Product Document

Published by
ams OSRAM Group

Application Note

AN001044

AS7050 SpO2 Calibration

Overview of SpO2 Measurement & Guidelines for Calibration

v1-00 • 2022-Apr-07

Content Guide

1 Introduction

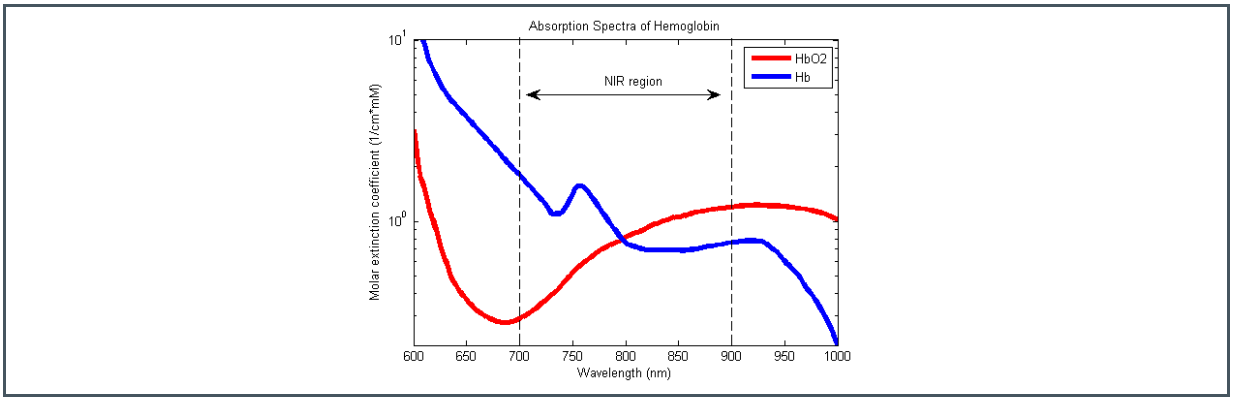
Every cell in the human body relies on a functioning supply of oxygen. Therefore, a measure is the oxygen saturation, which is given in percent and provides information about the functionality of the oxygen transport. In the past, pulse oximeters were used primarily in the medical environment, to monitor the respiratory functionality of patients. At a time of increasing interest in home monitoring, pulse oximetry is also gaining more and more importance. Furthermore, the Covid-19 pandemic is leading to an increasing interest in monitoring respiratory function.

2 Principles of Reflective SpO_2 Measurement

2.1 Light Absorption by Oxygenated Hemoglobin and Deoxygenated Hemoglobin

The principle of SpO_2 measurement is based on the fact that a red blood cell enriched with hemoglobin (HbO_2) absorbs light to a different extent than deoxygenated hemoglobin (Hb). The absorption of light by oxygenated and deoxygenated hemoglobin is much higher than for the surrounding human tissue and water in the visible and near-infrared (NIR) wavelength range. The absorption is described by the extinction coefficient. The higher the extinction coefficient, the more light is absorbed in the given substance. Figure 1 shows the absorption at different wavelengths for oxygenated hemoglobin and deoxygenated hemoglobin.

Figure 1:
Extinction Coefficient of Oxygenated Hemoglobin and Deoxygenated Hemoglobin for Different Wavelengths[1]



It can be seen in Figure 1 that the extinction coefficient for red light (λ = 680 nm) is much higher for deoxygenated than for oxygenated hemoglobin. The absorption at higher wavelengths (e.g. infrared, λ = 900 nm) is stronger in the case of HbO_2 than Hb.

2.2 Photoplethysmography: Measuring the Pulsating Nature of Blood

The blood volume in the blood vessels pulsates according to the heartbeat. By recording a photoplethysmographic signal (PPG), this pulsatile nature can be made visible. This is done by irradiating the skin with light (e.g. fingertip). A part of the light is absorbed and the remaining parts are either reflected, scattered, or transmitted as shown in Figure 2. Depending on the positioning of the photodetector, the PPG signal can be measured using the transmitted or the reflected light. The PPG signal consists of pulsating (AC) and non-pulsating (DC) components. While the AC component

indicates the change in arterial blood volume, the non-pulsating part is mostly derived from the venous blood, surrounding tissues, and the ambient light; and is overlaid by a low-frequency drift (caused by breathing and movements of surrounding tissue).

Figure 2:
Reflection, Transmission, Absorption, and Scattering of Light

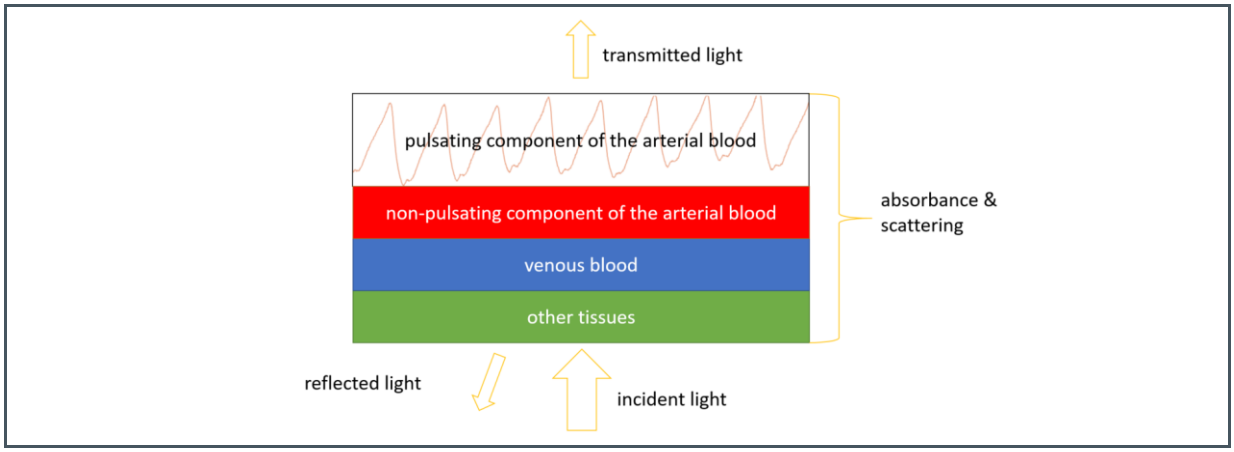
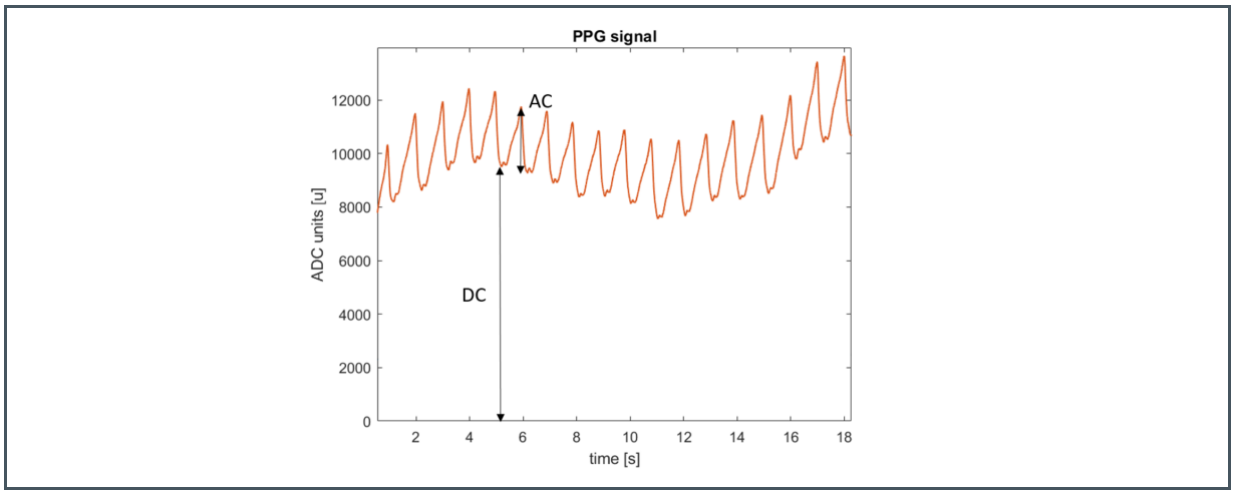


Figure 3 shows a reflection mode PPG measurement performed on the fingertip, using the ams OSRAM biosensor AFE AS7050.

Figure 3:
Photoplethysmographic Signal Measured on the Fingertip Using the Reflective Measurement Principle(1). Each Peak of the Signal Can Be Assigned to a Heartbeat as It Shows the Blood Volume Change in the Arteries.



(1) The DC part presented is cropped, due to the use of a photodiode offset current and is, in reality, greater by a factor of about 10. The use of the photodiode offset current will be explained in more detail within sections 3.2 and 3.3.

2.3 The Ratio of Ratios: R

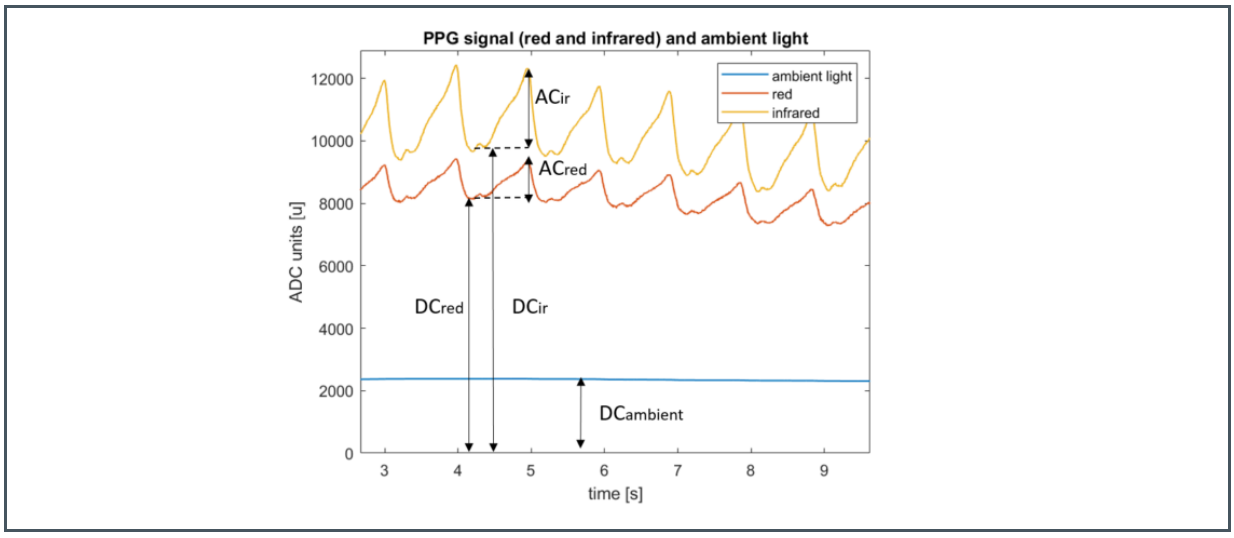
The pulsatile nature of the PPG signal makes it possible to determine the occurring absorbance effect and differentiate it from the influences of the surrounding tissue. This means, the absorbance due to the surrounding tissue and venous blood does not affect the measurement. The usage of red and infrared (IR) wavelengths makes it possible to obtain a measure of the oxygen saturation, requiring no absolute calibration with respect to the overall person-specific tissue absorbance. However, due to device-specific optical behavior, calibration of the pulse oximeter is needed. The ratio of ratios R (Equation 1) is calculated out of two synchronously measured PPG signals, derived from the usage of red and infrared LEDs.[2]

Equation 1:

$$R = \frac{\frac{AC_{red}}{DC_{red}}}{\frac{AC_{ir}}{DC_{ir}}}$$

AC_{red} is the pulsatile part and DC_{red} is the non-pulsating part of the PPG signal derived by the measurement with the red light. AC_{ir} and DC_{ir} are derived from the measurement using the infrared LED. Figure 4 shows how these components are determined in the PPG signal.

Figure 4:
AC and DC(1) Parts of the Red and Infrared PPG Signal



(1) The DC parts presented are cropped due to the use of a photodiode offset current and are, in reality, greater by a factor of about 10. The use of the photodiode offset current will be explained in more detail within sections 3.2 and 3.3

3 Signal Acquisition with the AS7050

3.1 Quasi-Synchronous Data Acquisition

For the determination of the oxygen saturation, a synchronous acquisition of the red and infrared PPG signal is necessary. While the red signal is measured, the infrared LED is switched off and vice versa. For the SpO_2 calculation, the ambient light also has to be determined. Therefore, measurement is done while both LEDs are switched off. This LED switching and clocked timing is done internally in the AS7050.

3.2 Automatic Gain Control (AGC) – Algorithm for High AC Signal Resolution

The AGC algorithm is included in the product evaluation software. It controls the applied photodiode offset current, and/or the LED drive current to ensure that the PPG signal amplitude is within a defined range of ADC values.

The measured PPG signals are overlaid by a low-frequency drift, which is caused, among other things, by breathing and movements of the surrounding tissue. The non-pulsating (DC) part is much higher than the pulsating (AC) part of the signal. Nevertheless, it is necessary to achieve a high resolution for the AC part, to obtain precise results with the SpO_2 algorithm.

The higher the intensity of the incident light, the higher the intensity of the reflected and transmitted signal. Therefore, the AGC algorithm controls the red and infrared LED current. Also, a third variable, the offset current, is controlled as well. The offset current is injected in the opposite direction to the photocurrent to avoid device saturation and to reduce the DC component of the PPG signal. The higher this current, the lower the DC part of the PPG signal. This leads to an enhanced resolution of the AC part.

3.3 Ambient Light Cancellation and Correction of the Photodiode Offset: Correction of R

To obtain AC and DC values that are independent of the environment and the photodiode offset, it is necessary to make some corrections. The ambient light must be taken into account because it affects the DC component. To make the R values independent of the AGC algorithm settings, the photodiode offset has to be taken into account as well. A change in the LED current leads to a change in the measured signal, but this has an equal effect on the AC and the DC part, therefore R is not affected. However, the ratio of the AC and DC part is changed by applying an offset current, as here, only the DC part is affected. The implemented algorithm eliminates these influences on the DC components of the red and the infrared signals to obtain the corrected R values (Equation 2):

Equation 2:

$$DC_{red_{corrected}} = DC_{red} - DC_{ambient} + PD_{offset\_current} \cdot PD_{off\_fact\_red}$$

$$DC_{ir_{corrected}} = DC_{ir} - DC_{ambient} + PD_{offset\_current} \cdot PD_{off\_fact\_ir}$$

4 Determination of Device-Specific Photodiode Offset Factors

The resulting factors for the DC compensation, $PD_{off\_fact\_red}$ and $PD_{off\_fact\_ir}$, for the evaluation kit, depend on the different settings of the ADC range, the PD offset range, and the PPG clock frequency. For example, smaller ADC ranges and greater PD offset ranges require a higher compensation factor PD_{off_fact}. The factors for certain configurations are provided in Figure 5. Note that further changes in the settings are not examined, and if such are carried out, the PD_{off_fact} should be re-determined.

Figure 5:
Factors for the DC Compensation for Different ADC and PD Offset Ranges Set at a Clock Frequency of 10 MHz

PD Offset Range/ ADC Range	32 µA	16 µA	8 µA	4 µA	2 µA	1 µA
128 µA	525	1042	2046	3964	7417	13198
64 µA	262	521	1023	1982	3708	6599
32 µA	131	260	511	991	1854	3299
16 µA	65	130	255	495	927	1649
8 µA	32	65	127	247	463	824
4 µA	16	32	63	123	231	412

Information

The cells marked in grey are ADC range/PD offset range combinations that are not recommended.

Figure 6:
Factors for the DC Compensation for Different ADC and PD Offset Ranges Set at a Clock Frequency of 5 MHz

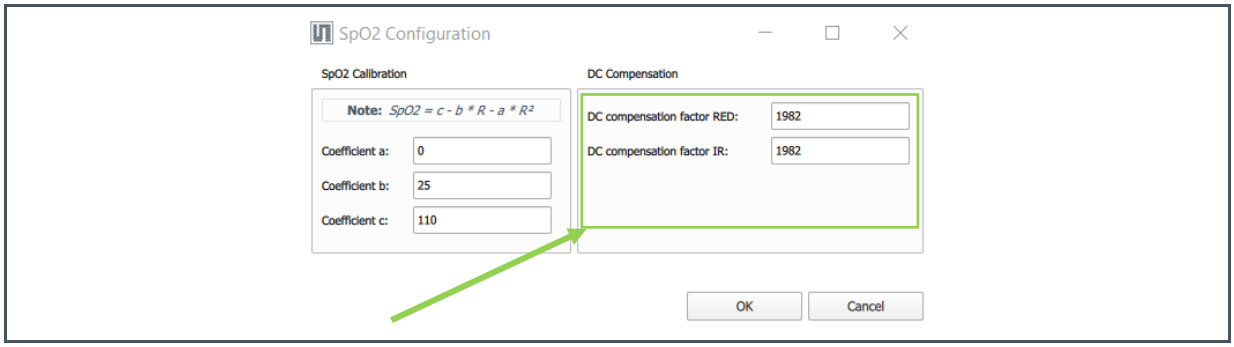
PD Offset Range/ ADC Range	32 µA	16 µA	8 µA	4 µA	2 µA	1 µA
128 µA	506	1004	1975	3833	7207	12887
64 µA	253	502	987	1916	3603	6443
32 µA	126	251	493	958	1801	3221
16 µA	63	125	246	479	900	1610
8 µA	31	62	123	239	450	805
4 µA	15	31	61	119	225	402

Information

The cells marked in grey are ADC range/PD offset range combinations that are not recommended.

These factors associated with the specific settings of the AS7050 must then be entered in the SpO_2 configuration settings. In the user interface of the evaluation kit, these settings can be found under *Application settings -> SpO2.*

Figure 7:
SpO_2 Configuration Window of the Evaluation Kit. *Application settings -> SpO2*



5 Calibration of the SpO_2 Model

5.1 Calculation of the Oxygen Saturation Using R

The R value, calculated by the firmware, is used to calculate the oxygen saturation. Different models are proposed in the literature for this purpose. For the AS7050, both the quadratic (Equation 3) and the linear model (Equation 4) are implemented:

Equation 3:

$$SpO2 = -a \cdot R^2 - b \cdot R + c$$

Equation 4:

$$SpO2 = -b \cdot R + c$$

Equation 5 is an example of proposed coefficients from related literature[3].

Equation 5:

$$SpO2 = -25 \cdot R + 110$$

The firmware calculates the R value with all aforementioned corrections directly. These R values can be used for performing the calibration procedure.

5.2 Calibration of the SpO_2 Algorithm

In addition to the absorption, depending on the wavelength of the light and the oxygen saturation, the incident light is further weakened by scattering processes. The optical behavior and the scattering vary, depending on the design of the pulse oximeter and the implemented optical system. To be able to determine correct SpO_2 values, the integrated AS7050 biosensor AFE and the corresponding optical system must be calibrated. This can be done in a laboratory environment. There, the oxygen saturation of the test subjects can be varied using an oxygen-controlled environment, and at the same time, the R values can be recorded with the device to be calibrated. The test subjects breathe through a regulated oxygen mask to reach a certain oxygen saturation level. Afterward, the recorded R values derived from the biosensor AFE AS7050 can be assigned to the known SpO_2 values from a reference device. Thus, the relationship between the R values and the reference SpO_2 values can be modeled using a linear or quadratic regression. The requirements for the calibration procedure are defined in the following guidelines:

- ISO 80601-2-61:2017: Medical electrical equipment — Part 2-61: Particular requirements for basic safety and essential performance of pulse oximeter equipment
- Pulse Oximeters - Premarket Notification Submissions [510(k)s]: Guidance for Industry and Food and Drug Administration Staff

This chapter should give an overview of the calibration process. A more detailed description of the non-invasive laboratory testing is described in ISO 80601-2-61:2017 in Annex EE.3. In the case of non-invasive calibration, a calibrated reference pulse oximeter can be used as a so-called secondary standard pulse oximeter.

The FDA recommends the procedure for invasive laboratory testing described in Annex EE.2 of the standard ISO 80601-2-61:2017, or an equivalent method, to validate the SpO_2 accuracy of the pulse oximeter system by comparing each value from the system and a simultaneously obtained value from the oximetry of an arterial blood sample.

5.2.1 Requirements for the Calibration Procedure

In the scope of a controlled desaturation study, the oxygen saturation should be varied in the range between 70%-100%, and at least 200 equally distributed data points (paired observations: pulse oximeter under test & reference pulse oximeter) have to be recorded from at least 10 healthy adult subjects. The subjects should vary in their physical characteristics, age (18 - 50), gender, and skin color (according to the FDA, at least 2 subjects, or 15% of the subject pool, should be darkly pigmented, whichever is larger).

ISO 80601-2-61:2017 criteria for inclusion in study:

- Age: 18 – 50
- Positive Allen's test (test of arterial flow in hand)
- ASA category 1 (healthy person)

ISO 80601-2-61:2017 exclusion criteria:

- Pregnancy

The clinical evaluation should show that the root mean square error (RMSE) is below 3% for transmission and 3.5% for the reflection mode (AS7050).

5.2.2 Execution of the Clinical Trial

This chapter describes the procedure of the data acquisition in the laboratory on test subjects.

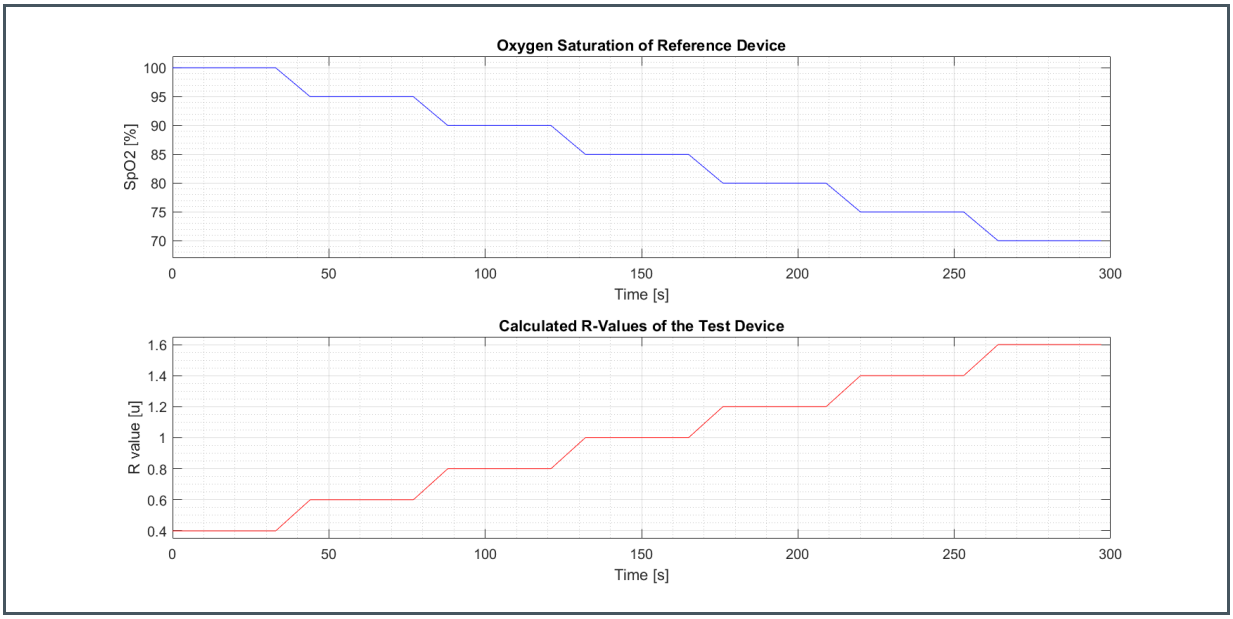
Initial Steps

1. In the first step, the healthy test subjects are informed about the process and the further procedure.
2. The biosensor AFE (AS7050) is placed in the same way as it should be done in the intended use of the device. Subsequently, the measured PPG signals must be checked for sufficient quality, to ensure high-quality R values. Therefore, it is suggested to use the graphical user interface of the evaluation kit.
3. The sensors of the calibration device (reference pulse oximeter) are also positioned as described in the provided instructions for use. It should be ensured that the test person is in a comfortable position in which he or she can remain for a few minutes without moving.

Calibration Procedure

1. The oxygen mask is placed on the subject, and the subject breathes 100% oxygen to achieve maximum oxygen saturation. The recording of R values obtained by the biosensor AFE (AS7050) and of the SpO_2 values obtained by the reference device is started. In case the evaluation kit software is used, click on "*Log*" --> "*Start Log…*", and enter the target file name.
2. The oxygen saturation is lowered in a controlled manner from 100% to 70% in steps of, for example, 5%. It must be ensured that each level is held for at least 30 seconds to allow the oxygen saturation to settle. The theoretical course of the oxygen saturation and the theoretical associated R values are shown in Figure 7.
3. The file containing the recorded R values of the AS7050 and the file containing the reference SpO_2 values are saved.
4. After a short break for the volunteer, the process can be repeated starting again from 100% oxygen saturation, in order to get two measurements of each subject.

Figure 8:
Theoretical Course of the Oxygen Saturation and Associated R Values, Assuming a Linear Relationship.

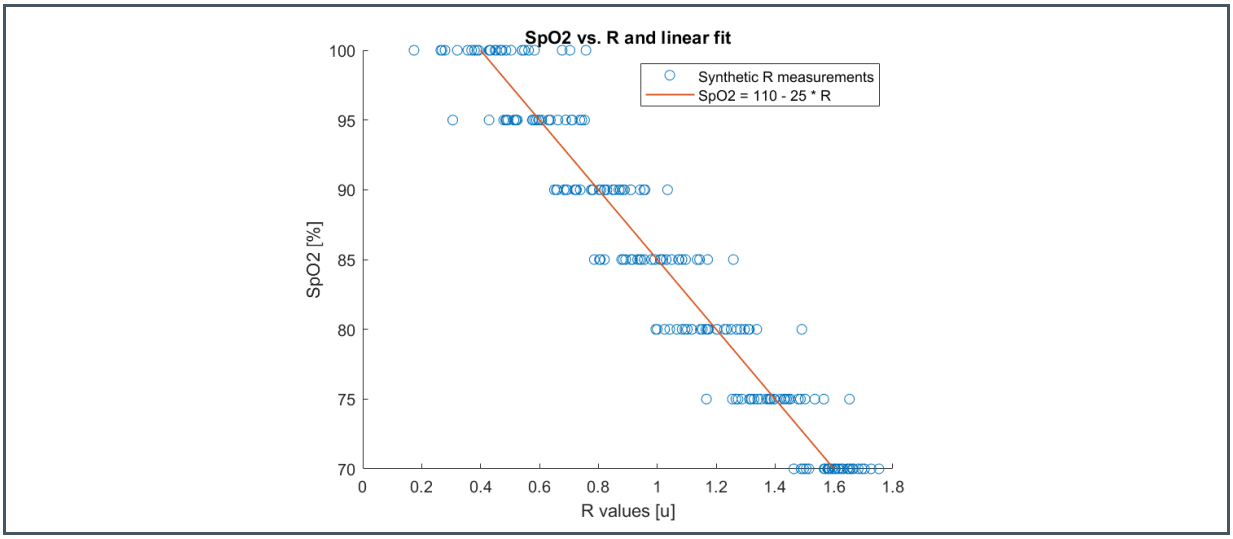


5.2.3 Determination of the Calibration Coefficients

The clinical trial results in two corresponding files for each measurement. One contains the oxygen saturation values of the reference device (SpO2_reference), and the other, the associated R values (R_AS7050). The final data set should contain at least SpO_2 levels in the range of 73% to 97%. In the first step, the sampling rates have to be adjusted to each other. For this purpose, it is recommended to use a linear up-and-down- sampling function. The algorithm of the AS7050 delivers one R value each second.

Afterward, the files can be aligned in terms of time. It is recommended to use the cross-correlation function to define the time lag between both files. Between the R values of the sensor (R_AS7050) and the SpO_2 reference values (SpO2_reference), there is a negative correlation. The transient responses after stepping from one SpO_2 level to another should also be excluded, to have a more precise calibration. After successful alignment and exclusion of the transient parts, use all measurements of all subjects to form pairs of SpO_2 and R values. Then, determine the coefficients (a, b, c) for a quadratic (Equation 3) or the coefficients (b, c) for a linear fit (Equation 4). How the results could look like for a linear fit is shown in Figure 9.

Figure 9:
The Relationship Between Calculated R Values and Corresponding SpO_2 Values Can Be Represented Using a Linear Model(1)



(1) In some cases a quadratic model may be a better fit

Since the behavior of the AS7050 was not investigated in a medical laboratory, only oxygen saturation levels that could be achieved in a simple way, such as holding the breath or decreasing breathing frequency, were examined. However, for these oxygen saturation levels (between 90% and 100%) it was possible to obtain precise results. The following linear fit (Equation 6) for reflective measurements on the fingertip was obtained for our evaluation kit.

Equation 6:

$$\mathrm{SpO2\_AS7050} = -28.43 \cdot \mathrm{R\_AS7050} + 113.13$$

5.2.4 Error Calculation and Overall Accepted Error

After the regression coefficients (b and c) have been determined in the scope of the calibration procedure, an error calculation must be carried out for the derived model. For this purpose, the SpO_2 value has to be determined using the recorded R values and the obtained linear (Equation 7 or quadratic (Equation 8) model.

Equation 7:

$$\mathrm{SpO2}_{\mathrm{AS7050}} = -\mathrm{b} \cdot \mathrm{R}_{\mathrm{AS7050}} + \mathrm{c}$$

Equation 8:

$$\mathrm{SpO2}_{\mathrm{AS7050}} = -\mathrm{a} \cdot {\mathrm{R}_{\mathrm{AS7050}}}^2 - \mathrm{b} \cdot \mathrm{R}_{\mathrm{AS7050}} + \mathrm{c}$$

The root mean square error (RMSE) has to be determined and is defined as follows:

Equation 9:

$$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}$$

Where *n* is, in this case, the total number of *SpO2_AS7050* and *SpO2_reference* pairs, y_i is *SpO2_reference*, and $\hat{y}_i$ is *SpO2_AS7050*. The requirements for the different measurement principles and sites are given in the related documents. A short overview is given in Figure 10.

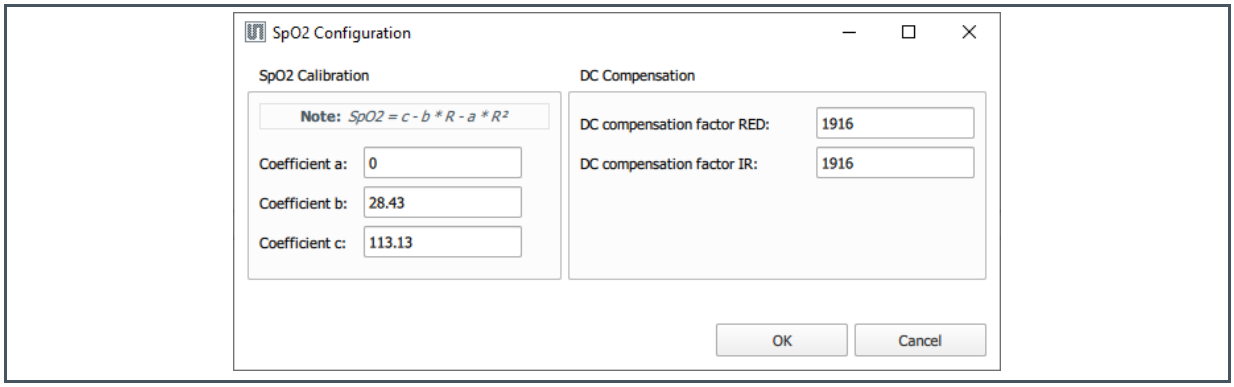
Figure 10:
Maximum RMSE for Optical Pulse Oximeter According to FDA

	Transmittance	Reflectance	Ear Clip
RMSE	≤3 %	≤3.5 %	≤3.5 %

5.2.5 Usage of the Determined SpO_2 Coefficients

After the coefficients have been determined, and the requirements regarding the error calculation have been satisfied, they can be easily implemented into the algorithm. For this purpose, the coefficients a, b, and c can be entered in the graphical user interface of the evaluation kit.

Figure 11:
SpO_2 Configuration Window of the Evaluation Kit. Application Settings -> SpO_2



6 Additional Documents

For further information, please refer to the following documents:

1. Wikipedia. (2021, Feb. 11). *Pulse Oximetry* [Online]. Available: Pulsoxymetrie – Wikipedia
2. Webster, John G., ed. *Design of pulse oximeters*. CRC Press, 1997.
3. Lazakidou, Athina A. *Handbook of research on distributed medical informatics and e-health*. Ed. Konstantinos M. Siassiakos. Medical Information Science Reference, 2009.

7 Revision Information

Changes from previous version to current revision v1-00	Page
Initial version	all

- Page and figure numbers for the previous version may differ from page and figure numbers in the current revision.
- Correction of typographical errors is not explicitly mentioned.

8 Legal Information

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