BIOPHOTONICS

APPLICATION NOTE

sensL
SENSE LIGHT

BENEFITS OF USING AN SPM

DETECTOR SIZE AND GEOMETRY

The ability to vary Silicon Photomultiplier detector size from ~25 mm2 down to <0.01 mm2 and optimize the sensitive area geometry to specific requirements while maintaining highly uniform optical response over the entire sensor area.

HIGH SIGNAL GAIN AND SHORT RESPONSE TIMES

Allow fluorescence based bioimaging to be performed with shorter exposure times and reduced illumination intensities. This enables faster image acquisition, hence reducing the risk of photobleaching.

PEAK SPECTRAL SENSITIVITY

Reaches well over 20% photon detection efficiency and can be optimized for the emission wavelengths of most fluorophores in the visible and near infrared domain.

EASY OPERATION

High signal gain and low operating voltage simplifies both detector operation and signal readout.

BIOPHOTONICS APPLICATIONS

FLOW CYTOMETRY

Techniques used to count and size biological systems such as cells and biopolymers by suspending them in a stream of fluid and passing them through an electro-optical detection apparatus

BIOIMAGING SYSTEMS

A broad range of rapidly evolving techniques and systems that use optical methods to obtain in vivo, in vitro or ex vivo optical images of biosystems

FLUORESCENCE ANALYSIS & IMAGING

Enhanced bioimaging systems that can visualize targeted biosystems and provide time resolved analysis of biological processes

SPECTROSCOPY

An enabling technique for many bioimaging systems providing the means to target select fluorophores (fluorescence based imaging) and energy discriminated bioprocesses in both spatial and time resolved modes

Market Overview

Thanks to the rapid evolution of signal processing and light source technologies, the field of biophotonic imaging has enjoyed spectacular advancements over the last 15 years. A diverse range of imaging techniques is now solidly established in both the laboratory and specialized diagnostics spaces. Yet, the enabling instrumentation remains bulky, complex, costly and difficult to operate. The trend now is to simplify and miniaturize these systems and to combine complementary imaging modalities into single instruments.

The drive towards smaller and more highly integrated systems hinges on progress in four key areas: photodetection, light sources, sample handling, optics and filters. Tight integration and miniaturization of these elements will lift advanced bioimaging out of the specialized research environment into clinical and point-of-care settings.

The silicon photomultiplier or SPM addresses the challenge of integrating single photon detection and timing capabilities both at desktop and MEMS scale instrumentation.

Phototodetectors In Biophotonic Imaging

The majority of biophotonic imaging systems relying on low light detection such as Confocal Microscopy, OCT, TIRF and FLIM employ the venerable photomultiplier tube (PMT). Both the technical and operational benefits of replacing this technology with a semiconductor detector such as the SPM are evident.

Yet, compared to PMT, semiconductor detectors exhibit one perceived disadvantage: they produce higher levels of noise or dark counts. This fact tends to discourage systems developers who are accustomed of working with PMT.

In most biophotonic applications this dark count problem can be overcome by exploiting two key features of the SPM:

1. The SPM dark count rate is proportional to its sensitive area.
2. SPM dark count rates can be substantially reduced through cooling of the detector.

Adapting the light path to concentrate photons on a small spot is, in most cases, straight forward and may even serve to simplify the system layout. Thermo-electrically cooling the SPM is a well established technique and, due to the small mass of an SPM, can be achieved with low power and low heat dissipation.

Furthermore, SPM dark counts have highly uniform pulse heights. When SPM signals can be time integrated (e.g. FLIM), gated (e.g. Confocal Microscopy) or threshold discriminated (e.g. Flow Cytometry) dark count contributions can be mitigated through appropriate baseline subtraction or statistical treatments.

Application Examples

SensL silicon photomultipliers have been successfully used in a range of advanced biophotonic detector systems – notably:

A bioMEMS, microfluidic two stage flow cytometer / cell sorter. A fiber optical cable is used to carry the light to an uncooled 9 mm2 active area SPM. The SPM signals are Sigma-Delta modulated and the system is capable of discriminating down to 100 FITC molecules at acquisition rates of 500Hz. This example clearly demonstrates that dark count effects can be mitigated through appropriate statistical methods.

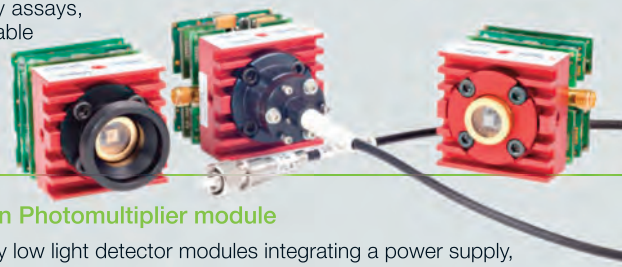
A shoe box sized PCR system combined with stimulated fluorescence detection allows for the simultaneous analysis of eight samples distributed in a glass capillary. Uncooled 1 mm2 SPMs are placed behind a low pass filter in close proximity to the capillary and read out using low cost transimpedance amplifiers.

Silicon Photomultiplier Benefits

All biophotonic imaging modalities where light is highly focused or collected in an optical fiber are intrinsically compatible with silicon photomultipliers. SPM geometry and size can be tailored to the source. In bioMEMS applications, SPM can be integrated directly on the device or easily placed in close proximity.

Being a solid state detector, filters can be efficiently integrated on the detector package or directly on the silicon die. The ability to optimize spectral sensitivity, in particular in the green through near IR region, sets SPM apart from PMT.

SPM are manufactured in a CMOS process offering highly attractive economies of scale. For clinical and point-of-care applications as well as high density assays, SPM can be integrated into disposable units creating design opportunities not feasible with alternative photodetectors.



SensL Mini – Integrated Silicon Photomultiplier module

The SensL Mini is a family of turnkey low light detector modules integrating a power supply, transimpedance amplifier and a 1 mm2 or 9 mm2 silicon photomultiplier mounted on a two stage photoelectric cooling element. Spectral response spanning the visible and near IR range covers the bulk of biophotonic applications. An optional range of light coupling solutions facilitate integration and assure optimal light collection.

Bringing fluorescence analysis to the desktop of every doctor:
A hand held and battery driven fluorescence analyzer stimulating blood samples with 340 nm ultraviolet light. Delayed fluorescence in the red spectral region is analyzed through integration of SPM signals over a 400 µsec time period. The analysis is repeated at a 1 kHz rate providing for high statistics and analytical power.

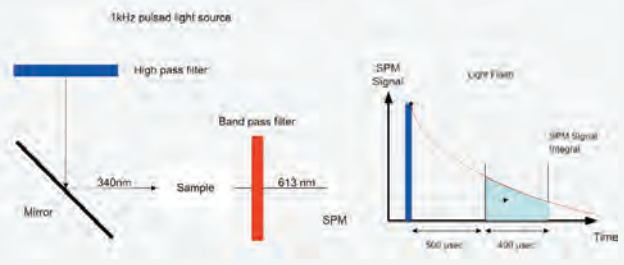


FIGURE 1: (Schematic and signal readout for a handheld fluorescence analyzer)