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(54) Title: RAMAN SPECTROSCOPY

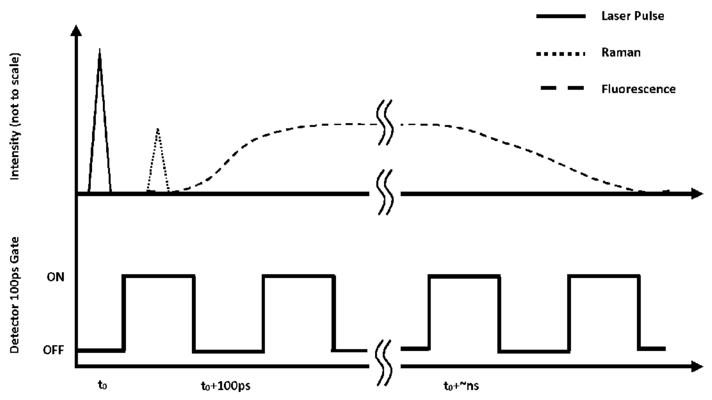

Fig 1 the measurement concept

(57) Abstract: The present invention relates to Raman spectroscopy, particularly to time-resolved Raman spectroscopy. We describe a Raman spectroscopic instrument comprising a time-resolved Raman spectrometer with a static Fourier transform spectrometer and a single-photon avalanche diode (SPAD) array detector; wherein the detector provides a response in the form of an electronic signal for every pixel, which signal comprises precise information on the arrival time of an initial photon and, after detection of an initial photon, every pixel enters a recovery period during which it is disabled from further detection.

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RAMAN SPECTROSCOPY

FIELD OF THE INVENTION

The present invention relates to Raman spectroscopy, particularly to time-resolved Raman spectroscopy.

BACKGROUND TO INVENTION

Raman spectrometry is an increasingly prominent tool in a variety of sectors, whereby all molecules provide a unique molecular signature that can be used as a finger print to identify the chemical composition of a substance. This has led the development of a variety of handheld systems that have been used for the identification of explosive materials, for example.

However, the performance of these systems is limited when organic substances are present as they emit a strong background fluorescent signals that can completely mask the Raman response. It has been proven that these signals can be separated temporally [Martyshkin. D.V., R. C. Ahuja., A. Kudriavtsev. And S. B. Mirov. “Effective suppression of fluorescence light in Raman measurements using ultrafast time gated charge coupled device camera” *Review of scientific instruments* **Vol 75 N° 3** (2004)], using so called time-resolved Raman spectrometers. Typically, the separation is achieved via either fast high-voltage gating of a sensitive detector or by the use of a fast chopper such as a Kerr gate [P. Matousek, M. Towrie, C. Ma, W. M. Kwok, D. Phillips, W. T. Toner and A. W. Parker “Fluorescence suppression in resonance Raman spectroscopy using a high-performance picosecond Kerr gate” *J. Raman Spectrosc.* **32**: 983–988 (2001)]. These systems work in combination with a short laser pulse (with a pulse length <= 50 ps).

In recent years, Geiger mode single photon avalanche photodiodes have been combined with fast timing electronics to perform time-of-flight LIDAR measurements [João Pereira do Carmo, B. Moebius, M. Pfennigbauer, R. Bond, I. Bakalski, M. Foster, S. Bellis, M. Humphries, R. Fisackerly and B. Houdou, "Imaging lidars for space applications", Proc. SPIE 7061, 70610J (2008); doi:10.1117/12.79370]. One of the properties of these detectors is that they respond to the first photon that they encounter and are then unable to record another signal for up to 50 ns. We have recognised that this feature, or detector dead time, is, in effect, a perfect shutter and we have exploited this to form a novel, time-resolved, Raman spectrometer. The first photon received by any detector element from a given laser pulse will be detected and will then disable that element, and any subsequent photons emitted for up to 100 ns later will be supressed. By identifying the arrival time of the first photon with sufficient accuracy (< 100 ps) it may be identified as either Raman or fluorescent in nature and hence the two signals can be separated. Further this timing can be improved by combing the detector with a static Fourier transform spectrometer (Harlander et al 1992). In these devices, unlike classical dispersive systems, all wavelength are observed by all pixels. This property can be exploited to improve the accuracy of any timing measurement.

SUMMARY OF INVENTION

Accordingly, in its broadest sense, the present invention provides a Raman spectroscopic instrument comprising a time-resolved Raman spectrometer comprising a static Fourier transform spectrometer and a single-photon avalanche diode (SPAD) array detector comprising a plurality of detector pixels; wherein the detector provides a response in the form of an electronic signal for every pixel, which signal comprises precise information on the arrival time of an initial photon and, after detection of an initial photon, every pixel enters a recovery period during which it is disabled from further detection.

Preferably, the detector recovery period is more than 1ns

Preferably, the detector is triggered to provide accurate timing of the returns; the signal is recorded by read-out electronics that time stamps the returned response; and the signal observed in the first timing period is then separated to extract the Raman response.

Preferably, all the pixels are used to provide and average of the time measurement, exploiting the response of the static Fourier transform spectrometer.

Preferably, the spectroscopic instrument further comprises a trigger for the detector to respond at or before the short pulse source is activated.

Preferably, the trigger signal is an electrical or photonic signal.

In certain embodiments, the detector is gated such that it is only on for a fixed period of time, in order to supress background light. Suitably the period of time is greater than or equal to 10 ns and preferably the position of this gate is controlled by the trigger of the system, to coincide with the location of the target.

Preferably, every detection element has an independent electronics channel capable of event timing. More preferably, the timing per electronics channel is better than 100 ps.

Preferably, every timing electronics channel comprises a discriminator with threshold such that the discriminator logic contains event timing information to an accuracy of less than about 100ps.

Preferably, every timing electronics channel performs time to digital conversion on the discriminator logic pulse to digitise the event time to better than 100 ps.

Preferably, the detector array has more than one detection element.

Preferably, a single detector element is used to precisely measure the distance to the target, allowing the trigger signal to be positioned for the extraction of the Raman signal.

Preferably, the spectroscopic instrument provides an output signal corresponding to a Raman signal response.

Preferably, the spectroscopic instrument further comprises an analysis function, preferably an analysis function adapted to record and analyse both Raman and fluorescent returns over a period of time.

Preferably, the instrument further comprises a source for a short pulse of monochromatic light, or near monochromatic light. More preferably, the source is a laser source.

Preferably, the source is arranged to excite a target sample and the assembly is further provided with an imaging or similar optical system to capture broadband continuum light emitted from the sample and pass the light to the detector.

Suitably, the spectroscopic instrument provides an output signal corresponding to a Raman signal response.

Preferably, the spectroscopic instrument includes an analysis function, more preferably, an analysis function adapted to record and analyse both Raman and fluorescent returns over a period of time.

The above and other aspects of the present invention will now be described in further detail, by way of example only, with reference to the accompanying figures, in which:

Figure 1 is a schematic view of the overall measurement functionality of an embodiment of a Raman instrument in accordance with the present invention;

Figure 2 is a schematic view of an embodiment of a spectroscopic instrument in accordance with the present invention;

Figure 3 is a schematic showing an embodiment of a spectroscopic instrument of the present invention comprising a static Fourier transform spectrometer; and

Figure 4 is a schematic of a typical electrical circuit used to read out the data from the detector and time the arrival time of the photon

DETAILED DESCRIPTION

According to one aspect of the invention, a short pulse from a monochromatic or near monochromatic source is combined with a spectrometer and linear Geiger mode or single-photon avalanche diode (SPAD) array detector.

The light from the source causes the sample to radiate Raman light and fluorescence. This broadband continuum light emitted from the sample is then captured via an imaging or similar optical system. The light is passed via a spectrometer unto the detector. The response of the detector is recorded by system electronics, with each pixel recording the time of arrival of the first photon detected to an accuracy of the order of 100 picoseconds or less. Once the first photon arrives at any pixel, that pixel enters its recovery period ensuring that no later contaminant signal is observed and thus acts as an ideal shutter. This recovery period is used to extract or separate the Raman signal from the fluorescent response. This process is illustrated in Fig 1.

The detector is triggered to respond at or before the laser pulse is fired. Once the photons have been recorded those observed in the first timing sector represent those emitted within 100 ps of the laser pulse starting to illuminate the sample, and are separated and identified as Raman signals by means of their recorded arrival times. Photons recorded in subsequent times are identified as fluorescence signals or unwanted signals. Once the signal photons have been recorded and converted into an electrical signal within the detector, fast timing electronics are then used to time stamp the photons with an accuracy of better than 100 ps. The time signature of each photon is thus used to identify them as either Raman or fluorescent/other photons.

The spectrometer used for the measurement is a static Fourier transform device. , (Fig 2) [Harlander. J., R. J Reynolds and F. L. Roesler., " Spatial Heterodyne Spectrometer for the exploration of diffuse emission line a far ultraviolet wavelengths" *Astro Phys Journal* **396** (1992)]. In this arrangement all the photons from all the targeted wavelengths are able to be observed in all the pixels of the detector. Therefore all pixels can be used to determine properties of the light such as time of arrival. This property can used to improve the accuracy of timing of any measurement. The timing results may be averaged to improve the quality of the return. By averaging the timing of the response, accuracy of the system may be improved. Additionally, the Raman signal is spread over many pixels allowing detection of multiple simultaneous Raman photons compared with a conventional spectrometer where Raman photons are collected only by one or few pixels, and therefore quickly saturate the detector.

The trigger signal is suitably electrical in nature or may be photonic and may be generated by an external source or directly from the incident monochromatic light source.

In certain embodiments, a signal corresponding to a Raman signal response is output from the spectroscopic instrument.

In certain preferred embodiments, the spectroscopic instrument includes an analytic function to record and analyse both the Raman and fluorescent returns.

In a further embodiment of the invention, the detector is gated such that it activates for a fixed period of time to supress background light. The time is suitably greater than or equal to 10 ns, where the position of this gate is controlled by the trigger of the system, to coincide with the location of the target.

Figure 1 is a schematic view of the overall measurement functionality, where a laser pulse is shown in the left hand side of the image, which is followed by a “Raman” pulse from the sample. The detector records the photon and enters the recovery period (of 1 to 50ns). The final pulse is the fluorescent signal observed 200ps after the Raman pulse;

Figure 2 is a schematic view of an embodiment of a spectrometer of the present invention. The laser is incident on a sample that could be solid, liquid or gas in nature. The scattered/ emitted light is captured by the receiving lens and passed through a filter to remove the laser light. The light is then analysed in a spectrometer and focused onto the SPAD array;

Figure 3 is a schematic showing an embodiment of a static Fourier transform spectrometer of the present invention used to analyse the sample. The incoming light is separated by a beam splitter, where the two paths strike a dispersive element (e.g a reflective diffraction grating). These reflective signals then interfere forming a fringe pattern which is observed at the detector. A Fourier transform of the raw data is then applied to extract the spectral signal.
Figure 4 is a diagram of the timing electronics used on every pixel within the detector to time the incoming photons. The signal from the SPAD array is passed to the event timing circuit that consists of a pre amp, discriminator and time to digital converter.

Use of Raman systems has hitherto been limited due to the presence of unwanted fluorescent responses found in most organic targets. Separating the signals in time is the most accurate method of extracting the Raman signature from the fluorescent background. Currently these measurements are performed using either fast high voltage (HV) gated detectors or Kerr gate technology, both of which, are complex, leading to large, expensive bench-top systems.

We have demonstrated that this measurement can be performed using a Geiger mode single photon avalanche detector (SPAD), combined with a static Fourier transform spectrometer . The single element SPAD detects the first arriving photon and then enters a deadtime period that effectively disables further photon detection in that particular pixel, preventing pile up of signals. This property is in effect a perfect shutter and thus can be used to separate the Raman signal. This invention, while employing a detector similar to that discussed in US2013/0342835 [Jordana Blacksberg "Time resolved laser Raman spectroscopy using a single photon avalanche diode array"], uses an additional novel step whereby the timing of each photon is measured to an accuracy of 100 ps or less by means of fast electronics while the detector is gated on. Additionally, time gating as described in US2013/0342835 is used not for resolving short duration signals from longer duration signals but rather to provide additional information such as distance to the target etc.

Further, the target instrument combines a high etendue static Fourier transform spectrometer (SFTS) and a linear array of greater than 100 pixels Geiger mode SPAD detector and electronic readout capable of time to digital conversion to provide a timing accuracy of ca. 100 ps. In the SFTS every pixel observes every wavelength of light simultaneously, unlike a classic dispersive system. Therefore, instead of a single pixel measurement being used to determine the timing, every pixel can be used no matter the nature of the signal. This provides a far greater statistical base for the timing measurement and hence improve the overall system accuracy.

CLAIMS

1 A Raman spectroscopic instrument comprising a time-resolved Raman spectrometer comprising a static Fourier transform spectrometer and a single-photon avalanche diode (SPAD) array detector comprising a plurality of detector pixels; wherein the detector provides a response in the form of an electronic signal for every pixel, which signal comprises precise information on the arrival time of an initial photon and, after detection of an initial photon, every pixel enters a recovery period during which it is disabled from further detection.

2 A spectroscopic instrument as claimed in claim 1 wherein the detector recovery period is more than 1ns

3 A spectroscopic instrument as claimed in claim 1 or claim 2 wherein the detector is triggered to provide accurate timing of the returns; the signal is recorded by read-out electronics that time stamps the returned response; and the signal observed in the first timing period is then separated to extract the Raman response.

4 A spectroscopic instrument as claimed in any preceding claim wherein all the pixels are used to provide and average of the time measurement, exploiting the response of the static Fourier transform spectrometer.

5 A spectroscopic instrument as claimed in any preceding claim further comprising a trigger for the detector to respond at or before the short pulse source is activated.

6 A spectroscopic instrument as claimed in claim 5 wherein a trigger signal is an electrical or photonic signal.

7 A spectroscopic instrument as claimed in any preceding claim wherein the detector is gated for a predetermined period of time, to supress the detection of background and fluorescent light.

8 A spectroscopic instrument as claimed in claim 7 wherein the predetermined period of time is greater than or equal to 10ns.

9. A spectroscopic instrument as claimed in any preceding claim wherein every detection element has an independent electronics channel capable of event timing.

10. A spectroscopic instrument as claimed in claim 9, wherein the timing per electronics channel is better than 100 ps.

11. A spectroscopic instrument as claimed in any preceding claim wherein every timing electronics channel comprises a discriminator with threshold such that the discriminator logic contains event timing information to an accuracy of less than about 100ps.

12. A spectroscopic instrument as claimed in any preceding claim wherein every timing electronics channel performs time to digital conversion on the discriminator logic pulse to digitise the event time to better than 100 ps.

13. A spectroscopic instrument as claimed in any preceding claim, where the detector array has more than one detection element.

14. A spectroscopic instrument as claimed in any preceding claim wherein a single detector element is used to precisely measure the distance to the target, allowing the trigger signal to be positioned for the extraction of the Raman signal.

15 A spectroscopic instrument as claimed in any preceding claim wherein the spectroscopic instrument provides an output signal corresponding to a Raman signal response.

16 A spectroscopic instrument as claimed in any preceding claim further comprising an analysis function, preferably an analysis function adapted to record and analyse both Raman and fluorescent returns over a period of time.

17 A spectroscopic instrument as claimed in any preceding claim further comprising a short pulse monochromatic or near monochromatic source.

18 A spectroscopic instrument as claimed in claim 17 wherein the source is a laser source.

19 A spectroscopic instrument as claimed in claim 17 or claim 18 wherein the source is arranged to excite a target sample and the assembly is further provided with an imaging or similar optical system to capture broadband continuum light emitted from the sample and pass the light to the detector.

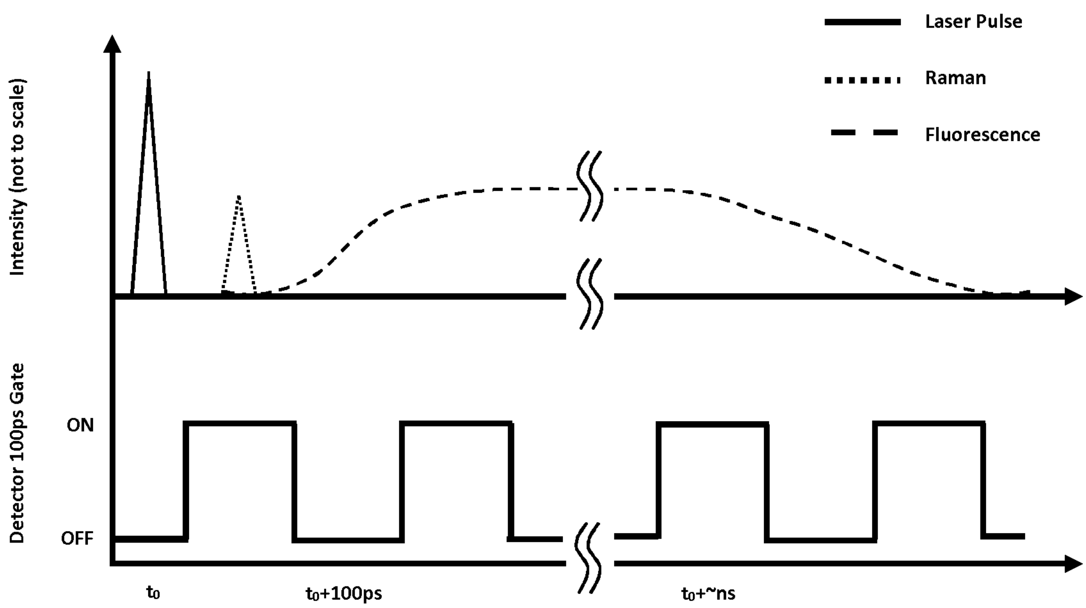

Fig 1 the measurement concept

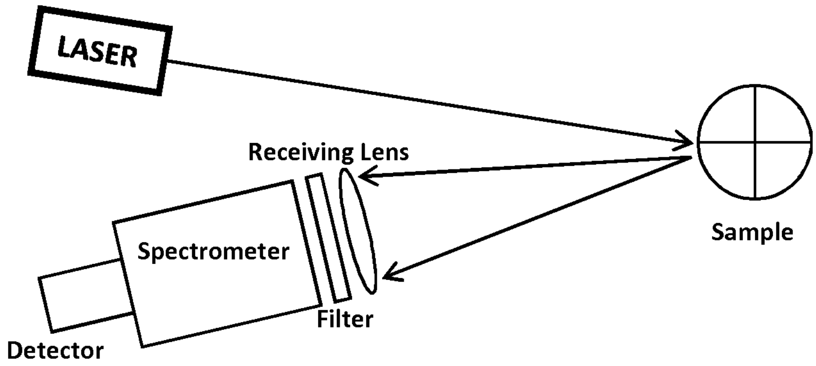

Fig 2 Schematic of the instrument

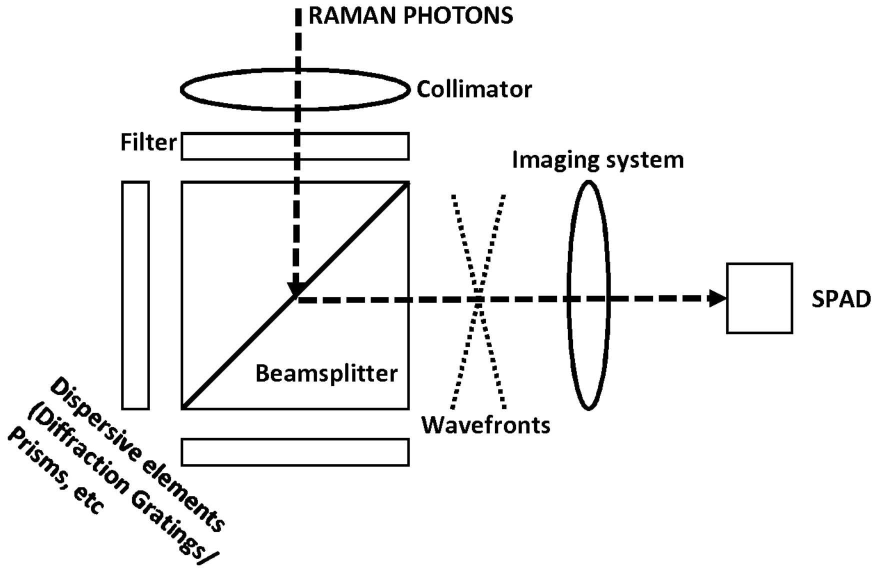

Figure 3 Schematic of a static Fourier transform spectrometer

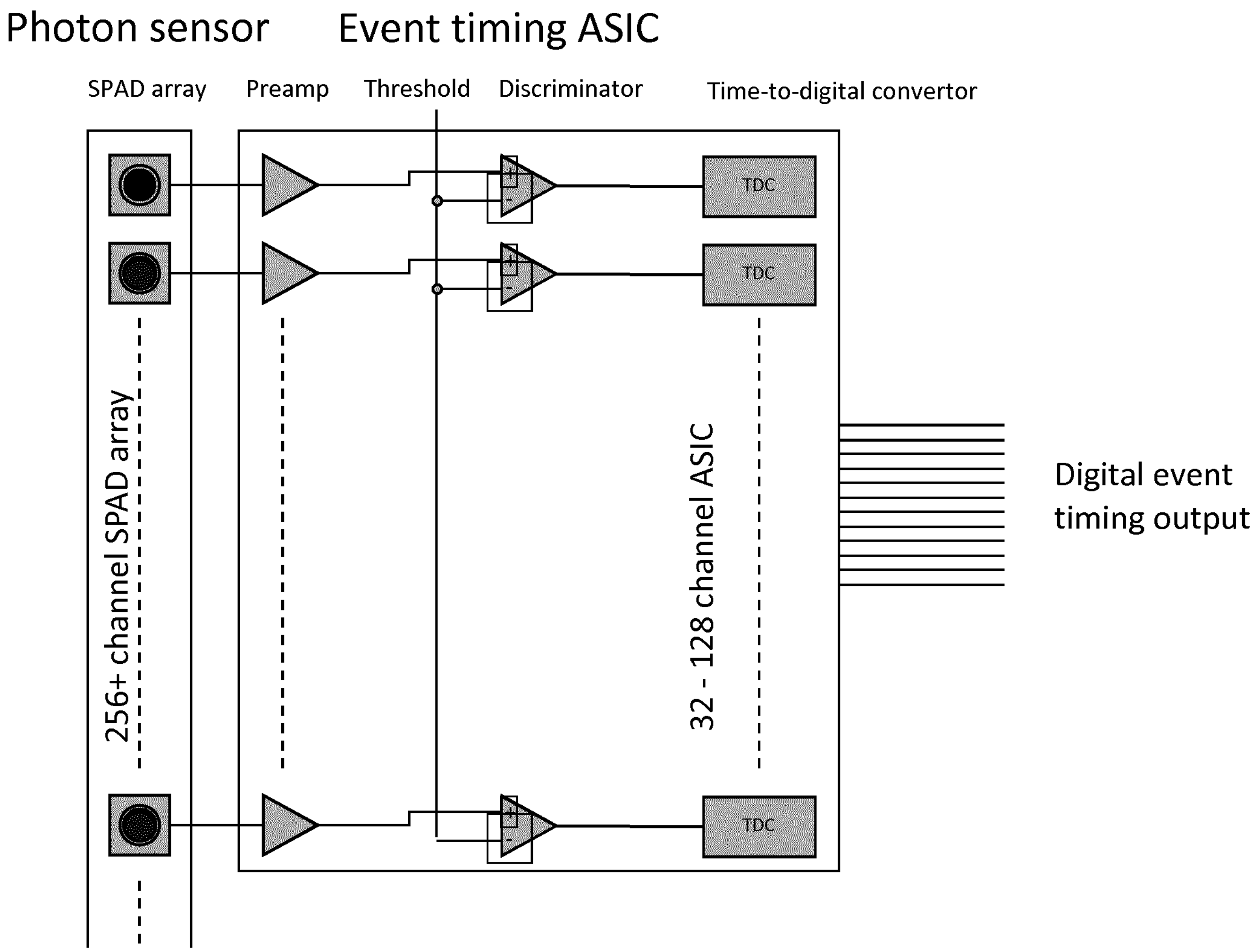

Figure 4 System timing electronics

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. G01J3/28 G01J3/44 G01J3/453
ADD. G01J1/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2013/342835 A1 (BLACKSBERG JORDANA [US]) 26 December 2013 (2013-12-26) paragraphs [0012], [0016], [0057], [0058] - [0062], [0077], [0080]; figures 1B, 1F -----	1-19
Y	WO 2014/018140 A2 (UNIV WAYNE STATE [US]) 30 January 2014 (2014-01-30) paragraphs [0033], [0034], [0037], [0043], [0049], [0051]; figure 3 -----	1-19
A	US 8 947 659 B1 (BAASTIANS GLENN [US] ET AL) 3 February 2015 (2015-02-03) claim 1 -----	12
Y	US 2015/285625 A1 (DEANE PETER [US]) 8 October 2015 (2015-10-08) claim 1 -----	14

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2017/067901

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2013342835 A1	26-12-2013	NONE	
WO 2014018140 A2	30-01-2014	US 2015085284 A1	26-03-2015
		WO 2014018140 A2	30-01-2014
US 8947659 B1	03-02-2015	NONE	
US 2015285625 A1	08-10-2015	CN 106165399 A	23-11-2016
		DE 112015001704 T5	29-12-2016
		JP 2017520134 A	20-07-2017
		KR 20160142839 A	13-12-2016
		US 2015285625 A1	08-10-2015
		WO 2015157341 A1	15-10-2015