

Keywords

- Real Time Polymerase Chain Reaction (qPCR)
- Point-of-Care (POC) diagnostics

Techniques

- Multispectral sensing

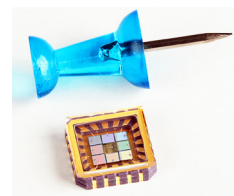
Applications

- qPCR
- Real-time PCR
- POC diagnostics

Breakthrough Sensor for PCR at Point-of-Care

Abstract

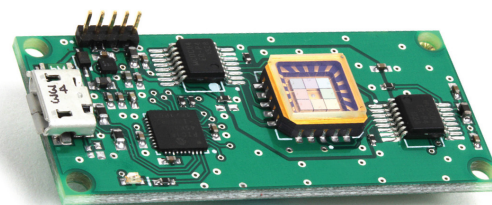
As point-of-care (POC) molecular diagnostics transforms medicine by bringing sophisticated diagnostic testing to the patient, the need for compact optical and detection technologies is increasing. Highly integrated multispectral sensors fill this niche well, reducing the complexity, footprint and cost of OEM instrumentation significantly. In contrast to the full spectrum acquired by a spectrometer, a multispectral sensor collects data only at the wavelength bands of most interest to the application. By integrating filtering and detection into monolithic elements in an array of up to 8 channels, the breakthrough PixelSensor™ multispectral sensor from PIXELTEQ provides even greater multispectral detection efficiency in a package the size of a fingernail.



PixelSensor™ PCR Detector

Getting Point-of-Care Instruments in Hand

Once considered a research tool, advanced molecular diagnostics now allow the medical community to draw on a much wider range of available assays for routine use in patient care, from infectious disease diagnosis to genetic testing. While analysis is often performed at dedicated hospital or off-site laboratories due to the cost and size of the instrumentation, the desire for faster diagnoses has sparked a trend toward decentralized diagnostic testing at the point-of-care (POC) or near the patient. When care or triage is needed immediately or when access to the patient is limited due to lack of, or distance from medical facilities, POC diagnostics provide rapid testing results and lead to both better patient engagement and decreased risk of lost patient follow-up appointments.

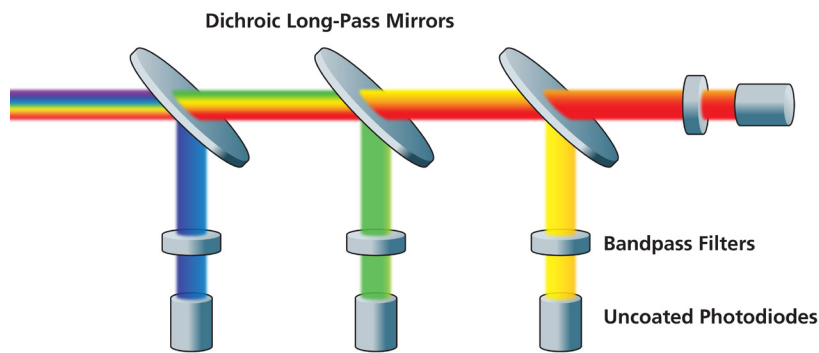


Simple Electronics for Seamless Device Integration

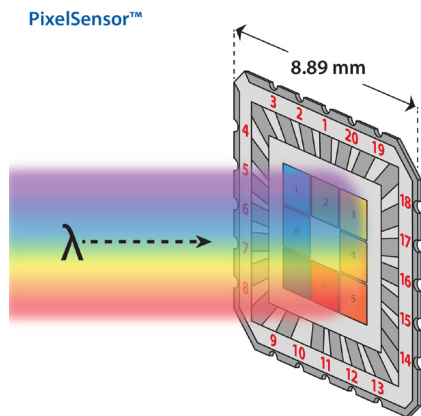
To be an effective alternative for and supplement to laboratory testing, POC instruments need to be smaller, less costly, faster and more robust than their larger counterparts, without sacrificing accuracy or the flexibility to detect the multiple fluorophores used in different assay test kits. This is accomplished by combining micro-fluidics, micro-optics, and advanced detection reaction chemistries to create smaller, portable or handheld instruments capable of delivering quick results at the patient bedside or in the field.

With space at a premium, multispectral sensors offer significant

advantages over the traditional optical filter train, simultaneously sensing light from multiple wavelength bands in a compact footprint and reducing cost. Each sensor element directly filters and detects a specific band of wavelengths, eliminating the need for wavelength separation using discrete bandpass and dichroic filters and the space required for this type of optical layout. By mixing and matching sensor elements, multiple bands of interest can be combined to analyze a given assay. The PixelSensor takes this concept one step further, coating the bandpass filter directly onto the surface of each photodiode to create a more optically efficient and robust sensor.



Traditional Optical Filter Train



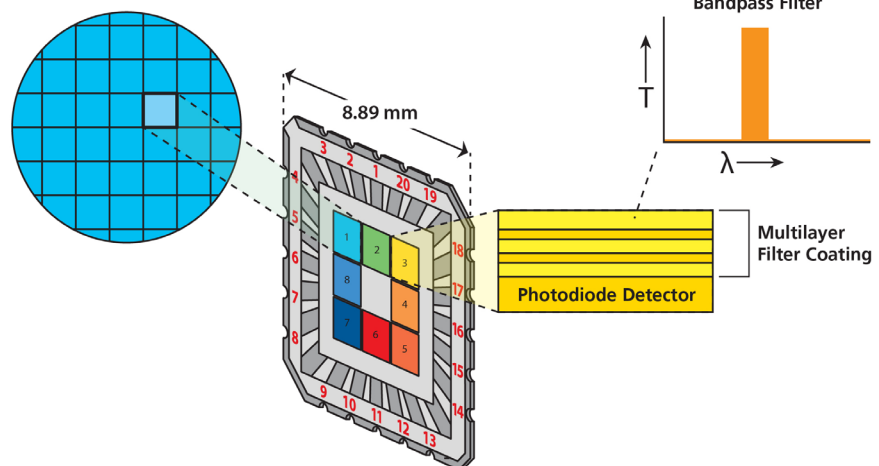
PixelSensor™ Simultaneous Wavelength Sensing

Light from the PixelSensor™ Perspective

While most multiple-wavelength sensors assemble a discrete filter with a photodiode to create a single channel, the unique on-chip coating technology at the heart of PixelSensor reduces losses attributed to multiple optical surfaces and maximizes the alignment, optical efficiency, and reliability benefits offered by multispectral sensing. Patented micro-patterned optical filters are directly deposited at the wafer level onto the surface of active photodiodes, which are then diced and recombined in a two-dimensional array. The specific photodiodes are chosen to detect the spectral bands corresponding to a specific diagnostic test or assay chemistry. Up to 8 detector elements (channels) may be accommodated in the 9 x 9 mm LCC package. Each channel may be customized to filter a desired set of VIS-NIR wavelengths, with additional out of band blocking for ambient light.

Designed for low noise and fast response time, the 20-pin LCC package can be surface- or socket-mounted, providing a single component from a single vendor for streamlined sourcing and assembly.

Micro-Patterned Photodiode Wafer



Anatomy of a PixelSensor™

An evaluation kit, including an electronics board, software, and sampling optics is available for proof of concept testing and prototyping. Also, the reference design of the electronics board is available to help reduce time to market. ⁱⁱ



PixelSensor™ Evaluation Housing and Accessories



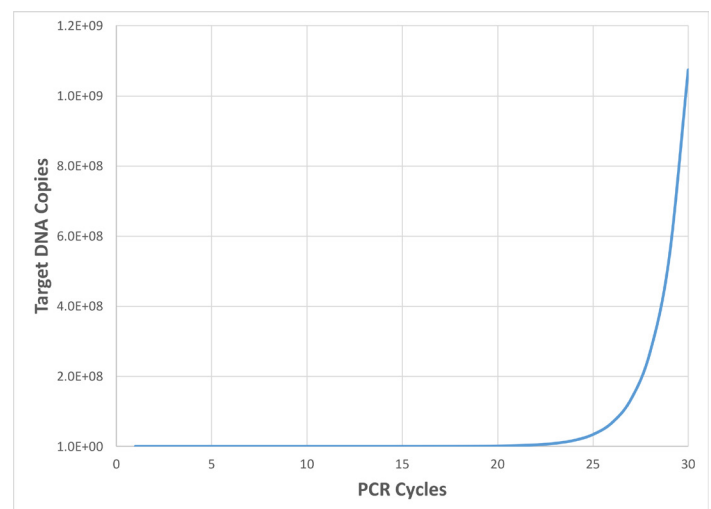
PixelSensor™ Software

Downsizing Molecular Diagnostics – Handheld PCR Hits the Big Time

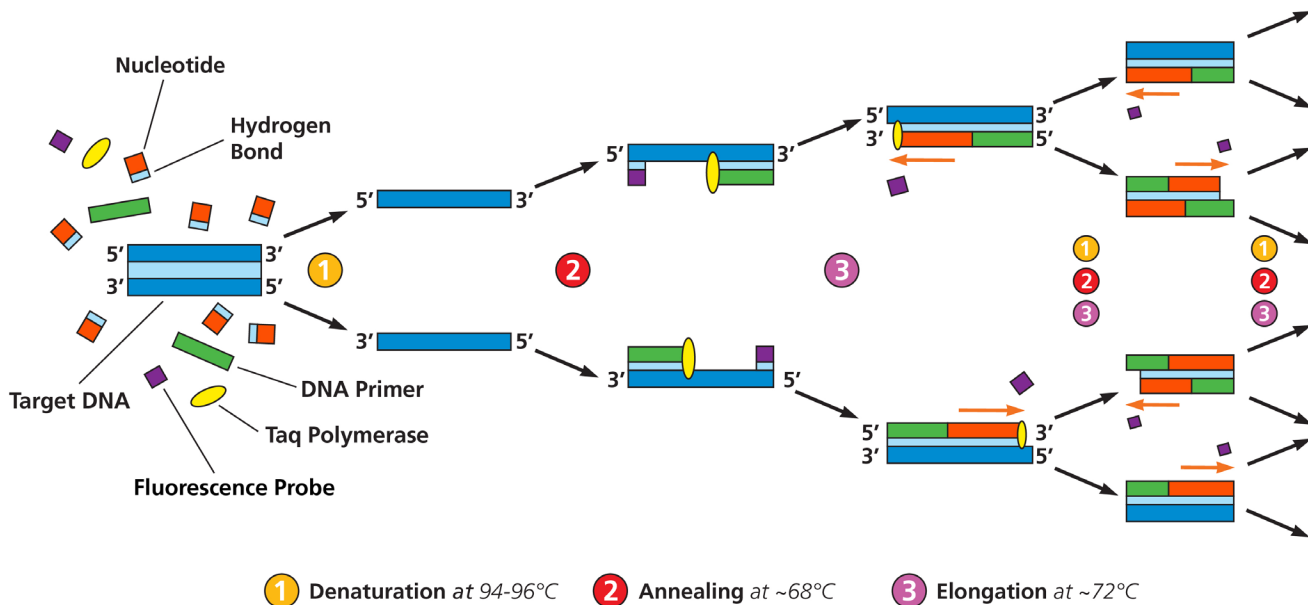
Polymerase chain reaction (PCR) is a prime example of a POC application beginning to benefit from multispectral sensing. In PCR, a DNA fragment of interest within a sample is copied millions of times, providing enough signal amplification to detect the markers for a disease or a virus using a very small amount of blood or tissue.

PCR is a highly specific, accurate and fast DNA amplification technique, often referred to as DNA “photocopying.” Invented in 1985 by Kary Mullis at the Cetus Corporation, PCR was awarded the 1993 Nobel Prize in Chemistry ⁱⁱⁱ, and has proved vital to developing the field of genomic sequencing ^{iv}. Each thermal cycle in the PCR process doubles the amount of DNA through three steps: denaturation of target DNA strands, annealing of primer molecules to the denatured DNA, and elongation of the target strands via a polymerase enzyme reaction. Repeated many times, the process produces exponential amplification of the target DNA sequence.

The advent of real-time or quantitative PCR (qPCR) ^v in the 1990s has further enabled the growth of molecular diagnostics by automating the detection of DNA concurrently with amplification in the same instrument. Rather than performing electrophoresis at the end of the amplification process, qPCR integrates fluorescent tags specific to the desired DNA sequence before thermal cycling begins. The amplification reaction can then be monitored in real time, with the fluorescence signal proportional to the quantity of target DNA. The more target DNA is present initially, the faster amplification will occur, allowing qPCR to detect not only the presence of a desired DNA sequence, but also its initial concentration within a sample. This can be valuable in assessing the viral or microorganism load in a patient’s body, allowing physicians to gauge efficacy of treatment and deliver personalized medicine in addition to basic diagnostics.



PCR Amplification of DNA



Real-Time Polymerase Chain Reaction (qPCR)

Parallel advances in microfluidics, test chemistry and instrument design have allowed OEMs to move toward the development of smaller, portable qPCR instruments for POC molecular diagnostics with vastly decreased cycle times – delivering results in minutes rather than hours. As engineers continue to shrink instrument footprints and simplify optical designs, they seek compact alternatives to filter-based optical trains with comparable accuracy. They also need the specificity to detect multiple fluorophores independently, as used in the multiplexed assays emerging with improvements in probe and primer chemistry. By incorporating multiple fluorophores, each tagged to a specific DNA sequence and with their own key detection wavelengths, multiplexed assays enable simultaneous detection and diagnosis of multiple infectious disease and pathogen targets.

The high degree of flexibility offered by PixelSensor in customizing multiple independent channels in a mix-and-match format offers optical engineers forward compatibility with a wide range of current and future assays in a single, compact, cost-effective package. From basic 2- or 4-color handheld systems to more sophisticated yet compact tabletop instruments with up to 8 channels for multiplexed assays, PixelSensor is a scalable platform for optical detection in qPCR.

Small Answers with Big Impact

Compact and handheld PCR instruments will soon open up a whole new world for physicians – one in which sophisticated molecular diagnostics can be performed in the office, at a home-care visit, or within mobile clinics in remote areas with no access to traditional labs. Not only will this result in faster diagnosis and treatment, but it will also increase use of molecular diagnostics to assess treatment effectiveness and improve patient outcomes.

As portable diagnostics continues to develop and expand, it needs scalable technologies that can adapt with it to deliver accurate answers to more assays in a smaller footprint. PixelSensor is one such enabling technology – a multispectral sensor with up to 8 custom-designed detection channels in a compact, robust package. It allows the optical designer ultimate flexibility in spectral detection, from choice of optical filter bands to number of channels, package type, and electronics.

About PIXELTEQ

PIXELTEQ provides OEM spectral sensing and imaging solutions, patterned optical filters, and custom electro-optical devices for a variety of aerospace, biomedical, industrial, scientific, and security applications. At the heart of each multispectral device is an array of pixel-level spectral filters purpose-built for your application. Leveraging comprehensive expertise in thin film coating and micro-patterning, PIXELTEQ specialists collaborate to provide expert design assistance and custom-engineered solutions — from rapid prototyping through high-volume OEM production.

References

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- iv. <https://molecular.roche.com/innovation/pcr/history/>
- v. <http://www.news-medical.net/life-sciences/Real-Time-PCR-An-Overview-.aspx>

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