Summary of the PhD Thesis

Measurement of the Blood Flow and Perfusion Based on the Laser Speckle Contrast Analysis

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Introduction

When coherent light falls on an optically rough surface, and the scattering radiation is caught by a canvas, speckle pattern is formed on it. The phenomenon is used in industrial, medical, etc. applications. However one can find the phenomenon in such common devices as the laser optical mouse.

One of the medical applications is the measurement of the blood flow or blood perfusion based on the laser speckle contrast analysis (LASCA). With this technique, the cerebral or ocular tissue is illuminated by laser light, which is primarily scattered by the red blood cells and is imaged by a camera. One of the objective properties of the speckle image is its contrast, which is defined by the ratio of the intensity values of the pixels on a selected segment of the image: $K = \sigma / \langle I \rangle$. The contrast is generally calculated over 5×5 pixel segments of the image (i. e. *local* contrast), and, as a result, the contrast map of the examined area can be determined. In the following part of the summary the average of the local contrast values over a selected area (e. g. the area corresponding to a vessel) will be referred as contrast. If the illuminated sample moves or contains moving scattering parts (e. g. red blood cells), the speckle pattern changes in time which results in the blurring of the time-integrated image. In the case of such a sample, the contrast is strictly monotonically decreasing as a function of the exposure time (T), and its boundaries are $\lim_{T\to 0} K(T) = \beta \le 1$ and $\lim_{T\to\infty} K(T) = 0$, where β is a correction factor related to the illumination and the imaging system. By the use of these asymptotic values and the actual contrast value, one can determine the autocorrelation time (shortly: correlation time, τ) related to the changes of the intensity values shown by the pixels of the imaging chip which is supposed to be inversely proportional to the characteristic speed of the moving scatterers. The first applications were able to characterize these changes qualitatively, especially in the case of skin, since the static parts of the sample (i. e. the skin surface) add an offset to the square of the contrast, $\lim_{T\to\infty} K(T) > 0$. As the amplitude of this offset cannot be determined by the use of one exposure time, the results of measurements performed on different persons or under different circumstances cannot be compared to each other reliably.

Objectives

The aim of my study was to extend the applicability of LASCA and the creation of a method and a system which can be used easily in the daily routine. The goal of my work was to make this system able to provide near-to real-time results which could be quantitatively compared to each other even if they were determined under different circumstances.

- I aimed to provide the proper software background. I intended the implementation of a measurement protocol which was able to record images by the use of several exposure time values for post processing.
- I purposed the creation of a synthetic sample for the modelling of living samples to examine the effect of the static scattering centres on the contrast. Based on the results, I targeted the elaboration of a modified contrast – exposure time relationship which was able to correct the effects of the static scatterers and determine the real correlation time when combined with a proper sampling method.
- I aimed to extend the capabilities of the system by several enhancements of the protocol and the devices to be able to perform near-to real-time measurements. I had to introduce a method which was not used on the field yet and which could provide an extremely cost-effective solution for the tuning of the exposure time from frame to frame. As the recording and the analysis of the images consisted of 4 parts, each lasting for 0.1 to 0.3 seconds, it was quite a challenge to optimize and parallelize the steps to make the system able to record and process 5 images within a second.
- I intended to test the method elaborated by me during the measurement of the blood perfusion of cerebral and cutaneous tissue.

Scientific results

When the flow or perfusion rate is evaluated by the use of one exposure time, the contrast value is compared to the pre-determined $\lim_{T\to 0} K(T) = \beta \leq 1$ value. Unfortunately, the static scattering parts of the examined sample can give an offset to the square of the offset. Since the amplitude of this offset cannot be determined by the use of one exposure time, it can prohibit the determination of the intensity of the perfusion or the flow. When several exposure times are applied, the contrast values determined at each exposure time can be compared to *each other* instead of a pre-determined value. I performed the measurements on latex

microsphere suspension filled in a cuvette which was covered by 50 and 100 μm thick Teflon foil and tracing paper. This sample provided similar scattering properties to those of living tissues containing non-moving parts.

1. I elaborated a modified expression to describe the dependence of the contrast on the exposure time. The use of this makes one able to determine the scattering properties of the sample and the real correlation time by fitting a curve on the contrast values measured at different exposure times. I used the $\lim_{T\to 0} K(T)$ and the $\lim_{T\to \infty} K(T)$ asymptotic contrast values as fitting parameters which characterize the scattering properties of the sample and the properties of the illumination and the imaging system. The results provided by this method are only a little bit or not affected by the static scattering of the sample [T1].

I examined the applicability and necessity of the application of multiple exposure times during the measurement of cerebral blood perfusion and flow rate. I compared the results to the results evaluated by the use of one exposure time.

2. I showed that during the evaluation of blood perfusion and flow rate of tissues which do not contain static scattering parts, the use of one exposure time and the $\beta = \lim_{T\to 0} K(T)$ correction factor should provide adequate results. However, to achieve the optimal result, the exposure time should be near to the inflexion point of the exposure time – contrast curve which can be found generally between 1 and 5 ms for the mentioned type of tissue. The use of longer or shorter exposure time may detrimentally affect the results as the contrast values may show saturation [T2].

I examined the applicability of the multi-exposure LASCA method for the evaluation of the changes (post occlusive reactive hyperaemia) of the skin perfusion. I evaluated the results to them of two singe-exposure methods. I performed 20 measurements on the forearm of 8 volunteers. Simultaneously, I monitored the perfusion rate by the use of a Doppler system which is used in the daily medical routine. I compared the results of the LASCA methods to the results of the latter system as I them as standard reference values.

3. I showed that the multi-exposure LASCA method elaborated by me can provide more accurate information regarding to the changes of the blood perfusion rate of the skin of the forearm than the LASCA methods utilizing only one exposure time combined or not combined with the $\beta = \lim_{T\to 0} K(T)$ correction factor [T3].

4. I showed that the scattering properties of the skin as well as the $\lim_{T\to 0} K(T)$ and $\lim_{T\to \infty} K(T)$ values might change considerably if the perfusion rate of the tissue varies significantly. This may lead to false results if only one exposure time is applied, however, the changes can be followed by the use of multiple exposure times [T3].

A considerable drawback of the original LASCA method I developed utilizing multiple exposure times is the low temporal resolution which is insufficient for the real-time measurements, since at least 5 images have to be recorded for each exposure time to reduce the statistical noise. The variable neutral density filter which needed relatively long time to be positioned further reduced the temporal resolution. To resolve the problem, I looked for a cost-effective method to change the exposure time from frame to frame within a few milliseconds.

5. I showed that the switching mode control of the current of the laser diode was a fast, reliable and cost-effective method for the control of the exposure time providing mode hop-free illumination and constant light intensity. Each exposure consisted of the same number of similar flashes, and the exposure time could be controlled by the separation time between the flashes from frame to frame. The integration time of the camera could be constant which decreased the effects caused by the nonlinearity of the camera [T4].

The next step of the development was the introduction of a technique which is able to provide near-to real-time measurements even by the use of multiple exposure times.

6. I elaborated a sampling and analysing process which – next to the initialization of the fitting parameters – provides the full-field perfusion map of the sample following every second frames, while it is able to re-tune itself continuously according to the

changes of the scattering properties of the sample. This method combined the high speed and short reaction time with the single-exposure methods with the high accuracy of the multi-exposure one developed by me.

I combined the laser speckle contrast analysis based on the use of multiple exposure times with the adjustment of the exposure time by the switching mode control of the driving current of the laser diode and a sampling and approximation method. This technique provides the cost-effective and reliable monitoring of the skin perfusion over large areas simultaneously. A medical device based on the methods described above could be extremely useful in the case of the examination of burn injuries, transplanted tissues, diabetic dermadromes, or cancerous mutations.

References

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