Research of photon correlation technology

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Abstract: Photon correlation technology is an important technology in the field of nanoparticle measurement at present. This paper expounds the research significance of photon correlation technology, introduces the research background and basic concepts of this technology, and studies and analyzes the research status of the correlation algorithm of the new photon correlator. Finally, prospect and application development trend of this technology are analyzed, from the aspects of practicability, application environment and hardware conditions, the difficulties faced by the photon correlation technology are put forward. There are some difficulties when the photon correlator needs to meet the requirements of accuracy, small sampling interval and large dynamic range, this article presents some possible solutions.

1. Introduction

Fluorescence Correlation Spectroscopy (FCS), counts the photon pulse data of detected photoelectric signals and performs correlation operations to obtain the light intensity function, which is used to detect the concentration, size and interaction between molecules under specific experimental conditions [1, 2]. By calculating the time correlation of light fluctuation of scattered by particles, the size of nanoparticles in solution can be obtained by photon correlation spectroscopy, and various motions of polymer chain can be deduced. The concept of Fluorescence Correlation Spectroscopy was put forward in the 1970s, as an interdisciplinary discipline consisting of physics, material science, biochemistry and electronic informatics, it didn't get the actual application and research progress. In the 1990s, with the rapid development of computer technology, laser focusing technology and optical detection technology, fluorescence correlation technology was gradually applied in various fields [3]. With the increasing demand of fluorescence correlation measurement devices in various research and application departments, the processing speed, accuracy and dynamic range of photon correlator are required more and more. As an interdisciplinary subject, the technical progress in this field can promote the development of multiple fields, but it is also restricted by other fields, such as the accuracy of photoelectric data acquisition.

Photon correlators require specialized hardware to obtain and calculate the intensity correlation of rapidly changing input signals, so photon correlators are usually relatively expensive, and most of the correlator instruments are used at the laboratory level. It has great practical significance that the fluorescence correlation spectrometers with independent core technologies are used at the industrial or commercial level. This paper analyzes and summarizes the recent researches in the field of photon correlator, and puts forward the direction of improving the performance of photon correlator from the perspective of the implementation method of photon correlator.
2. Basic concepts of photon correlation technology

2.1 Measurement of nanoparticles size by photon correlation technique

After the subjects are labeled with fluorescence, the fluorescence particles in the sample solution are subjected to Brownian motion by collisions of surrounding particles. Concentration of particle can be determined by measuring Brownian motion-related diffusion coefficients. When the laser is irradiated into the solution containing nano-fluorescence particles, scattering light is generated. Scattered light is converted into TTL level signal by photoelectric detection system, and the signal is processed by amplification, reshaping, etc, and the number of photons in each cycle is obtained by the photon counter. The number of photons in the sampling time is used as the input of the photon correlator to obtain the correlation function, which is used to obtain the concentration of fluorescent labeled particles result to the upper computer.

2.2 Photon correlator experimental device

The laser excited labeled fluorescence particles, and the optical path system transmitted the fluorescence signal reflected by the fluorescence particles to the photoelectric detection device, Photon correlator finally carries out photon counting and correlation operation [4, 5]. After the front-end processing of the signal, the photoelectric signal becomes a pulse string in the form of level, and the pulse number within the sampling time is the function of light intensity. Photon correlator deals with the real-time correlation algorithm of light intensity function and saves the result in the host computer. The composition of the experimental device of photon correlator is shown in Fig.1.

![Fig.1 Diagram of experimental device of photon correlator](image)

2.3 Light intensity autocorrelation function

The scattered light intensity signal varying with time can be obtained through the time autocorrelation of the light intensity function, refer with: Eq.1,

\[ G(\tau) = \langle I(t)I(t + \tau) \rangle = \lim_{T \to \infty} \frac{1}{T} \int_0^T I(t)I(t + \tau)dt. \]  

In Eq.1, \( I(t) \) and \( I(t + \tau) \) represents the scattering light intensity signal at \( t \) and \( t + \tau \) moment, brackets \( <> \) represents the average operation, \( T \) represents the total experimental time. In the delay time is very small, \( I(t) \) and \( I(t + \tau) \) is almost equal, two signal correlation is very strong, the larger delay time \( \tau \) is, the weaker the correlation is.

Eq.1 is the autocorrelation function of light intensity in the continuous case. In fact, it is in discrete form, refer with: Eq.2,

\[ G(i\Delta t) = \frac{1}{M} \sum_{j=1}^{M} n(j)n(j + i). \]  

\( M \) is the total sampling times, the total experimental time is \( M\Delta t \), \( \Delta t \) is the single sampling time, \( n(j) \) is the number of photon pulses obtained by the photon correlating device during the j.th sampling time, and \( n(j + i) \) is the number of photon pulses during the \( j + i \).th sampling time. Eq.2 actually refers to the estimation of the light intensity autocorrelation function with \( i\Delta t \) in a finite time, and the experimental time and the sampling time will affect the estimation error of light intensity autocorrelation function.
3. Improved photon correlator

3.1 FPGA based hardware correlator

The photon correlator processes the counting value obtained from the photon counter, and separate the value according to the sampling period. The current sampling period is multiplied by the value of different delay sampling periods, and the results are added to finally complete the correlation operation [6]. The delay, multiplication, accumulation, and cache output of a particular delay signal consists of delay modules, multiplication modules, and accumulation modules, which are called a channel in the hardware implementation, and the photon correlator consists of these channels. The dynamic range of correlation calculation can be increased by increasing the number of correlator channels. As a high-speed integrated chip, the actual number of channels is limited by internal resources of FPGA, cannot blindly increase channels [7]. The delay unit is realized by the shift register. When the number of channels is fixed, increasing the sampling time can also increase the dynamic range of correlation calculation, but reduce the resolution of correlation function curve.

In 1985, Klaus Schatzel of Germany first proposed the multi-sampling time related technology [8]. The structure of photon correlator proposed by him can guarantee the resolution of correlation function curve and enlarge the dynamic range of correlator within a limited number of channels. Multi-delay photon correlation structure groups correlator channels according to sampling time. Each group of channels has the same sampling time, and different groups of channels have different sampling time. The whole correlator can be regarded as an organic connection of multiple linear correlation modules. In the structure of multi-sampling-time correlator, the time for sampling number of photons remains the same in the group, and the time for sampling number of photons doubles between groups. There are 16 linear channels in group 0, and 8 linear channels in the other group, as shown in Fig.2.

![Multi-sampling time correlator structure diagram](image)

3.2 Software correlator based on Labview

In 2003, Davide Magatti and Fabio Ferri developed a multi-sampling time correlator using software [13, 14]. The correlator consists of a standard photon counting unit, a fast timer (6602-pci) and a PC unit.
When the delay time is small, the input signal has a great impact on the result of correlation function, records accurate time data. When the delay time is large, the accurate information of data is abandoned to improve the operation speed. The measurement system combining the two methods can calculate the correlation function online. Software has natural advantages in data processing, and software correlator is more flexible [15]. Software can be used to reduce the cost effectively. Limited by the performance of computer and electronic equipment, software correlator lacks competitiveness in running speed. However, with the continuous development of electronic equipment field, software correlator also has great development potential.

4. Development difficulties and solutions of photon correlator

4.1 Combination of software and hardware to achieve a large dynamic range

In radio astronomy, materials science and other application fields, the dynamic range of correlator is required to reach at least $10^{12}$, and the experimental time can last more than 100 hours. In the implementation of photon correlator with large dynamic range, hardware correlator is expensive, and the number of channels and other parameters are fixed. The hardware resources cannot be extended indefinitely, and the delay time need to be quite large. The software correlator has slow operation speed, low precision and low performance. So far, the implementation of photon correlator is in a state of "hard or soft". Although some scholars have put forward similar Suggestions, there is no new low-cost photon correlator combining hardware and software.

Presented here based on multi-sampling-time correlation technology, combined with the advantage of software and hardware parts. When the sampling time is small, using the speed and performance advantage of the hardware implementation method to process the correlation function in real-time. When the sampling time is large enough to be minutes or seconds, some correlator channel calculation can be calculated by software, and can save cost of correlator, and improve the correlator flexibility. The hardware part of the photon correlator carries out real-time correlation operation and collection of photon counting signals. When the collection and calculation reach a certain time, the data will be transferred to the upper computer, and the hardware part itself will be cleared to start the next round of work again. The PC processes and stores each round of data it receives. In this way, high-density processing and operation are completed in the hardware part, and low-density processing and operation are completed in the upper computer software. However, there is a difficult control problem in the process of software and hardware interaction.

4.2 The development difficulty of software correlator

The photoelectric signal extraction of software correlator is different from that of hardware correlator. It needs to collect data to upper computer through a high-performance data acquisition card. There are errors in the optoelectronic pulse width from photomultiplier tube and the frequency of weak signal detection circuit, so there is an error in the photoelectric signal collected by the data acquisition card. Existing photomultiplier tubes have recovery time (or dead time), which affects the minimum sampling time of correlator. The minimum sampling time of existing correlators is generally 25ns, which requires a more sensitive photoelectric detection system to reduce the minimum sampling time. If the signal collected by the photon correlation system is the photon arrival signal, all the information collected by the photon signal can be retained, and part of the information will not be lost due to multiple pulses within two adjacent sampling times. How to improve the performance of the data acquisition system is a difficult problem.

5. Summary

Based on the development of photonic correlation technology in recent 20 years, this paper reviews the basic concept, implementation method and research status of this technology. Taking the new photon correlator as the research focus, this paper summarizes the key problems existing in the field of photon correlator technology from two aspects of hardware and software correlator, and puts forward possible
improvement of directions. The current development of photon correlation technologies requires more accurate and economical measurement methods to be commercialized or industrialized. It is hoped that this paper can provide some references and inspirations for researchers in the field of measuring instruments and photons.

References
[1] Liu Tiegen, Zhang Fan, Meng Zhuo. Research status and development of methods for detecting the size and distribution of nanoparticles [J]. Optical technology, 2005 (01):96-100.
[2] Saffarian S, Elson E L. Statistical analysis of fluorescence correlation spectroscopy: The standard deviation and bias [J]. Biophysical Journal, 2003, 84(3):2030-2042.
[3] Elson E L. Fluorescence Correlation Spectroscopy: Past, Present, Future [J]. Biophysical Journal, 2011, 101(12):2855-2870.
[4] Liu W, Shen J, Sun X. Design of Multiple-Tau Photon Correlation System Implemented by FPGA[C]/ International Conference on Embedded Software & Systems. IEEE, 2008.
[5] Lee H Y, Lin H Y, White J D, et al. High-speed low-cost correlator for single molecule fluorescence correlation spectroscopy[J]. Proceedings of SPIE - The International Society for Optical Engineering, 2009, 7185:71850R-71850R-8.
[6] Mocsár, Gábor, Kreith, Balázs, Buchholz J, et al. Multiplexed multiple-\tau auto- and cross-correlators on a single FPGA [J]. Eprint Arxiv, 2011.
[7] Chen Haibin. Design of hardware system of fluorescence related spectrum analyzer [D]. Shanghai jiaotong university, 2013.
[8] Klaus Schäzel, Martin Drewel, Sven Stimac. Photon correlation measurement at large lag times: improving statistical accuracy [J], Journal of Modern Optics, 1998, 35(4): 711-718.
[9] Cheng y t. research on multi-channel time-delay photon correlator [D]. Shandong university of technology, 2009.
[10] Cheng yanting, shen jin, liu wei, sun xianming, Yang yan. Normalization method of autocorrelation function in multi-tau photon correlator [J]. China laser, 2009,36(02):444-448.
[11] Cheng yanting, shen jin, liu wei, et al. A method and implementation of dynamic range adaptive adjustment of photon correlator [J]. China laser, 2008, 35(s2).
[12] Wang lipeng. Research on dynamic light scattering nanometer particle size measurement method based on FPGA [D]. Qilu university of technology, 2014.
[13] Davide Magatti and Fabio Ferri, Fast multi-tau real-time software correlator for dynamic light scattering[J], Optical Society of America, 2011
[14] Magatti D, Ferri F. 25 ns software correlator for photon and fluorescence correlation spectroscopy [J]. Review of Scientific Instruments, 2003, 74(2):1135.
[15] Schaub, Emmanuel. High countrate real-time FCS using F2Cor [J]. Optics Express, 2013, 21(20):23543.