeters is adequate for monitoring patients during surgical operation, where the clinical information that is needed is the absence of dramatic deterioration in the respiration efficiency. However, the error in pulse oximetry is too high for the clinical assessment of lung function, probably because of the need for calibration in the available technique.

The use of two wavelengths in the infrared, instead of one wavelength in the red and one in the infrared region, enables the use of pulse oximetry without calibration. The technique can also be used for determining venous blood saturation, which is important for assessment of the adequacy of tissue blood supply. The simple technique of difference oximetry

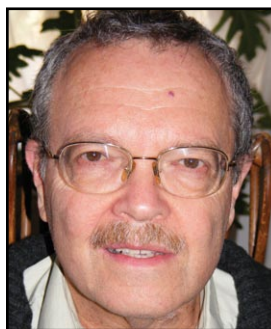
## The use of two wavelengths in the infrared...enables the use of pulse oximetry without calibration.



and the more sophisticated techniques of NIRS need further improvement in order to be of clinical significance.

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<b>HAVE 2008</b> Haptic Audio Visual Environments	10–12 October 2008	Ottawa, Ontario, Canada	<a href="http://ieee-ims.org/site/conferences.php">ieee-ims.org/site/conferences.php</a>	59
<b>ROSE 2008</b> Robotic and Sensors Environments	17–18 October 2008	Ottawa, Ontario, Canada	<a href="http://ieee-ims.org/site/conferences.php">ieee-ims.org/site/conferences.php</a>	59
<b>SAS 2009</b> Sensors Application Symposium	17–19 February 2009	New Orleans, Louisiana, USA	<a href="http://www.sensorapps.org">www.sensorapps.org</a>	N/A

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