A new method of short-coherence-interferometry in human skin \textit{(in vivo)} and in solid volume scatterers

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ABSTRACT

We adapted a method, the „coherence radar“, that was originally developed for the precise measurement of surface topology, to measure bulk properties within strongly scattering media. The sensor is based on short-coherence-interferometry. It enables the two-dimensional observation of light propagation in scattering media with a high temporal resolution (<100 fs). The measurements are carried out by observing photons that traveled from an entrance focus through the bulk of the sample, and back to the surface. The source of information is the speckle contrast. One important result is that during the propagation a sharp photon horizon evolves. This photon horizon can be used for the detection of inhomogeneities in the scattering properties. In solid samples we measured absorbing obstacles with a depth of 320 µm and a depth uncertainty of <5%. The measuring time is about 30 seconds. The observation of the photon horizon can also be realized in „life“ volume scatterers with moving scattering particles. First \textit{in vivo} measurements of human skin have been successful.

1. INTRODUCTION

Optical Coherence Tomography is an important tool for medical diagnosis of biological systems such as artery, eye or skin \textsuperscript{1,2,3,4,5}. One specific implementation is the detection of inhomogeneities of the scattering characteristics in human skin \textit{in vivo} for the diagnosis of skin cancer.

However, the use of light in the visible or near infrared range causes multiple scattering during the propagation in the skin \textsuperscript{6}. As a result of multiple scattering, photons which have run the same optical path length could have traveled along different individual paths reaching different depths in the scatterer. This affects the depth uncertainty that can be achieved in the measurements.

In order to investigate the influence of multiple scattering we worked out a method which enables us to observe the propagation of light in volume scatterers by short-coherence-interferometry \textsuperscript{7}. The temporal resolution of the observation only depends on the coherence length of the light source and is about 100fs. The object is observed by imaging with a finite aperture. This causes subjective speckle in the image plane. It has been shown that these speckle are the actual source of information. One particular result shows the light propagation in a volume scatterer with an absorbing obstacle (Fig. 1). The cross section of the object is observed. The light is focused onto the surface and it is scattered. (The white region at the focus is due to saturation of the camera.) All black spots are caused by photons which have run the same path length but along different individual paths (t is the propagation time of the photons in the sample). It is obvious that photons with the same propagation time reach different depths. However, there are photons for which the depth reached in the scatterer is unambiguously determined by the traveled optical path length. These photons form a sharp curved edge in front of the impulse response: the photon horizon PH (e.g. see Fig. 1b,d). It can be seen how the PH propagates around the absorber just by multiple scattering. The time of its reappearance at the surface encodes the information about the depth of the absorber. Furthermore the reappearance at the surface enables the observation of the surface (non invasive observation in reflection).

The observation of the surface is not coaxial (Fig. 2) to the illumination. This kind of observation has one specific advantage: If photons of the PH emerge at any point of the surface, no other photons emerge simultaneously which have propagated the same run length but which have reached only lower depths thereby. This separation cannot be achieved by coaxial methods.

The experimental data were confirmed by coherent simulations of the light propagation in volume scatterers \textsuperscript{8}. A method is introduced which only observes the propagation of the photon horizon. We call this method: Detection of the Photon Horizon (DPH). Fast and quantitative measurements in reflection of the
depth of an absorber by DPH are presented in this paper. Furthermore we are able to observe the light propagation in human skin in vivo by DPH.

Fig. 1: Observation of light, scattered around an absorbing obstacle (cross section)\(^7\).

2. EXPERIMENTAL SETUP

Fig. 2: experimental setup
Our basic experimental setup is a Mach-Zehnder-Interferometer (Fig. 2). The light source is a superluminescent diode in the near infrared range with a short coherence length \(l_C\) (SLD, \(P=4\) mW, \(\lambda=850\) nm, \(l_C=30\) \(\mu\)m). A light spot is focused onto the surface of the sample. The optical axis of the illumination is inclined by an angle \(\alpha=45^\circ\) to the normal of the surface of the object. The light is penetrating the sample and is scattered. We observe the scattered light that is reaching again the surface by imaging that surface onto a CCD camera (dynamic range of about 48 dB). The axis of observation is
perpendicular to the surface of the object. The plane reference wave is separated by a beamsplitter in the illumination arm and propagates via the displaceable reference mirror to the camera target, where the plane reference wave and the object wave superimpose. Interference contrast occurs in the image of the object only where the optical path length of the photons scattered back from the object differs from the optical path length of the photons from the reference by less than the coherence length.

3. SIGNAL FORMATION

In order to understand the basic principle of the DPH, we first have to examine the light propagation in the scatterer. Partially coherent light is focused onto the surface of the object. The focus F is located at \( F(x_F, y_F) \) in the image plane (Fig. 3a). The light propagates into the object, is scattered, and partly hits the surface again. Due to multiple scattering the photons which emerge at one certain point \((x, y)\) from the surface, ran different optical path lengths \( l \) in the object. There is a minimum and a maximum optical path length, \( l_{\text{MIN}}(x, y) \) and \( l_{\text{MAX}}(x, y) \) for each point \((x, y)\). With partially coherent illumination, all photons arriving at the image plane which have traveled the same optical path length \( l_i (\pm l_c) \), have to be considered as a distinct set of photons \( P_i \). The imaging with a finite aperture causes subjective speckle in the image plane. Each set \( P_i \) will generate its own coherent speckle pattern with the intensity \( S_i(x, y) \).

The different speckle patterns \( S_1, ..., S_i, ..., S_N \) are incoherently superimposing to a total speckle pattern \( S(x,y)=\Sigma S_i \).

Fig. 3: Propagation of the spatial impulse response at the surface of a homogeneous scatterer.

In a first step we are interested in finding the regions of the surface where photons with a certain path length \( l_i \) emerge. This region is closely related to the spatial impulse response at the corresponding time. The selection of the path length \( l_i \) is done by the superposition of the reference wave with the proper path length \( l_R = l_i \). Hence only photons from set \( P_i \) are able to interfere with the photons from the reference. High interference contrast occurs just at locations where these photons emerge. In order to measure the interference contrast, the reference is continuously shifted. The velocity of the shift is adapted to the wavelength in such a manner that the shifted distance within one exposure is \( \lambda/3 \). Two subsequent exposures are subtracted. The incoherent fractions of the signal are the same in both exposures. Therefore the difference of these two frames contains only the coherent part of the signal. The difference of \( \delta l_R=\lambda/3 \) of the reference shift has the advantage, that within three subsequent exposures one difference will be definitely high. The difference corresponds with the interference contrast. We call it difference contrast \( \overrightarrow{C} \). In our experiments \( \overrightarrow{C} \) is the normalized difference between two exposures of a CCD camera of 48 db dynamic range. Figure 3 shows the propagation of the spatial
impulse response (region from which these photons emerge that are coherent with the photons of the reference) for different reference lengths. All black spots are caused by photons which have run the same path length but along different individual paths. The sample is a solid polyester (n=1.54) with embedded monodispersive SiO$_2$-spheres (made by H. Rinneberg, Physikalisch Technische Bundesanstalt, Berlin). The scattering coefficients of the sample at a wavelength of $\lambda=850\,\text{nm}$ are: $\mu_s=55\,\text{cm}^{-1}$ and $g\approx0.8$. There is a main direction of the propagation along the x-axis, due to the specific geometry of illumination. The photon horizon propagates symmetrically to the x-axis.

4. DETECTION OF THE PHOTON HORIZON (DPH)

![Graphs showing photon horizon detection](image)

Fig. 4: a) Difference contrast $C$ versus the run time of the photons at the pixel $(x_A, y_A)$ in a solid scatterer,

b) Difference contrast $C$ versus the run time of the photons at the pixel $(x_A, y_A)$ in human skin (under arm, inside) in vivo,

c) $C_{\text{MAX}}$ versus the distance of the observed pixel to the focus F in a solid scatterer,

d) $C_{\text{MAX}}$ versus the distance of the observed pixel to the focus F in human skin (under arm) in vivo

In each of the frames of Fig. 3 the photon horizon is the point of interest. The photon horizon is the sharp curved edge of the impulse response. The photons of the photon horizon have the specific feature that they have propagated the longest distance from the illumination point F in the scatterer while running the same optical path length.

For the quantitative localisation of the photon horizon the reference mirror is continuously shifted. The length of the reference arm is $l_R$, the run time of the photons in the reference is $t(R)$. For a certain length
of the reference arm the difference contrast \( C(x, y, l_r) \) is measured for each pixel \((x, y)\) by the difference of two subsequent exposures. For a continuous shift of the reference, the contrast \( C(x, y, l_R) \), or \( C(x, y, t_R) \), can be regarded as the temporal impulse response at the pixel \( P(x, y) \). The behavior of the contrast \( C \) is shown in Fig. 4a for one pixel \( P_A(x_A, y_A) \), which is located at the x-axis at a distance of 465\( \mu \)m from the focus \( F \) (Fig. 3a). In the region where \( l_R < l_{MIN}(x_A, y_A) \), only the camera noise \( C_N(\approx 0.03) \) appears. If the optical path length in the reference arm is increasing, the first photons emerging at \((x_A, y_A)\), are able to interfere with the photons from the reference, and a contrast \( C \) can be measured that exceeds the camera noise (Fig. 4a, at t_{THR_1}=3.13\,ps). Due to multiple scattering, most photons emerge at the point \((x_A, y_A)\) at later times. The contrast steeply increases and after the maximum contrast \( C_{MAX}=0.063 \) (t_{MAX}=3.8\,ps) is reached, \( C \) softly drops. Finally, for \( l_R > l_{MAX}(x_A, y_A) \) (t_{THR_2}=4.53\,ps) the contrast \( C \) again equals the camera noise \( C_N \). \( C_{MAX} \) drops for an increasing distance between the focus and the pixel of interest\(^7\). Figure 4c shows the decrease of \( C_{MAX} \) along the x-axis. A contrast cannot be measured around the focus \((x_F=352\,\mu\text{m}, \varnothing=110\,\mu\text{m})\) due to the saturation of the camera. The measured contrast on the left side of the focus in Fig. 4c is just the camera noise \( C_N \), because hardly any light is scattered in this direction. The behavior of the graph of \( C \) is well confirmed by Monte Carlo simulations of the light propagation in volume scatterers\(^9\).

In order to obtain the run time profile of the photon horizon, that reference length \( l_R \) has to be stored for each pixel, where \( C \) exceeds the camera noise threshold for the very first time (\( l_R = l_{MIN}(x, y) \)). With a threshold \( C_{THR} = 0.04 \) in our experiments the extension of the temporal impulse response is \( \Delta t = t_{THR_2} - t_{THR_1} = 1.4\,\text{ps} \) (Fig. 4a).
5. EXPERIMENTAL RESULTS ON SOLID SCATTERERS

Investigations of various samples have been performed with the setup of Fig. 2.

In a first measurement we observed the run time profile of the photon horizon in a homogeneous scatterer. Figure 5 shows the propagation of the photon horizon of the polyester phantom mentioned above. The grey scales encodes the time when the first photons emerge. The photon horizon propagates symmetrically to the x-axis. Inhomogeneities at the surface will cause a deformation of the photon horizon.
Fig. 6: Run time profile of the PH in an inhomogeneous sample. During the propagation around an absorbing obstacle of varying depth the symmetry is destroyed.

Quantitative measurements of inhomogeneities (e.g. absorbers) can be performed with this method. Figure 6 shows the polyester phantom with an embedded obstacle. The obstacle is a pencil lead (diameter of 440µm). The axis $a$ of the lead is inclined at an angle with the normal $n$ of the surface. The oblique cross section at the surface is an ellipse. Because of the inclination of the lead its depth at the lower side of Fig. 6 is larger than at the upper side. This leads to the destruction of the symmetry of the propagation. Light that emerges topright at Fig. 6 will emerge earlier than from the corresponding point bottomright. From the specific shape of the photon horizon the depth of the obstacle can be measured. We succeeded in measuring the depth of several leads along the x-axis up to a depth of 320µm (the width of this obstacle at the surface is 640µm) with a depth uncertainty $<5\%$.

The limitation of the measuring range is caused by the output power of the light source, the dynamic range of the camera and the scattering characteristics of the sample.

6. APPLICATIONS OF THE COHERENCE RADAR FOR FAST MEASUREMENTS

If we use the hardware of the coherence radar $^{10}$, which does the routine of the DPH with a specific image processing system in wired logic $^{11}$, the measuring time of the experiments in Figure 6 takes 30 seconds only.

7. APPLICATIONS OF THE DPH FOR IN VIVO MEASUREMENTS IN HUMAN SKIN

The former measurements have been made on solid phantoms. In human skin the scattering particles (mitochondria, blood cells) are moving. Therefore it has to be investigated, if DPH can be applied to in vivo measurement.
We first consider the behavior of the signal formation in dynamic scatterers. According to chapter 3, subjective speckles result from imaging the object surface with finite aperture. These speckles are the actual signal carriers. Due to the movement of the scattering particles the speckle pattern is not stationary in the image plane. Hence, the finite exposure time (40 ms) of the CCD camera averages the intensity in each pixel and the interference contrast drops. The interference contrast $C$ is measured by the subtraction of two subsequent exposures. Figure 4b shows the graph of the averaged interference contrast $\bar{C}$ for the *in vivo* measurement of a human under arm. The pixel of interest $P_A(x_A, y_A)$ has the same distance to the focus as in the measurement of Fig. 4a (see Capt. 4). In our experiments we find that the under arm *in vivo* displays stronger scattering than the phantom shown above. Therefore the signal arrives earlier at the observed pixel ($t_{THR_1}=1.2 \text{ps}$) and the temporal extension of the impulse response is larger ($\Delta t=2.0 \text{ps}$). Due to the temporal averaging of the contrast $\bar{C}_{\text{MAX}}$ is only 0.055. Figure 4c shows the decrease of $C_{\text{MAX}}$ along the x-axis. The region of the saturation of the camera at the focus is widened due to stronger scattering. The comparison with the corresponding diagram for a solid scatterer (Fig. 4c) shows the smaller contrast for each pixel as well as the smaller deviation between adjacent pixels caused by the averaging due to the movement of the scatterer. As a conclusion of this considerations the exposure time has to be as short as possible. Nevertheless, we could measure light propagation in human skin (under arm) *in vivo* with a standard exposure time of 40 ms. The result is shown in Fig. 7.

### 8. DPH IN DILUTIONS OF MILK WITH VARYING SCATTERING COEFFICIENT $\mu_s'$

DPH measurements have been made in milk-water-dilutions with different concentrations. Different concentrations of milk correspond to different densities of the scattering particles (drops of fat) and therefore to different scattering coefficients $\mu_s'$. Figure 8 shows the DPH for dilutions of milk (3.5% fat) in water with different concentrations: 2 vol%, 25 vol% (scattering coefficients approximately of bloodless skin tissue $12^2$) and for 50 vol%. The corresponding scattering coefficients are vol% / $\mu_s'$: 2% / 0.8cm$^{-1}$, 25% / 9.5cm$^{-1}$, 50% / 17.6cm$^{-1}$. It can be seen that for increasing concentration the region of backscattered light is widened, the PH arrives earlier for each point of the surface and the maximum path
length ($l_{\text{MAX}}$) which can be observed decreases (conc. / $l_{\text{MAX}}$: 2% / 2.8mm, 25% / 1.8mm, 50% / 1.6mm).

Finally we can observe the light propagation in the geometrical shadow of an absorbing obstacle in a dynamic scatterer. The phantom is a vessel with a thin wire ($\varnothing=200\mu$m) at the backside of the front glass. The vessel is filled with 25 vol% dilution of milk. The light is focused on the left side of the wire. Figure 9a shows a single video frame of the illuminated phantom. With the superposition of the reference wave the light propagation can be observed. The measurements are carried out with the standard exposure time of 40ms.

9. CONCLUSION AND PROSPECTS

Short-coherence-interferometry with detection of the photon horizon (DPH) makes it possible to observe light propagation in two dimensions, at the surface of strongly scattering media with a resolution better than 100 fs. The formation of the photon horizon is an important feature of the propagation, which can be used for the detection of inhomogeneities of the scattering properties. In solid scatterers we achieve a depth uncertainty <5%. The measuring range is about 350µm in depth.
With the technology of the coherence radar, the measuring time takes 30 seconds only. The DPH for a whole image can be applied for in vivo measurements too. First measurements of human skin have been carried out successfully. Because of these encouraging experiments we suggest to use the DPH method for the detection of pathological alterations of human skin (e.g. melanoma maligna). Furthermore we will investigate the processes of the signal formation in human skin in vivo with regard to the behavior of the speckle.

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11. REFERENCES