DEVELOPMENT OF A PULSEOXIMETER TO MEASURE THE OXYGEN SATURATION AND THE HEARTRATE OF SEDATED MICE

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Abstract: *Continuous monitoring of the oxygen saturation and the heart rate of sedated laboratory mice is achieved by adapting the principles of a human pulse oximeter. Using a measuring hardware with the proper analysis software in a micro-controller it is possible to calculate and display those vital signs periodically on a LCD and supply the digital data via a USB connection to a MATLAB GUI for further investigations. The results show an overall agreement with the theory and allow to use this work in preclinical studies to control the anaesthesia gases and the ventilation of sedated mice during research processes.*

Keywords: *pulse oximetry, noninvasive, vital signs, oxygen saturation, heart rate*

Introduction

To analyse the state of health it is possible to measure and check several parameters like the blood pressure, the body temperature, the pulse rate, the respiratory rate and the oxygen saturation ([1]). Besides other methods like ECG or blood pressure measurements, only the pulse oximeter makes it possible to draw conclusions about the transport of oxygen and thus indirectly to make statements about the effectiveness of breathing ([1]).
Using two LEDs with different wavelengths (infrared and red) the absorption of the arterial blood gets measured. This time varying signal gives information about the perfusion of the analized tissue and the oxygen saturation of the pulsating blood. Additionally this signal is used to determine the heart- and subsequently the breathing rate. This mechanism is well-known in human monitoring systems and gets adapted in this project to monitor the vital state of small rodents during anaesthesia.

Methods

Through the use of a modified pulse oximeter sensor to fulfil the small dimensions, the time varying absorption of oxihemoglobin and desoxihemoglobin at two different wavelengths in the arterial blood can be measured and used to calculate the peripherial oxygen saturation.

Mathematical model: Based on the assumptions of a monochromatic light source, a homogeneous distribution of the hemoglobin, no light scattering and a simultaneously measurement, it is possible to derive, starting from the Beer–Lambert law, a calculation rule for the peripherial oxygen saturation as it is given in Eq. 1 (reproduced from [2]).

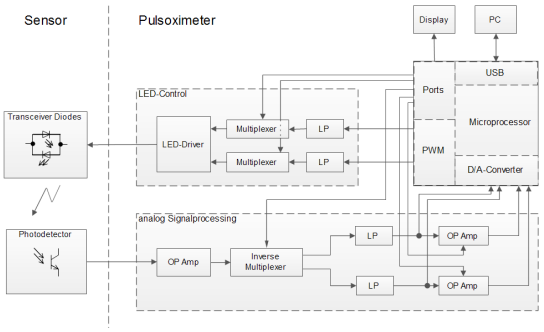

Figure 1: Block diagram of the pulse oximeter hardware

$$SpO_2 = \frac{\epsilon_{Hb}(\lambda_R) - \epsilon_{Hb}(\lambda_I R)R}{\epsilon_{Hb}(\lambda_R) - \epsilon_{HbO_2}(\lambda_R) + [\epsilon_{HbO2}(\lambda_I R) - \epsilon_{Hb}(\lambda_I R)]\,R} \quad (1)$$

This theoretical equation consists of the differential ratio between the measured pulse amplitudes (R), the extinction coefficients for hemoglobin (ϵ_{Hb}) and desoxyhemoglobin (ϵ_{HbO_2}) evaluated at the wavelengths of the light sources for visible red (λ_R) and infrared (λ_{IR}).
Non linearity and missing prerequisites for the use of the beer-lambert law makes it necessary to fit the behaviour of the formula shown in Eq. 1 by equation 2 to avoid large errors especially in areas with a low saturation ($SpO_2 < 80\%$, [2]).

$$SpO_2 = k_1 - k_2 R = 110.28 - 17.51R \quad (2)$$

The model parameters ($k_1 = 110.28$ and $k_2 = 17.51$) are fitted from literature data ([3]) to map the oxygen saturation regarding the amplitude-ratio that is calculated out of the measured and preprocessed data from the alternating infrared signal ($I_{vr_{AC}}$) and the alternating visible red signal ($I_{ir_{AC}}$) as it is demonstrated in Eq. 3.

$$R \approx \frac{I_{vr_{AC}}/I_{vr_{DC}}}{I_{ir_{AC}}/I_{ir_{DC}}} \overset{I_{vr_{DC}} \equiv I_{ir_{DC}}}{\cong} \frac{I_{vr_{AC}}}{I_{ir_{AC}}} \quad (3)$$

Implementation: The hardware consists of a MCU that controls the amplitude and the alternating time-profile of the LED-currents for the infrared and the visible-red LED. The controlled variables are the digitalized values of the transformed and preprocessed light intensities measured by the phototransistor as it can be seen in Fig. 1.

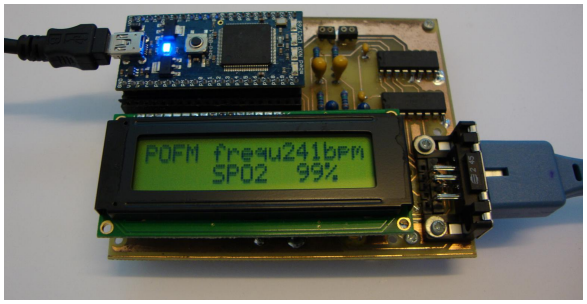

Figure 2: Hardware output in the continuous measurement mode

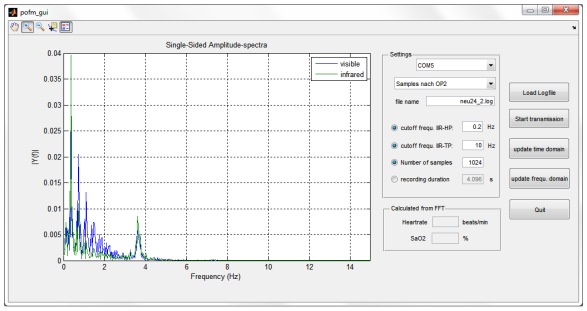

Figure 3: Representation of the FT-spectra of rodent pulse waves and superimosed breathing waves using the MATLAB GUI (green: infra-red, blue: visible-red)

This set-up is given by the anti-parallel LED design and the fact that only one photodetector is used, which allows us to neglect static errors from the phototransistor, the gain and the analog filter process due to the ratiometric calculation rule (see Eq. 3). After the analog pre-processing (current to voltage transformation and an active/passive high and low pass combination) the signals get digitalized and postprocessed by digital IIR-filter. Instead of a signal analysis and computation in the time domain we make use of the powerful microcontroller to transform the signal data to the frequency domain which enables an easier and more accurate [2] frequency decomposition and therefore a more precise calculation of the oxygen saturation. Side products of the FT are the heart rate and the breathing rate that are present as local maxima in the spectra of the time signals. One of those values is displayed periodically, together with the oxygen saturation, on the LCD. The digital data that is stored temporarily in the memory of the microcontroller can be transferred via a USB connection to a PC with the propper MATLAB GUI to process and analyze the pulse waves graphically.

Results

The results of the pulse oximeter are shown exemplarily in Fig. 2 and 3, respectively. The calculated variables in form of an LCD-output are given in Fig. 2 and show the heart rate described as "‘frequ"’ and the functional oxygen saturation caracterised as "‘SPO2"’. Fig. 3 show the graphical representation of the measured pulse waves for the visible light source (blue) and the infrared light source (green) in presence of breathing artefacts.

Discussion

During our research we found out, that the absorption peaks of a mouse-pulse-signal are up to the factor 10^3 smaller than the amplitudes that are measured in conventional human pulse oximetry ([2]). These extremly low currents require special noise considerations in the hardware design to keep the signal-to-noise ratio on an evaluable level. This could be satisfied by the use of optimized op amps, a 12 bit A/D converter and a moving average of the computation window.
By using a powerful 32-bit ARM Cortex-M3 Processor it is possible to take equally spaced discrete samples, perform a digital post processing and control the LED-currents while calculating periodically two 1024 point FFTs in order to compute the oxygen saturation and the heart rate. Although the hardware is designed to work stand alone and without the presence of a PC, it is possible to connect the hardware via a USB-cable with a MATLAB GUI and exchange data. This allows the user to analyze the raw data along with preprocessed data or other steering variables and print them graphically.
With the developed hardware and adapted methods of human pulse oximetry it could be shown despite the extremely low signal intensities, that it is possible to perform a continuous measurement and a periodical calculation of the oxygen saturation as well as the heart rate of sedated mice. During extended continuous measuring, with a maximum duration of three hours, the correct physiological behaviour of the calculated SpO_2- and the heart rate-values are successfully attained. Due to the increasing effect of Isoflurane over time, which results in a decreased heart rate and an initiation of an agonal respiration of the mouse, the SPO2-values are decreasing, indicating an upcoming severe health problem. The final test, a calibration with a subsequent validation, was not performed in this study and will be covered by a follow-up project.

Bibliography

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