Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Single-photon Counting: System Design, Characterization and Application to DNA-sequencing

By

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The objective of the proposed research is to design and characterize single photon counting systems (SPCSs) for detecting ultra-weak fluorescent signals in various biomedical applications, our application being DNA-sequencing. This thesis investigates the feasibility of designing cost-effective, SPCSs to perform fast, high performance DNA-sequencing at low cost.

This thesis presents design, development and characterization of unique single-channel and multi-channel (16 and 32 channel) SPCSs based on a large-area single photon avalanche diode (SPAD) having 0.5mm diameter (model C30902S-DTC from Perkin Elmer Optoelectronics (PKI)). A novel logic circuit for generating precise quench and reset delays in the quenching circuit is presented. Further, the developed SPCSs are integrated into DNA-sequencing instruments. Excellent DNA sequencing results, demonstrating single fluorescent molecule sensitivity are presented. Thus, for the first time, experimental evidence of the application of large area SPAD for highly sensitive detection of DNA-sequences is demonstrated.

Recently, low-cost, solid-state replacement for PMT called Silicon Photomultiplier (SiPM) has become available. Being an analog detector (output signal proportional to number of input photons) that is insensitive to magnetic fields, it is mostly used in applications in fields such as nuclear physics, nuclear medicine, where the incoming photons usually arrive simultaneously in few numbers. That is, SiPMs are used for photon number resolving, unlike SPADs that are used for counting photons. Another aspect of this thesis is to investigate the feasibility of SiPM as detectors for high-speed photon counting applications such as DNA-sequencing. This work shows that, under certain conditions, high sensitivity, acceptable DCR and high-speed photon counting is possible. This work then provides, for the first time, experimental evidence of excellent DNA sequencing results with SiPM, opening up a new application area for the device. This work proves that SiPM can replace SPAD for high-performance DNA sequencing, potentially decreasing the cost of photon detection by approximately 10 fold, resulting in significant cost-reduction in DNA-sequencing, especially for multi-channel systems.

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