35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Lock-in Amplification for Implantable Multiwavelength Pulse Oximeters

Michael Theodor, Utku Karakas, Dominic Ruh, Hans Zappe, *Member, IEEE* and Andreas Seifert

***Abstract*— Standard as well as multiwavelength pulse oximetry as established methods for measuring blood oxygen saturation or fractions of dyshemoglobins suffer from different kinds of interference and noise. Employing lock-in technique as a read-out approach for multiwavelength pulse oximetry is proposed here and strongly decreases such signal disturbance. An analog lock-in amplifier was designed to modulate multiple LEDs simultaneously and to separate the signals detected by a single photodiode. In vivo measurements show an improved signal-to-noise ratio of photoplethysmographic signals and a suppression of interference by means of the lock-in approach. This allows the detection of higher order overtones and, therefore, more detailed data for pulse wave analysis, especially for implantable sensors directly applied at arteries.**

I. INTRODUCTION

In a world of aging population, long-term monitoring of cardiovascular parameters for optimized therapy becomes increasingly important. Frequent measurement of blood oxygen saturation, heart rate and blood pressure is important, especially for patients recovering from surgery [1].

The most accurate way to determine blood oxygen saturation is by arterial puncture for blood gas analysis. Recent commercial solutions use non-invasive multiwavelength pulse oximetry [2], [3] to improve the accuracy of conventional pulse oximeters for oxygen and heart rate monitoring. Blood pressure is usually acquired either intra-arterially or by an inflating arm-cuff. All these methods are not convenient for the patient and not suitable for continuous measurements over longer periods.

An implantable, flexible multiwavelength pulse oximeter has been presented that is well suited for minimally invasive long-term monitoring of blood oxygen saturation as well as pulse wave analysis for blood pressure estimation [4]. This reflective photoplethysmographic (PPG) sensor is shown in Fig. 1.

However, photoplethysmographically acquired signals are prone to electrical and optical noise and interferences such that their detectability may degrade significantly. A typical spectrum for a PPG and its accompanying noise is shown in Fig. 2.

An analog lock-in amplifier was developed to address this issue and improve the signal-to-noise ratio of PPG signals measured with multiple wavelengths by modulating the sensor's light sources at different frequencies.

All authors are with the Department of Microsystems Engineering (IMTEK), University of Freiburg, Georges-Koehler-Allee 102, 79110 Freiburg, Germany, phone: +497612037569, fax: +497612037562

M. Theodor is holder of a Fritz-Huettinger-Scholarship `michael.theodor@imtek.uni-freiburg.de`

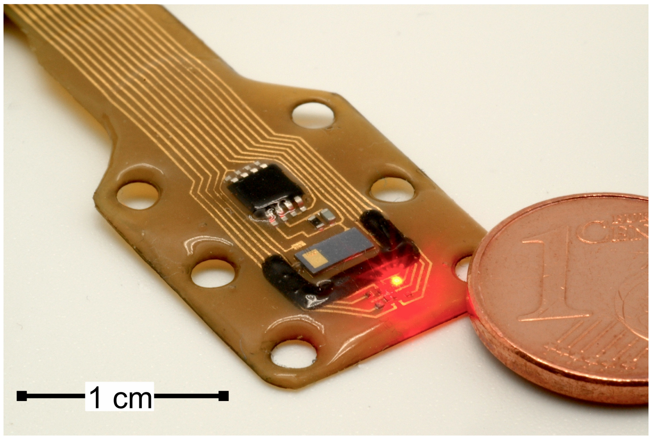

Fig. 1. Implantable, flexible pulse oximeter with eight LEDs, to be used on subcutaneous muscle tissue or perivascular, directly at arteries. [5]

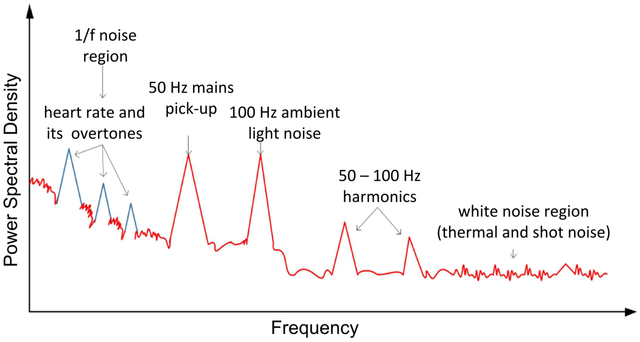

Fig. 2. Typical power spectrum of a photoplethysmographic measurement. The blue peaks indicate the actual signal consisting of components at the heart rate and up to 50 overtones. The red line symbolizes internal and external noise.

II. MULTIWAVELENGTH PHOTOPLETHYSMOGRAPHY

A. Implantable Sensor

The implantable pulse oximeter is based on a flexible polyimide substrate. The silicon photodiode as well as the 8 light emitting diodes (LEDs) are mounted as bare dies, to minimize the sensor area. The utilized wavelengths are 590 nm, 630 nm, 650 nm, 690 nm, 740 nm, 800 nm, 880 nm and 935 nm. An optical silicone barrier between light emitters and detector avoids direct illumination of the photodiode. For biocompatibility, the sensor is encapsulated in medical grade silicone rubber (NuSil MED-1000).

B. Detection of Hemoglobin Derivatives

To measure the arterial oxygen saturation and other important hemoglobin derivatives, the applied sensor uti-

978-1-4577-0216-7/13/$26.00 ©2013 IEEE

lizes the spectralphotometric method of reflectance pulse oximetry. The sensor is placed on subcutaneous muscle tissue, the light of 8 LEDs is emitted through the tissue's arterioles, and the backscattered light is detected by a photodiode. The different kinds of hemoglobin, such as oxyhemoglobin (O_2Hb), deoxygenated hemoglobin (HHb), carboxyhemoglobin (COHb), and methemoglobin (MetHb) cause a specific attenuation of light, dependent on their concentration and different absorption spectra. The use of the isosbestic wavelength of 800 nm allows the sensor to determine tissue perfusion, independent of oxygenation [5]. Due to lower capillary density, the signal intensity from subcutaneous muscle tissue is weaker compared to conventional extracorporeal measurements. To extract this weak signal, the system noise must be kept to a minimum.

C. *Measurement of Vascular Properties*

Applying two of such sensors directly on opposite sides of large arteries yields transmission mode PPG signals. As the PPG signal is generated by changes in optical path length, the sensor can detect the temporal expansion of a vessel.

This vessel expansion shows a characteristic curve defined by the heart ejection and the vascular properties. The heartbeats generate periodic pressure pulses in the arteries, which can be represented as a Fourier series with components at the heart frequency and its overtones [6]. A precise determination of the amplitudes of the overtones provides information on the arterial stiffness, a new but important parameter for diagnosis of arteriosclerosis. [7]

The sensor can also be used to estimate blood pressure by measuring the pulse transit time [4].

III. Lock-in Amplification of Photoplethysmographic Signals

A. *System Overview*

Conventional PPG sensors employ low-pass filtering algorithms to distinguish signal from noise, but actually, they are not able to discriminate true signals from noise. The detailed structure of the PPG signal is generally lost during this stringent filtering process. With a better noise reduction technique, detection of the overtones of the fundamental PPG frequency could deliver important information about vascular condition.

To receive light of different wavelengths, regular pulse oximeters either use several photo diodes with spectral filters or multiplex the LED signals by simply switching, which limits the sampling frequency and might distort the signal.

An analog lock-in amplifier was developed to address these issues, to avoid multiplexing and to improve the signal-to-noise ratio of signals measured with implantable PPG sensors.

Lock-in amplification is a modulation and phase sensitive detection technique for recovering small measurement signals from dominating noise background. The principle is visualized in Fig. 3 and was evaluated *in vivo* and *in vitro* with the multiwavelength pulse oximeter.

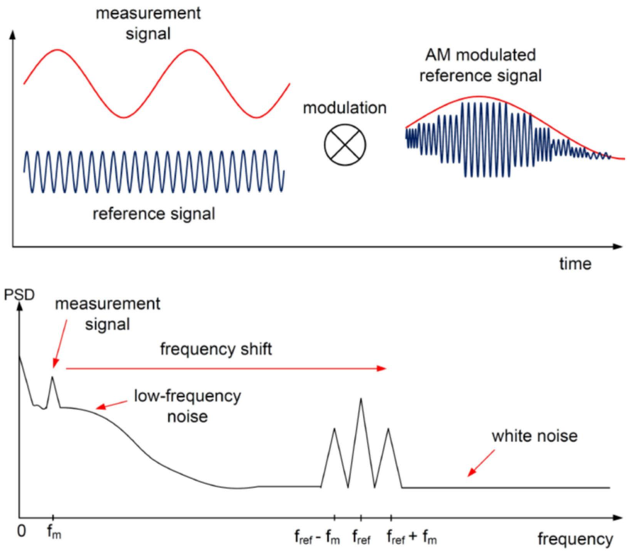

Fig. 3. Lock-in concept: The signal is modulated to higher frequencies, which is facing less 1/f-noise and external interference. This improves the signal-to-noise ratio.

In standard pulse oximetry, two or more wavelengths are sequentially toggled to separate the signals of different light sources. In lock-in technique, the separation is realized by modulation at different frequencies. Hence, the light sources can be operated continuously and several signals can be detected by one single detector simultaneously.

B. *Noise Sources in Photoplethysmographic Measurements*

Noise can be defined as the sum of all disturbances coming along with the genuine signal and hindering its detectability. For pulse oximeters, noise sources which affect the measurement can be separated into two groups: internal and external noise. Thermal and shot noise as white noise sorces as well as 1/f noise are the main internal noise sources [8]. Interference is of external origin and couples to the measurement system from a nearby electrical, optical or mechanical disturbance. 50 Hz power line pick-up noise and its harmonics, 100 Hz ambient light flickering and all kinds of electromagnetic interference belong to this category [9].

1/f noise (or flicker noise) in semiconductors originates from fluctuations of the carrier density when charges are randomly trapped at the Si - SiO_2 interface [9]. It dominates the low frequency power spectrum with a PSD function

$$S(f) = \frac{K_f I_{dc}}{f^n}, \tag{1}$$

where K_f is a device dependent constant, I_{dc} is the DC current in that device and $n \simeq 1$. Flicker noise falls off at about -10 dB/decade. Modern operational amplifiers have corner frequencies f_c, at which 1/f noise equals the white noise, ranging from a few Hz to several hundred Hz [10], [11]. Accordingly, slowly varying signals, such as PPG signals, should not be taken in the low frequency region where flicker noise additionally degrades the signal-to-noise ratio.

In a measurement system, the power spectral density function with 1/f and white noise can be expressed as

$$S(f) = N_f(1 + \frac{f_c}{f}), \tag{2}$$

where N_f is the constant white noise amplitude in V^2/Hz [10], [12].

C. Lock-In Approach

Lock-in amplification is an electronic method capable of extracting weak measurement signals from a dominating noise background. The idea is to modulate the measurement signal to separate it from low frequency noise and interference (see Fig. 3). This modulation approach makes the method different from other signal recovery techniques and enables it to distinguish signal from noise by phase sensitive detection. Fig. 4 shows the basic architecture of a lock-in amplifier.

The LEDs are modulated with a reference frequency ω_{ref} and amplitude A_{ref}. This modulated light is attenuated by pulsatile blood flow yielding the transmitted amplitude $A_s(t)$. Therefore, the signal $s(t)$ detected after the transimpedance amplifier can be expressed as

$$s(t) = A_s(t)\cos(\omega_{ref} \cdot t + \phi_s), \tag{3}$$

where ϕ_s is the phase shift $s(t)$ experiences during the experiment. The signal $s(t)$ is bandpassfiltered around the modulation frequency before demodulation, to eliminate the noise affected low frequency part and, for example, signals from other LEDs modulated at different frequencies. The reference signal $r(t)$ is also a sinusoidal voltage at frequency ω_{ref} and has an amplitude A_{ref}. Taking the product of these two signals for demodulation, yields

$$\begin{aligned} V_m(t) &= s(t) \cdot r(t) && (4) \\ &= \frac{1}{2}A_s(t)A_{ref}\cos[(2\omega_{ref})t + \phi_s + \phi_{ref}] && (5) \\ &+ \frac{1}{2}A_s(t)A_{ref}\cos[0 + \phi_s - \phi_{ref}] \end{aligned}$$

by using the trigonometric identity.

The frequency component at $2\omega_{ref}$ of (5) is filtered out by a lowpass and the remaining term is the output of the lock-in amplifier $V_{out}(t)$, which is proportional to measurement signal $A_s(t)$. The phase difference $\phi_s - \phi_{ref}$ should ideally be adjusted to zero by the phase shifter circuit so that $V_{out}(t)$ can attain its maximum amplitude.

This modulation technique allows the pulse oximeter to detect the signal in a frequency region around ω_{ref}, that is not facing flicker noise or interference.

IV. RESULTS

A. In Vivo Modulation of Two LEDs for Pulse Oximetry

Two lock-in amplifiers, operating at 14 and 22 kHz, respectively, modulated the red and infrared LEDs of the sensor concomitantly. The corresponding finger PPG signals of each LED could be extracted successfully by a single photodiode. The modulated PPG signals were separated by the bandpass filters of the lock-in amplifiers centered around the respective modulation frequencies. Fig. 5 shows both PPG signals amplified by lock-in technique, digitally low-pass filtered, and normalized to their respective DC values. The two modulation frequencies have to be chosen carefully, such that their overtones do not interfere with each other.

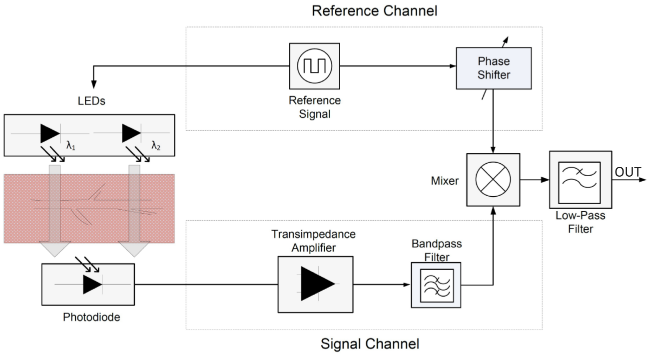

Fig. 4. Schematic of a lock-in amplifier for a pulse oximeter.

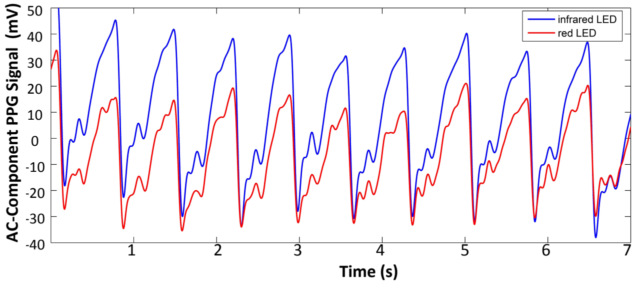

Fig. 5. Photoplethysmographic signal intensities of a red and infrared LED acquired in vivo at a finger by means of lock-in technique. The two LEDs were modulated at different frequencies and the signal was detected by only one photodiode. Demodulation could clearly separate the two signals.

Using lock-in technology, apparently improves the quality of the measured signals compared to conventional detector read-out. The spectra shown in Fig. 6 reveal that the lock-in system is able to detect more overtones of the heart frequency than standard technology, and additionally, clearer overtones. Furthermore, external 50 Hz noise is totally eliminated.

B. PPG Measured on Vessel

The implantable pulse oximeter is designed to be mounted on subcutaneous tissue or directly at a blood vessel.

The characteristics of the sensor at a vessel was evaluated by *in vitro* measurements at a specifically constructed artificial circulatory system. Two sensors were mounted on opposite sides of a stretchable tube. A fluid with similar absorption as blood was actuated by a peristaltic pump. The sensor was used in transmission mode and detected the change in optical path length due to the pulsatile extension of the artificial blood vessel. The pressure was measured concomitantly, directly inside the vessel with a tip-catheter. Fig. 7 shows the power spectra of both the pressure and the

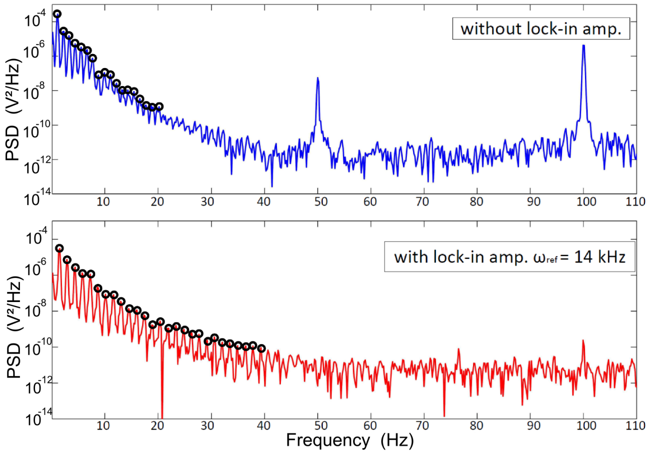

Fig. 6. Comparison of the power spectral density of PPG signals from a finger measurement with and without lock-in amplification. The black circles mark 17 and 25 overtones of standard and lock-in signal, respectively. The lock-in signal is not corrupted by the interferences at 50 and 100 Hz.

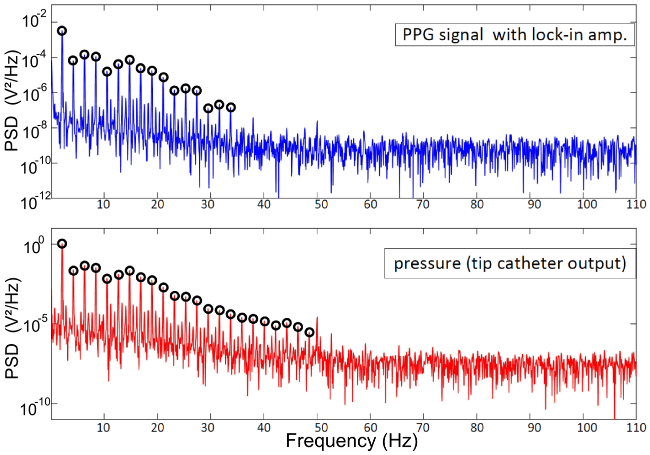

Fig. 7. Power spectral density of the blood pressure pulse and a PPG signal measured directly at an elastic tube using lock-in amplification *in vitro*.

optical sensor signal. They exhibit strong similarity, in particular in their lower frequency overtone characteristics. The signal-to-noise ratio of the developed pulse oximeter shows comparable quality with the commercial, intra-vascular blood pressure sensor. The seven overtones above 35 Hz, seen in the pressure signal, are missing in the PPG. This might be due to the damping properties of the artificial vessel, which was not developed for high-frequency signals.

Standard low-pass filtering for the sensor read-out, as in common instruments, is not able to provide the information contained in the overtones, since they are facing high 1/f-noise and interference in the low frequency region. This is completely avoided by use of lock-in technique.

V. DISCUSSION

The lock-in amplifier circuit has proven to be a useful tool for pulse oximetry. In particular, multiple modulated LED signals could be separated and noise could be decreased.

The amplifier employed for the measurements was fabricated on PCB level using discrete ICs. For the modulation, demodulation, band-pass and low-pass filtering, seven operational amplifiers are used per LED. This might not be a proper solution for an implantable device with, for example, eight wavelenghts. However, single-chip lock-in amplifiers with integrated photo detector on 0.35 µm CMOS basis have already been presented [13]. The small dimensions and power-consumption below 13 mW are well suited for use in implants with telemetric power transmission, as it is already established for cochlear implants.

VI. CONCLUSION

Implementing lock-in technique in pulse oximetry, leads to an improved signal-to-noise ratio of PPG signals at the finger and a suppression of interference. It was demonstrated that two lock-in amplifiers are able to modulate two LEDs simultaneously and filter out PPG signals detected by a single photodiode. Hence, the concept is well suited for conventional and in particular multiwavelength pulse oximetry.

In pulse wave analysis with a pulse oximeter mounted directly on an artery, the improved signal-to-noise ratio allows detection of more overtones for a better determination of vascular stiffness or generally vessel wall mechanics.

ACKNOWLEDGMENT

This work was supported by the Baden-Wuerttemberg Stiftung and by the Fritz Huettinger Stiftung.

The authors would like to thank their lab member Jens Fiala as well as their medical partners Katharina Foerster and Claudia Heilmann for their support during this project.

REFERENCES

[1] R. S. Irwin and J. M. Rippe, *Manual of Intensive Care Medicine*, R. S. Irwin and J. M. Rippe, Eds. Lippincott Williams & Wilkins, 2009.

[2] M. Cannesson and P. Talke, "Recent Advances in Pulse Oximetry," *F1000 Med Reports*, 2009.

[3] T. Aoyagi, "Pulse Oximetry: Its Invention, Theory and Future," *Journal of Anesthesia*, vol. 17, pp. 259–266, 2003.

[4] J. Fiala, P. Bingger, D. Ruh, K. Foerster, C. Heilmann, F. Beyersdorf, H. Zappe, and A. Seifert, "An implantable optical blood pressure sensor based on pulse transit time," *Biomedical Microdevices*, vol. 15, pp. 73–81, 2013.

[5] J. Fiala, R. Gehrke, N. Weber, P. Bingger, H. Zappe, and A. Seifert, "Implantable optical sensor for continuous monitoring of various hemoglobin derivatives and tissue perfusion," *IEEE SENSORS Conference*, 2009.

[6] S. C. Millasseau, R. P. Kelly, J. M. Ritter, and P. J. Chowienczyk, "Determination of age-related increases in large artery stiffness by digital pulse contour analysis," *Clinical Science*, vol. 103, 2002.

[7] D. Ruh, S. Sherman, M. Theodor, J. Ruhammer, K. Foerster, C. Heilmann, F. Beyersdorf, H. Zappe, and A. Seifert, "Determination of Vessel Wall Dynamics by Optical Microsensors," *Proc. 34th Annual International Conference of the IEEE EMBS*, pp. 2359–2362, 2012.

[8] Aldert Van Der Ziel, "Noise in Solid-State Devices and Lasers," *Proceedings of the IEEE*, vol. 58 no. 8, pp. 1178–1206, 1970.

[9] B. Razavi, *Design of Analog CMOS Circuits, International Edition.* McGraw-Hill, 2001.

[10] *Op Amp Noise Relationships: 1/f Noise, RMS Noise and Equivalent Noise Bandwidth MT-048*, Rev.0 ed., Analog Devices, October 2008.

[11] L. Smith and D. Sheingold, "Noise and Operational Amplifier Circuits," *Analog Dialogue*, vol. 3-1, pp. 13.25–13.34, 1969.

[12] M. L. Meade, *Lock-In Amplifiers: Principles and Applications.* Peter Peregrinus Ltd., 1983.

[13] A. Hu, "CMOS Optoelectronic Lock-In Amplifier With Integrated Phototransistor Array," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 4, 2010.