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Diffuse optical tomography by using time-resolved single pixel camera

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ABSTRACT

Diffuse Optical Tomography (DOT) and Fluorescence Molecular Tomography (FMT) generally require a huge data set which poses severe limits to acquisition and computational time, especially with a multidimensional data set. The highly scattering behavior of biological tissue leads to a low bandwidth of the information spatial distribution and hence the sampling can be preferably carried out in the spatial frequency source/detector space. In this work, a time-resolved single pixel camera scheme combined with structured light illumination is presented and experimentally validated on phantoms measurements. This approach leads to a significant reduction of the data set while preserving the information content.

Keywords: Time-resolved, diffuse optical tomography, fluorescence molecular tomography, compressive sensing, Hadamard

1. INTRODUCTION

Diffuse Optical Tomography (DOT) and Fluorescence Molecular Tomography (FMT) are novel biomedical techniques which aim at the 3D optical characterization of biological tissues at both preclinical[1] and clinical level[2–5]. In order to increase the spatial resolution of both techniques (DOT and FMT), a dense raster scanning of the point light source and highly parallel detection (e.g. CCD, CMOS) are generally adopted. This leads to a huge data set that poses severe limits to the acquisition time and computational tomographic inversion processes. The problem is further complicated when a multidimensional data set is needed, such as temporal and spectral (excitation and detection) information. The possibility to resolve in time, in fact, can improve the depth sensitivity and can disentangle absorption from scattering contributions[6,7]. The highly scattering behavior of biological tissue leads to a low bandwidth of the information spatial distribution and hence the sampling can be preferably carried out in the spatial frequency space. This has led, in the recent years, to the development of structured light based approaches[8–13]. The low bandwidth can be further exploited on the detection side by adopting compressive sampling schemes[14]. This leads to a significant reduction of the data set while preserving the information content, especially if the compression of both the source and detector space can be carried out at the acquisition level. In this work, a time-resolved single pixel camera scheme combined with structured light method is presented and experimentally validated on phantoms measurements. In particular the use of a single detector combined with Digital Micromirror Device (DMD) and Time Correlated Single Photon Counting (TCSPC) allows acquiring the time-resolved images of the diffuse light exiting the sample.

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2. METHODS

In this work we developed a time-resolved (TR) DOT/FMT system based on the single-pixel camera principle[15]. Output images from the sample are spatially modulated using Hadamard patterns. These patterns can be described mathematically by *NxN* squared matrixes H_k, with N a power of 2, composed by *+1* and *-1* elements[16]. The operation performed by the spatial modulator and the time-resolved single pixel detector can be represented by this equation:

$$C_k(t) = \iint I(x,y,t) h_k(x,y)\, dx\, dy \tag{1}$$

where $I(x,y,t)$ is the time-resolved spatial light profile exiting from the sample, $h_k(x,y)$ is the spatial implementation of the k-th Hadamard matrix and $C_k(t)$ is the k-th time-resolved coefficient representing the projection of $I(x,y,t)$ on the k-th Hadamard pattern.

Due to the fact that it is not feasible to have both positive and negative elements, two measurements for each Hadamard pattern were needed: the first with *0* in place of *-1*, and the other with *0* in place of *+1* and *+1* in place of *-1*. By performing the difference between these two images it is possible to measure one coefficient. This approach is redundant but it presents the advantage to provide a good background cancellation after subtraction.

Due to the orthonormality property of H_k it is possible to reconstruct an approximation of $I(x,y,t)$ by the following backprojection operation:

$$\tilde{I}(x,y,t) = \frac{1}{N^2} \sum_{k=1}^{N^2} C_k(t) h_k(x,y) \tag{2}$$

As an example, in the following 2x2 Hadamard matrixes are shown:

$$H_1 = \begin{bmatrix} 1 & 1 \\ 1 & 1 \end{bmatrix}, H_2 = \begin{bmatrix} 1 & -1 \\ 1 & -1 \end{bmatrix}, H_3 = \begin{bmatrix} 1 & 1 \\ -1 & -1 \end{bmatrix}, H_4 = \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix} \tag{3}$$

3. MATERIALS AND METHODS

The system schematic is depicted in Fig 1. A supercontinuum model locked laser providing pulse of tens of picoseconds at the repetition rate of 80 MHz (Fianium, SC450) is spectrally filtered by an interferential filter with center wavelength of 620 nm and 40 nm bandwidth. Light is then coupled to a Digital Micromirror Device (DMD Discovery kit 1100, Vialux, Germany) by an on-axis coupling system based on a Total Internal Reflection prism to create spatial patterns. The outcoming structured light is then imaged on the input plane of the sample over a 3x3 cm^2 area. The output plane of the sample is then imaged on a second DMD (DMD Discovery 4100, Vialux, Germany), by means of a lens (f=50 cm). The field of view is about 2x2 cm^2. The second DMD allows one to project patterns for compression, following the single pixel camera approach. The reflected light is focused on a 1mm diameter step-index fiber in order to direct the light on the active area (100 μm diameter) of Single-Photon Avalanche Diode (SPAD) (MPD, Italy) with time-resolved high resolution capability (IRF of ~70 ps FWHM). The SPAD is connected to a Time-Correlated Single Photon Counting Board (TCSPC) mounted on a Personal Computer (PC). By means of a flip mirror it is possible to image the DMD plane on a low noise 16-bit cooled CCD camera (Versarray 512, Princeton Instruments). In the case of fluorescence inclusions an interference filter and a high pass filter have been inserted in front of the detector (SPAD or CCD) to remove the excitation light and select the fluorescence signal. The selection of illumination and compression patterns, the acquisition of CCD image and time-resolved histograms is automated by a home-made LabView software.

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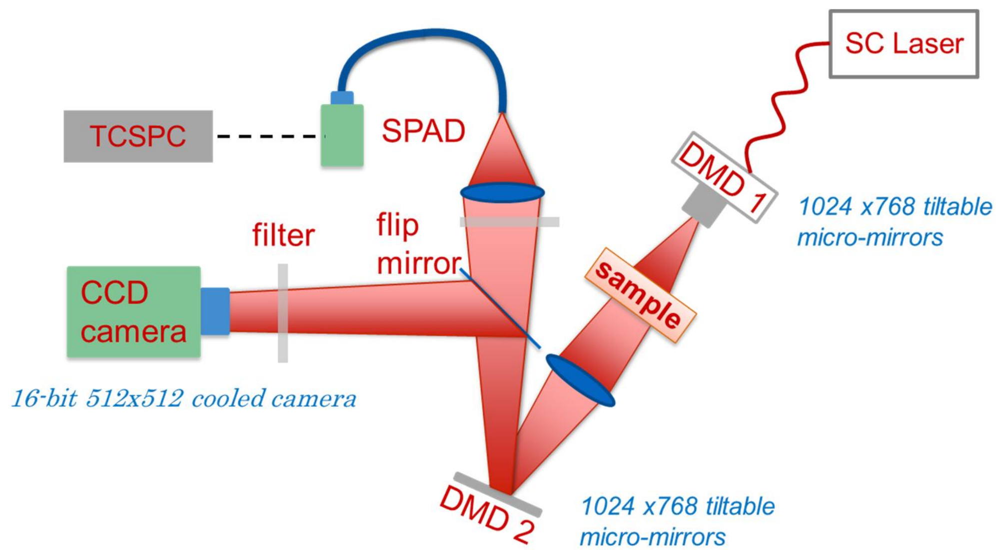

Figure 1. Schematic of the setup.

Measurements were carried out on a slab phantom (45 mm x 100 mm x 17 mm) made of epoxy resin, TiO_2 (as scatterer) and toner (as absorber) mimicking the optical properties of biological tissues[17]. This phantom has been previously calibrated using a broadband time-resolved spectroscopy system[18] giving an absorption of about 0.1 cm^{-1} and a reduced scattering coefficient of about 10 cm^{-1}. A small vertical cylindrical inclusion (height: 22 mm and diameter: 2 mm) was drilled into the phantom to allow the injection of a fluorescent dye (Nile Blue).

4. RESULTS AND DISCUSSIONS

First of all the imaging capability of the Time Resolved single-pixel camera has been tested. A white paper with a black "F" has been placed in the output plane of the phantom without fluorescent dye. A plane homogeneous illumination was produced on the input plane and 64x64 Hadamard patterns were sent on DMD 2. A reference image on the CCD was also acquired by activating all the elements of the second DMD. Figure 2 shows the CCD image compared to the reconstructed images using the single pixel camera by increasing the Hadamard order. As expected the image quality dramatically improves by increasing the Hadamard order used for reconstruction.

It is well known [8,2,5,6,7] that a scattering medium acts as a lowpass filter in the spatial Fourier domain, thus it is expected that an output image from a diffusive medium must be recovered by using only low frequencies components and consequently low order Hadamard patterns. Figures 3 and 4 show the reconstructed images of the bulk phantom without and with the fluorescent dye. For the last measurement a bandpass filter has been placed in front of the CCD and SPAD. In the same figures the root mean-square error (RMSE) plot is also shown. We observe that an 8x8 Hadamard transform for the homogeneous phantom and a 16x16 Hadamard transform for the fluorescence case allows a good approximation of the image information content. In fact by increasing the order of Hadamard patterns no significant improvements of RMSE value can be observed.

Finally, in Figure 5, it is possible to appreciate the time-resolved capability of the system. As an example it is shown the time resolved photons histogram corresponding to the pixel with the highest intensity in the fluorescence image. It is worth noting that the higher temporal sampling of the proposed method represents an important advantage compared to the use of a gated camera where the temporal sampling is serially performed.

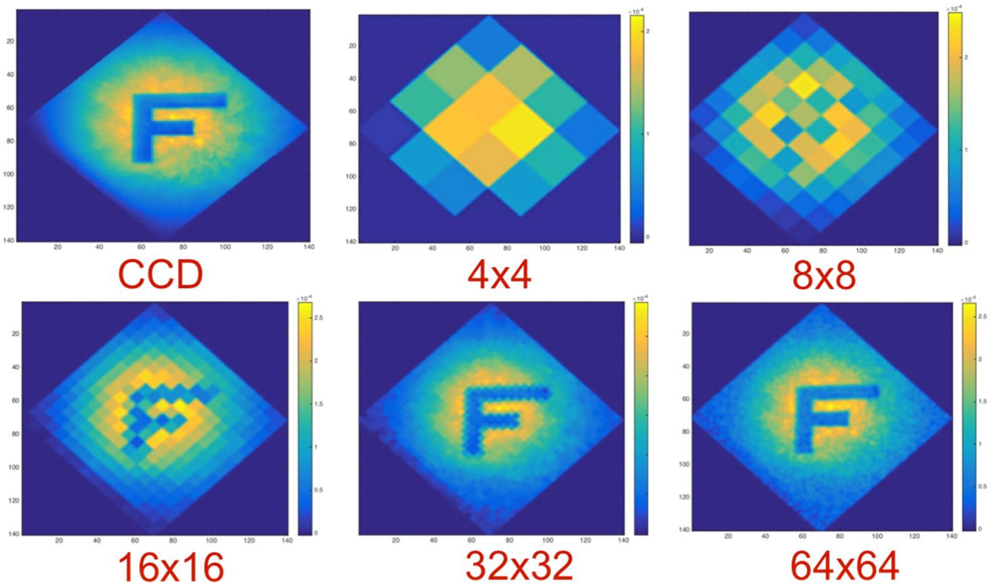

Figure 2. CW image reconstruction of the “F” letter using Hadamard patterns on DMD 2 and plane illumination.

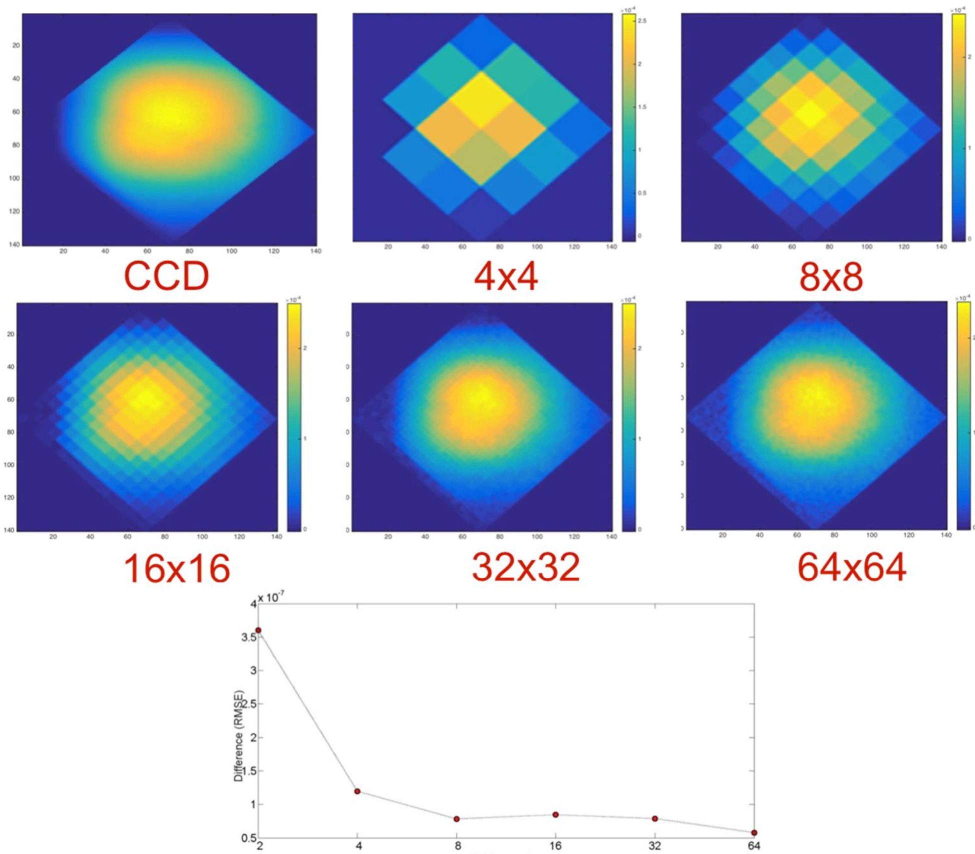

Figure 3. CW image reconstruction of output from an homogeneous phantom using Hadamard patterns on DMD 2 and plane illumination.

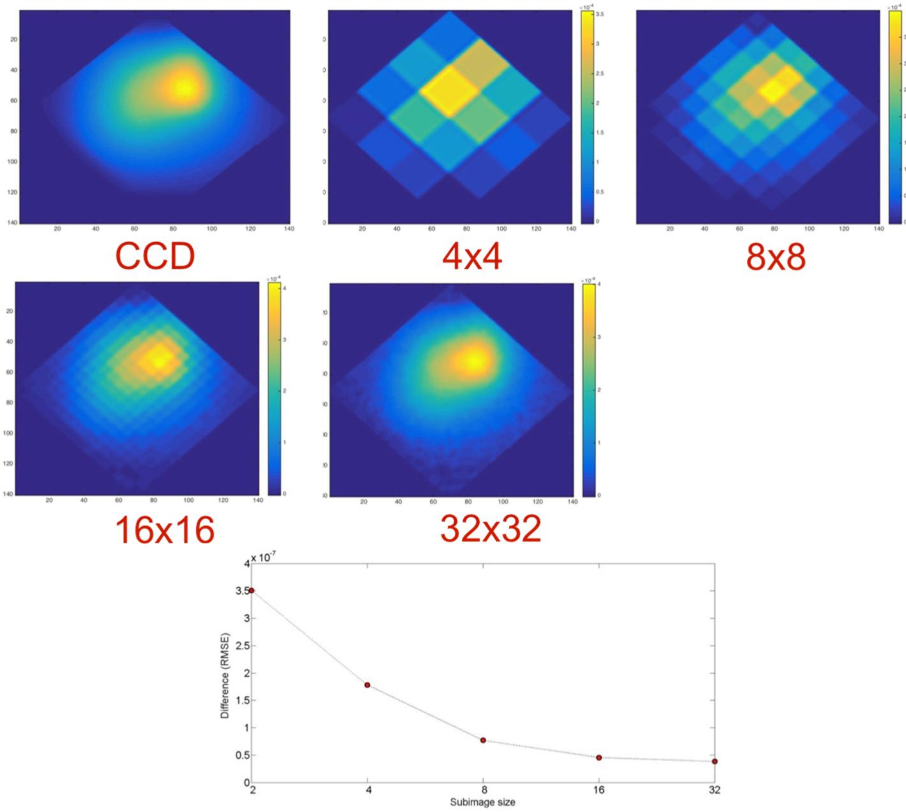

Figure 4. CW image reconstruction of output from an homogeneous phantom with an embedded fluorescent inclusion using Hadamard patterns on DMD 2 and plane illumination.

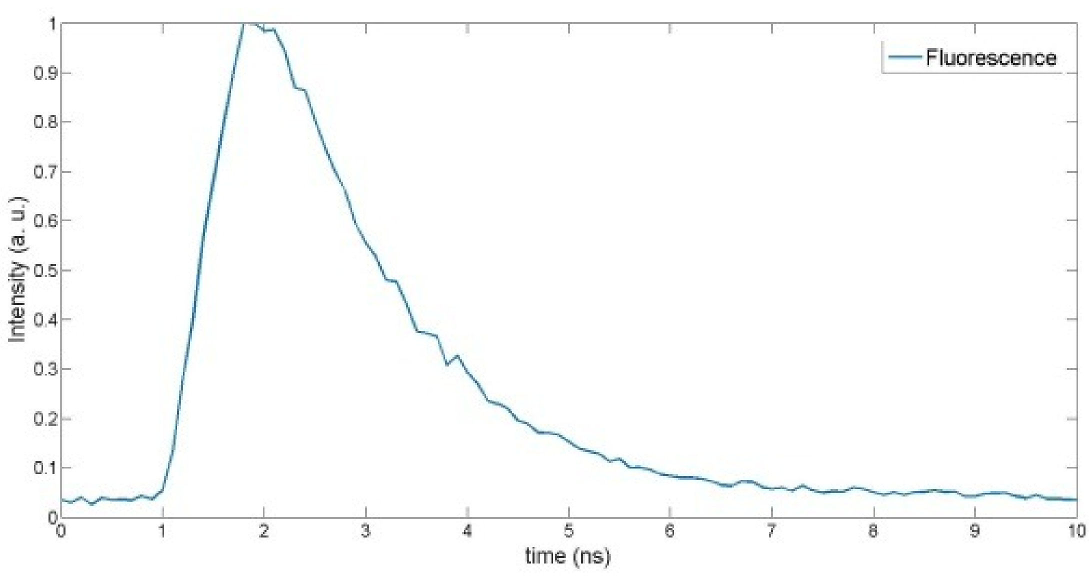

Figure 5. Time-resolved fluorescence decay extracted from the highest intensity pixel of the fluorescence image.

5. CONCLUSIONS

In this work a system suitable for Time Resolved DOT/FMT based on structured light illumination and compressive sensing was presented. Hadamard patterns have been used for compression and a fast detector (SPAD) was used for time-resolved capability. The imaging capability of the system has been obtained by comparing the CCD images with the one obtained with the single pixel camera. Future work will be devoted to perform optical tomography of complex shapes by exploiting the data set acquired with the proposed system. Moreover, the fluorescence spectrum in the case of FMT will be added by using an array of detectors following the scheme proposed by Pian[1]>.

6. ACKNOWLEDGEMENTS

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