Pseudo-random single photon counting for time-resolved optical measurement

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Abstract: We report a new time-resolved optical measurement method which combines single photon counting and the spread spectrum time-resolved optical measurement method. A laser diode modulated with pseudo-random bit sequences replaces the short pulse laser used in conventional time-resolved optical systems, while a single photon detector records the pulse sequence in response to the modulated excitation. Periodic cross-correlation is used to retrieve the impulse response. Feasibility of our approach is validated experimentally. A rise time around 150 picoseconds has been achieved with our prototype. Besides high temporal resolution, the new method also affords other benefits such as high photon counting rate, fast data acquisition, portability, and low cost.

OCIS codes: (120.0120) Instrumentation, measurement, and metrology; (300.6500) Spectroscopy, time-resolved; (170.3890) Medical optics instrumentation; (170.6920) Time-resolved imaging.

References and links

1. M. S. Patterson, B. Chance, and B. C. Wilson, "Time resolved reflectance and transmittance for the noninvasive measurement of tissue optical properties," Appl. Opt. **28**, 2331-2336 (1989).
2. J. R. Lakowicz, H. Szmacinski, K. Nowaczyk, K.W. Berndt, and M. Johnson, "Fluorescence lifetime imaging," Anal. Biochem. **202**, 316-330 (1992).
3. P. I. H. Bastiaens and A. Squire, "Fluorescence lifetime imaging microscopy: spatial resolution of biochemical processes in the cell," Trends Cell Biol. **9**, 48-52 (1999).
4. F. Gao, H. J. Zhao, and Y. Yamada, "Improvement of Image Quality in Diffuse Optical Tomography by use of Full Time-Resolved Data," Appl. Opt. **41**, 778-791 (2002).
5. M. Essenpreis, C. E. Elwell, M. Cope, P. van der Zee, S. R. Arridge, and D. T. Delpy, "Spectral dependence of temporal point spread functions in human tissues," Appl. Opt. **32**, 418-425 (1993).
6. W. Becker, A. Bergmann, M. A. Hink, K. König, K. Benndorf, and C. Biskup, "Fluorescence lifetime imaging by time-correlated single-photon counting," Microsc. Res. Tech. **63**, 58-66 (2004).
7. D.V. O'Connor, D. Phillips, "Basic Principle of the Single Photon Counting Lifetime Measurement," in *Time-correlated single photon counting*, (Academic, 1984), pp. 36-54.
8. Becker & Hickl GmbH, "The bh TCSPC handbook," http://www.becker-hickl.com/literature.htm.
9. D. Grosenick, H. Wabnitz, H. H. Rinneberg, K. T. Moesta, and P. M. Schlag, "Development of a Time-Domain Optical Mammograph and First *in vivo* Applications," Appl. Opt. **38**, 2927-2943 (1999).
10. R. Cubeddu, A. Pifferi, P. Taroni, A. Torricelli, and G. Valentini, "Compact Tissue Oximeter Based on Dual-Wavelength Multichannel Time-Resolved Reflectance," Appl. Opt. **38**, 3670-3680 (1999).
11. M. Prummer, C. G. Hübner, B. Sick, B. Hecht, A. Renn, and U. P. Wild, "Single-Molecule Identification by Spectrally and Time-Resolved Fluorescence Detection," Anal. Chem. **72**, 443 - 447 (2000).
12. P. Schwille, S. Kummer, A. A. Heikal, W. E. Moerner, and W. W. Webb, "Fluorescence correlation spectroscopy reveals fast optical excitation-driven intramolecular dynamics of yellow fluorescent proteins," PNAS, **97**, 151-156 (2000)
13. H. Eda, I. Oda, Y. Ito, Y. Wada, Y. Oikawa, Y. Tsunazawa, and M. Takada, "Multichannel time-resolved optical tomographic imaging system," Rev. Sci. Instrum. **70**, 3595-3602 (1999).
14. F. E. W. Schmidt, M. E. Fry, E. M. C. Hillman, J. C. Hebden, and D. T. Delpy, "A 32-channel time-resolved instrument for medical optical tomography," Rev. Sci. Instrum. **71**, 256-265 (2000).

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15. N. G. Chen and Q. Zhu, “Time-resolved diffusive optical tomography using pseudo-random sequences,” Opt. Express. **11**, 3445-3454 (2003).
16. N. G. Chen and Q. Zhu, “Time-resolved optical measurements with spread spectrum excitations,” Opt. Lett. **27**, 1806-1808 (2002).
17. N. G. Chen and Q. Zhu, “Spread spectrum time-resolved photon migration imaging system: the principle and simulation results,” Proc. SPIE **4955**, 474-479 (2003).

1. Introduction

Time-resolved techniques are important in optical instrumentation. Measurements of time-dependent transmittance, reflectance, and fluorescence in response to illumination by an ultrashort light pulse always contain rich information and researchers can use this information to retrieve important properties of the sample under investigation [1-3]. Two good examples are time-resolved diffuse optical tomography and fluorescence lifetime imaging. Time-resolved diffuse optical tomography measures temporal point-spread functions (TPSFs) which can be used for quantitative reconstruction of distributions of scattering and absorption coefficients [4], while fluorescence lifetime imaging measures the mean fluorescence lifetime of a chromophore at each spatially resolvable element of a microscope image [2, 3]. Both measurements are made in the time domain, in which short excitation pulses are used.

Currently, the temporal profile of the response to an ultrashort light pulse can be measured with either a streak camera [5] or a time-correlated single-photon counting (TCSPC) system [6, 7]. TCSPC is based on the detection of single photons of a periodical light signal, the measurement of the arriving time of the individual photons and the reconstruction of the waveform from the individual time measurements [8]. It provides a better dynamic range and temporal linearity than those using streak cameras, and thus is preferred in many applications. A few time-resolved systems for medical optical tomography have been reported, all of which use the TCSPC technique [9-14]. In spite of the advantages of TCSPC mentioned above, it has certain disadvantages. The principle of single photon counting requires that no more than one photon is detected in each cycle, otherwise the pile-up error will occur [8]. This causes a big problem in the data acquisition speed. The maximal count rate is limited by the repetition rate of laser pulses, the processing speed of electronic devices, and the time span of the impulse response. A typical count rate is 100,000 cps (counts per second), which leads to about 10 seconds to acquire around 10^6 photons for one temporal profile. In some applications, multiple detection channels are necessary. For example, F. E. W. Schmidt et al reported a 32-channel time-resolved instrument, which needs 10-20 minutes for a complete scan [14]. Modern TCSPC modules allow a count rate around 1 Mcps, but in this case the pile-up error may need to be corrected. For real-time or near-real-time imaging, a faster time-resolved method is desirable.

To achieve a higher measurement speed, a spread spectrum time-resolved (SSTR) optical measurement method that borrows ideas from spread spectrum communications was developed [15-17]. However, although this technique has better signal-to-noise ratio, shorter data-acquisition time, and low system cost as its main advantages, its time resolution is limited by the impulse response of detectors and is about one order lower than that of TCSPC.

In this paper, we present a novel approach that combines TCSPC and SSTR, which is termed pseudo-random single-photon counting (PRSPC). The basic principle and some preliminary simulation and experimental results are covered in the following sections.

2. Theory

The basic principle of the SSTR [12, 13] method is simple and straightforward. We denote $I(t)$ as the time-dependent response of a sample to the excitation of an ultra short pulse. A light source continuously modulated with a pseudorandom bit sequence (PRBS) is used to illuminate the sample. So the detected signal is proportional to the convolution of the impulse response with the excitation sequence:

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$$R(t) = AI(t) * (P(t)+1), \qquad (1)$$

where A is a constant representing the system gain and $P(t)$ is an N-bit long pseudorandom maximal length sequence with binary values +1 and -1. It has a circular autocorrelation function similar to a delta function:

$$g(\tau) = \langle P(t)P(t-\tau)\rangle$$

$$= \begin{cases} 1, \tau/T_0 = 0 \\ -1/N, \tau/T_0 = \pm1, \pm2, \ldots \end{cases}, \qquad (2)$$

where τ is the time delay and T_0 is the bit period. By circular correlating the ac component of $R(t)$ with $P(t)$ we will have

$$f(t) = \left\langle (R(t') - \left\langle R(t') \right\rangle) P(t'-t) \right\rangle = AI(t) * g(t), \qquad (3)$$

which is proportional to the original time spectrum $I(t)$ except a slight temporal spread determined by the bit period T_0.

In SSTR, the detected response $R(t)$ is acquired directly from the linear output of a photodetector, while the PRSPC method utilize single photon counting to accumulate the photon numbers in various time slots. The total number of time slots is the number of bit in the excitation sequence, and the width of each slot is identical to the bit period. The excitation sequence and pulse detection are synchronized with a universal clock signal.

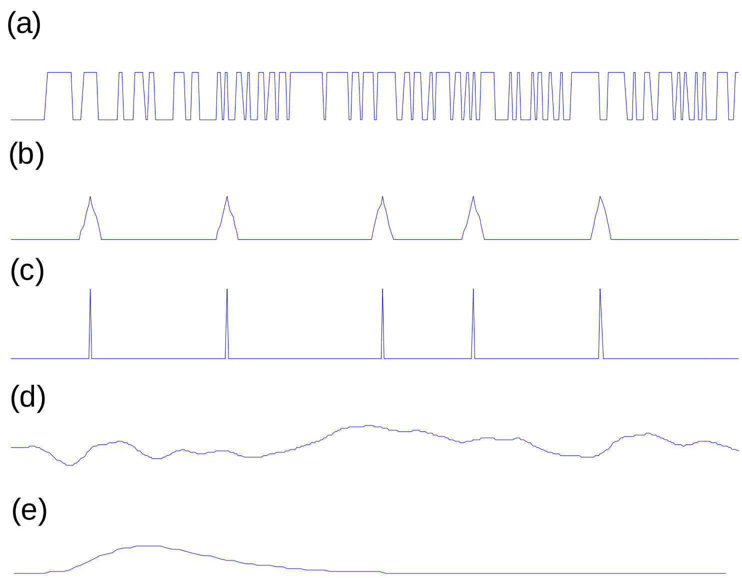

Fig. 1. Principle of PRSPC measurement.

The principle of PRSPC is illustrated in Fig. 1. Fig. 1(a) is the output of a transmitter intensity modulated with a PRBS; Fig. 1(b) is the detected pulses in response to the excitation. The pulse width is determined by the type of single photon detector used. Fig. 1(c) is the pulse

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sequence after post-processing, which can be performed with a circuit board or on a personal computer after digitizing. Each pulse is identified with its peak position in the time domain and has a much reduced pulse width. Then the photons are added to corresponding time slots. Repeating the process for a certain period of time, the detected signal $R(t)$ builds up (Fig. 1(d)). $f(t)$ is calculated by the use of Eq. (3) (Fig. 1(e)). A and $g(t)$ are system characteristics and can be obtained by calibration. Generally the original time spectrum $I(t)$ can be retrieved by deconvolution. However, if T_0 is sufficiently small, $f(t)$ is nearly proportional to $I(t)$ and no deconvolution is needed.

3. Simulation method and results

To validate the PRSPC method theoretically, we simulated time-resolved measurement of diffusive photon density waves by the PRSPC approach on a computer. A simulated PRSPC system virtually consists of a 5 Gb/s pattern generator, a 10 Gb/s transmitter, a single photon counting detector, and a 10 Gb/s digital transceiver and a computer for data processing. A 5 Gb/s 1023-bit long PRBS generated by the pattern generator is used to directly modulate the transmitter to generate an optical pulse sequence. The optical fibers coupled to the transmitter and the receiver are embedded in an infinite homogeneous turbid medium and separated by $6\,cm$. The reduced scattering coefficient of the medium is $8\,cm^{-1}$, while the absorption coefficient is chosen to be $0.05\,cm^{-1}$. The optical transmitter emits photons at a rate resulting in an average of 10 million photons per second arriving at the single photon counting (SPC) detector. The SPC output signal consists of a train of randomly distributed pulses due to the detection of the individual photons. It is assumed that the single photon counting detector outputs ideal digital pulses, which are sampled by the digital transceiver at a sampling rate of 10G and the photons are added to corresponding time slots. Repeating the process for 1 second, the detected signal builds up. Finally the cross-correlation operation is used to retrieve the original time spectrum. As shown in Fig. 2, the retrieved TPSF with PRSPC method agrees well with the original one.

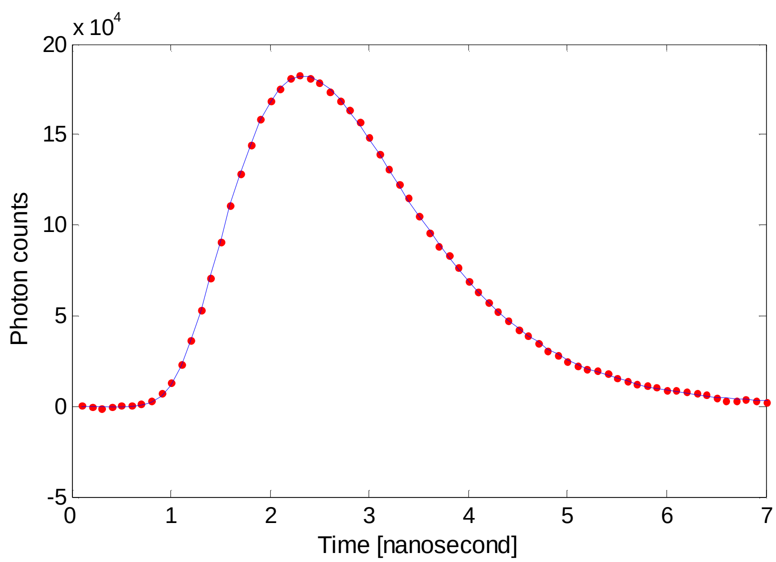

Fig. 2. Impulse response representing the TPSF of a diffusive photon density wave. Blue curve, theoretical prediction; red dots, reconstruction using PRSPC approach.

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4. Experimental setup

To validate the PRSPC method experimentally, we built a PRSPC prototype. The PRSPC experimental system consists of a 10 Gb/s pattern generator (PPG-E135, Lecroy), a 10 Gb/s 850 nm VCSEL transmitter (Model V-126) which has a maximal 1mW output power and is coupled to a multimode optical fiber, a single photon counting detector (PCDMini0100, SensL), a high speed oscilloscope (Agilent 54852A) which has a 2GHz bandwidth and an up to 10GHz sampling rate, and a personal computer (PC). A 5 Gb/s 1023-bit long PRBS generated by the pattern generator is used to modulate the transmitter to generate an optical pulse sequence. The light source is appropriately attenuated to control the actual counting rate. In the calibration experiment, the light source and the detector are aligned but separated by a distance around 5 cm. Only a very small portion of the diverging beam from the optical fiber reaches the small detection area of the detector (100 microns in diameter). Neutral density filters are inserted into the light path when necessary. The SPC detector converts the detected optical signal into electrical signal which is then acquired by the oscilloscope. The sampling rate of the oscilloscope is set to its maximal value 10GHz, corresponding to a time resolution of 100 picoseconds. A pulse sequence over a 26.2 μs time span is recorded at once and transferred to the PC through local area network (LAN). Reading data from the oscilloscope memory results in a dead time around 0.5 second. The process is repeated until the total acquisition time is reached. The PC is responsible for further processing the received data and finally performing cross-correlation to retrieve the TPSF, and also controls the data acquisition of the oscilloscope. The interaction between the PC and the oscilloscope is realized in the Matlab environment.

5. Experimental results

5.1 Calibration experiment

This experiment is to measure the impulse response of the PRSPC system. The beam emitted by the transmitter is attenuated by a neutral density filter (20%transmission), and then directly collected by the SPC detector. The acquisition time is set to be 1 second. As shown in Fig. 3(b), the rise time (20%-80%) is measured to be about 150 picoseconds.

5.2 Phantom experiment

This experiment demonstrates the potential application of our PRSPC system in time resolved diffuse optical tomography. In this experiment, solid tissue phantom slabs of various thicknesses are inserted between the transmitter and the single photon detector, and the temporal point spread function of light diffusing through the sample is measured. The tissue phantoms have similar optical properties as human breast tissue (μ_a~0.02 cm^{-1}, μ'_s~6 cm^{-1}). The acquisition time is set to be 1 second. Shown in Fig. 4 are TPSFs for tissue phantom slabs with a thickness of 1 cm (blue) and 2 cm (red), respectively.

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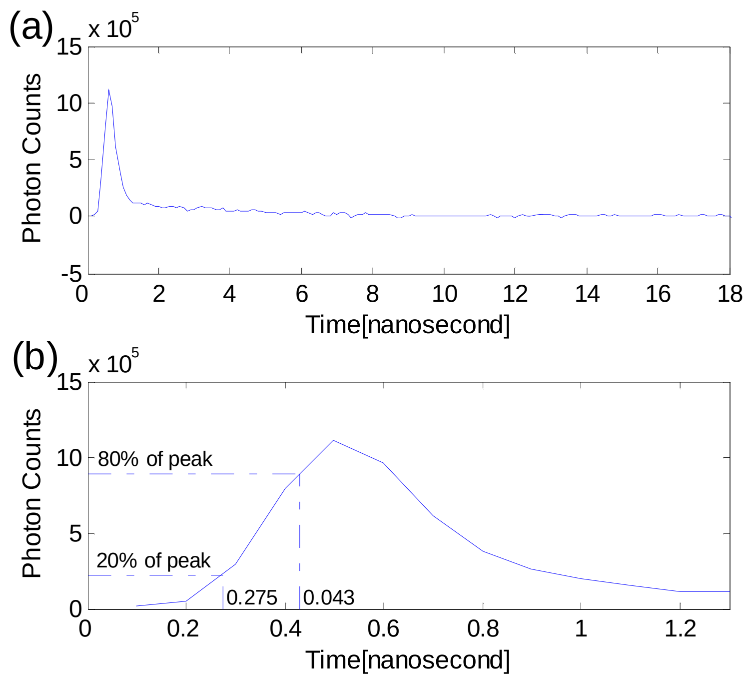

Fig. 3 Calibration result. (b) is partial magnification of (a).

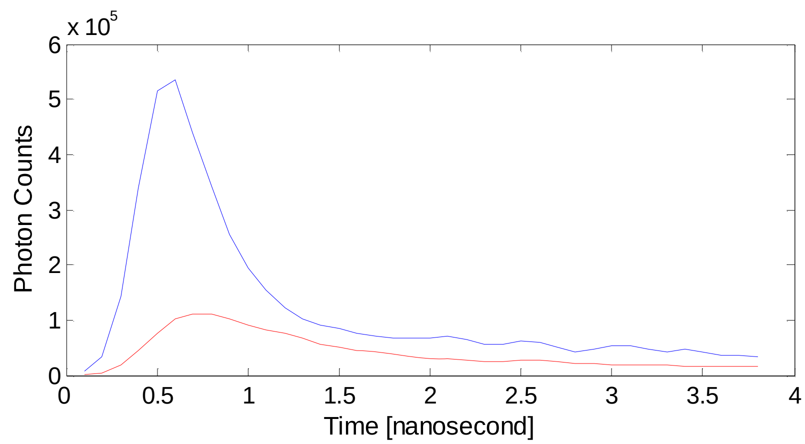

Fig. 4. TPSFs of light diffusing through solid breast tissue phantom. The thicknesses of the phantom are 1 cm (blue) and 2 cm (red), respectively.

6. Discussion

PRSPC combines SPC and SSTR, and it shares with TCSPC some desirable features such as high sensitivity and high time resolution. Our calibration experiment result has shown a remarkable time response of 150 picoseconds. However, it also offers many other advantages:

a. Higher photon count rate and faster data acquisition

There are two types of pile-up error in TCSPC. The type E error is caused by overlapping of two-photons that cannot be distinguished by electronics. The type S pile-up error, which dominates in standard TCSPC, results from the fact that a TCSPC device can detect only one photon per excitation period. If the detection rate is so high that the detection of a second photon within the recorded time interval becomes likely, then the temporal profile is distorted.

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It is commonly believed that the pile-up becomes a problem if the photon count rate exceeds 0.1 to 1% of the pulse repetition rate [2]. The typical repetition rate of pulsed lasers is about 100 MHz, which means a maximal photon count rate of 1 MHz. In PRSPC, we record every photon events and thus there is no type S pile-up error. The only pile-up is of type E, which is more tolerant of high count rate. A modified TCSPC system would be type E pile-up error free if it has multi-stop capability. However, this function is usually available for a low excitation repetition rate for commercial TCSPC modules. Even compared with modified TCSPC without type S pile-up error, our approach has another advantage in terms of type E pile-up error. The photon detection probability in a TCSPC setup is usually concentrated within a time window much smaller than the excitation period. For example, in fluorescence decay measurement, most photons tend to arrive at the detector immediately after the excitation pulse. In case of PRSPC, the excitation is close to continuous wave and the photon detection probability is more uniformly distributed in the time domain (Fig. 1(d)). As a result, there will be less type E pile-up error in PRSPC compared to TCSPC given the same counting rate. Generally speaking, the maximal photon count rate of PRSPC limited by pile-up error is about two orders higher than TCSPC, which implies a potential faster data acquisition. A 3M counts per second typical count rate has been achieved by our prototype in experiments with the 1-cm-thick phantom. This count rate is mainly limited by the dead time of the single photon detector used, whose typical value is 100 ns.

The development of our PRSPC prototype is to validate our PRSPC method experimentally. It is not the ultimate solution for real time data acquisition due to the long dead time spent on reading data from the oscilloscope memory. Currently our group is developing a digital time-tagged photon counting module on a FPGA (Field Programmable Gate Array) platform, which aims for real time data acquisition. PRBS generation will also be implemented on the same platform.

b. Portability and low cost

TCSPC requires a picosecond or femtosecond laser system, which is generally very bulky and of high cost. PRSPC uses small laser diodes as light sources. While a commercial TCSPC module (e.g., from Becker & Hickl) typically costs more than 8,000 €, we believe that the digital photon counting module we are developing will be significantly less expensive. Therefore, our whole system will become much more compact and of low cost. We expect our PRSPC system will be very competitive in terms of performance to cost ratio.

Our experimental results also show that, the noise level of our current PRSPC system is almost constant for all time delays, a phenomenon not desirable for detecting weak light away from the peak. This is due to the cross-correlation operation. We will explore possible approaches to reduce the noise level in our future study.

7. Conclusions

To conclude, we have developed a prototype of pseudo random single photon counting measurement system. The validity and performance of this system are verified by both simulation and experiments in time-resolved measurement of diffusive photon density waves. The new measurement system offers many advantages such as high sensitivity and high time resolution, faster data acquisition, portability, and low cost.

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