Technical Article

How Integrated Optical Receivers Future-Proof Point-of-Care Instruments

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Introduction

In vitro diagnostic (IVD) systems rely on optical receiver techniques to achieve highly sensitive and specific results. Established techniques such as ELISA and PCR utilize a fluorescence optical receive chain to perform diagnostic tests. It is no surprise, therefore, that the point-of-care (PoC) market has also adopted optical receivers as a powerful tool in creating a system that is accurate, flexible, and achieves a fast time to result. This article provides details on key considerations when designing an optical PoC receive chain and how integrated optical front ends can not only meet these performance demands but also provide a key advantage to those striving to create a platform for the future.

Fundamentals of Fluorescence Detection in Diagnostics

In a fluorescence-based IVD test, a sample containing fluorescent labels is excited with the light of a specific wavelength as shown by the green arrow in Figure 1. If the sample contains the analyte of interest, the fluorescent labels react to the excitation by emitting a light of a lower energy level. For example, in Figure 1, the fluorescent labels in the sample react by emitting red light. This emitted light is the fluorescence signal that needs to be detected to determine the presence, and possibly the amount, of analyte in the sample.

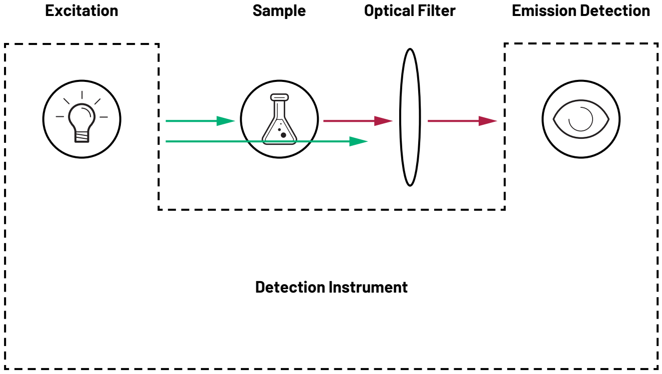

Figure 1. An IVD fluorescence detection system.

A fluorescence-based diagnostic test will have a threshold of what is considered reportable fluorescence. A fluorescence signal below the threshold level cannot confidently indicate the presence of the analyte in the sample. The electronics in the diagnostic detection instrument, along with other factors, contribute to the background noise, which forces the threshold higher. To reduce the threshold level and consequently achieve better sensitivity without sacrificing selectivity, a careful design of the optical detection system is needed to ensure that the electronic receive chain does not contribute to the background noise level.

A Typical PoC Fluorescence Detection System

A typical PoC diagnostic fluorescence detection system employs a light emitting diode (LED) to generate the excitation light and employs a photodiode (PD) to detect the fluorescence emission from the sample. The PD generates an electrical current that is proportional to the intensity of the fluorescence signal, which can be extremely weak. The PD current is often very small relative to the noise floor, necessitating careful electronic design for achieving high sensitivity detection without sacrificing selectivity. Figure 2 shows the main elements of a typical PoC fluorescence detection system. The current signal from the PD is converted to a voltage signal by the trans-impedance amplifier (TIA). The voltage signal is digitized by the analog-to-digital converter (ADC) and translated into a corresponding level of fluorescence.

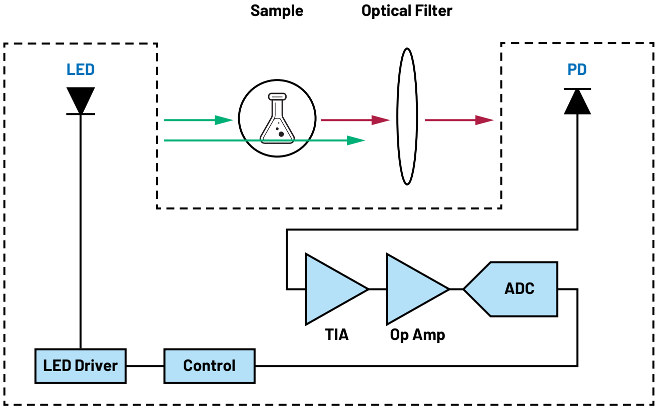

Figure 2. A typical PoC diagnostic fluorescence detection system.

The Performance Needs of a Fluorescence Detection PoC System

Designers of PoC systems strive to achieve maximum diagnostic sensitivity without sacrificing selectivity. In regard to PoC instruments, this goal translates into the requirement of reliably discerning very low PD current in response to LED excitation. For example, a high sensitivity system must be able to detect PD currents on the order of picoamperes in response to LED excitation currents on the order of 100 mA. That is, the system must be able to detect PD fluorescence given approximately 140 dB of optical attenuation.

To achieve such performance, a combination of electronic and system design considerations is necessary. The design of the analog front end (AFE) for the PD is particularly important. As the PD current is often very weak relative to the noise floor, the TIA needs to have a high gain and low input bias current. Additional important parameters are low TIA input offset voltage as well as a minimum distance between the PD and TIA.

The system design is also very important for achieving high sensitivity detection. Fluorescence detection must be synchronized with the LED excitation, hence the need for a controller that ensures this synchronicity. Averaging of multiple fluorescence readings is often needed for discerning the weak PD current signal from the noise floor. This averaging technique is an important function of the system controller. Ambient light and drift in LED lighting can contribute to a system error. A controller that allows the rejection of ambient light and that accounts for the impact of drift in LED lighting can enable an overall system performance advantage.

The Benefits of an Integrated Optical Front-End Receiver

When designing the electronic receiver chain for a PoC reader, there are two distinct architecture choices: a fully discrete solution as shown in Figure 2 or the use of an integrated optical front end, as shown in Figure 3.

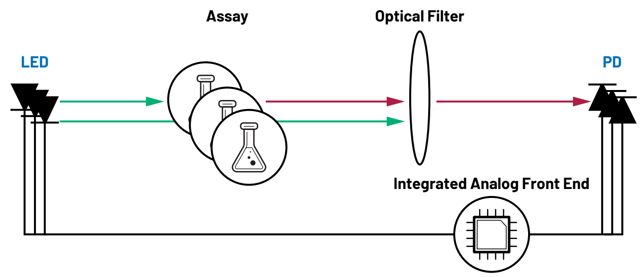

Figure 3. A PoC detection system using an integrated optical front end.

The first clear benefit of an integrated solution is the simplification in system design that it provides. The challenge of synchronizing the fluorescence detection with the LED excitation is removed as this is handled internally by the optical front end. Integrated optical front ends also provide a more compact solution with fewer electronic components. This reduces BOM and supply management complexity while enabling a smaller end device. The most critical benefit of an integrated optical front end is, however, the ability to adjust key configuration parameters, such as photodiode, LED driver, and signal filtering configuration, via firmware. Programmability is not available with a discrete solution without

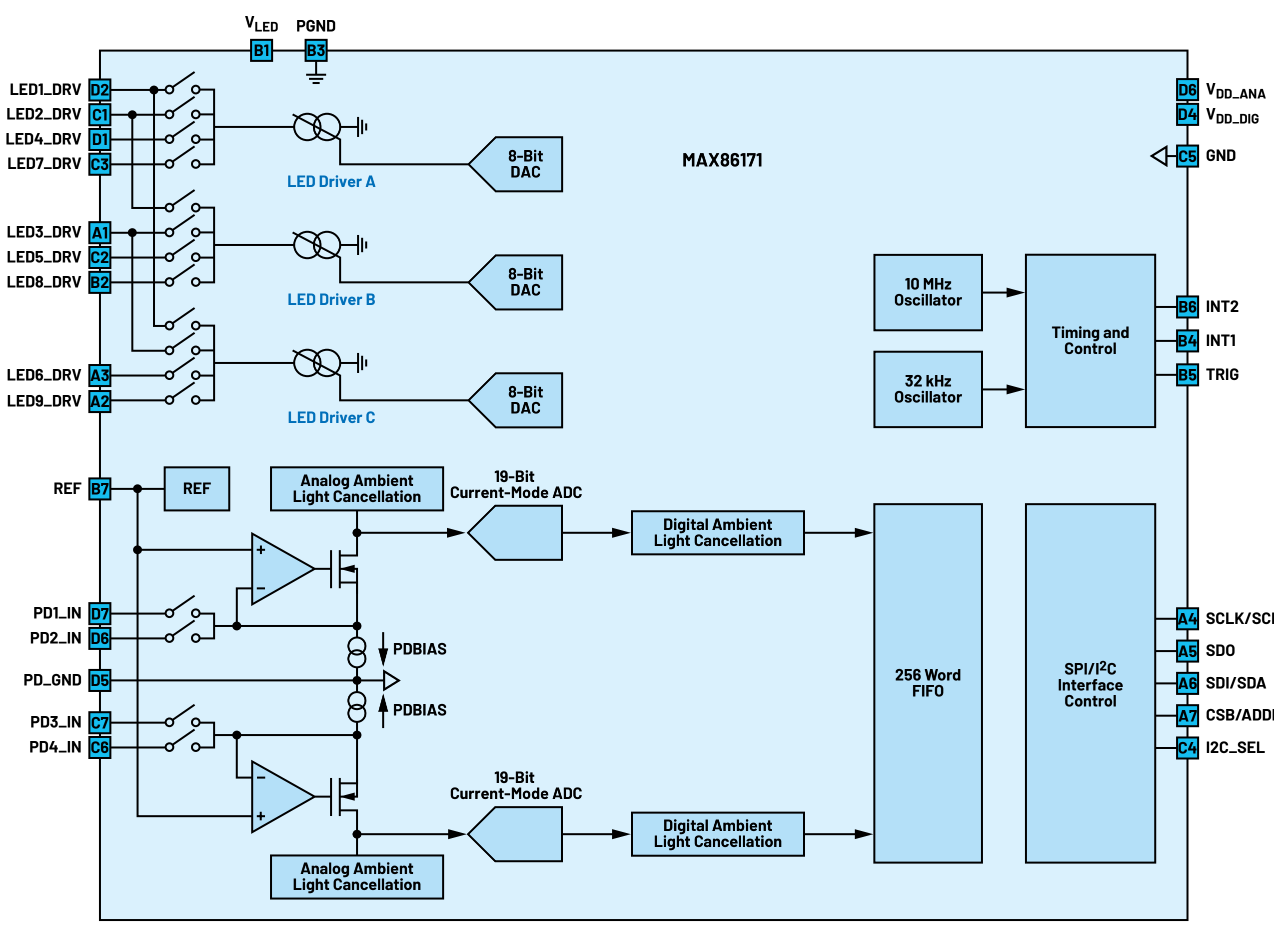

Figure 4. A block diagram of the MAX86171.

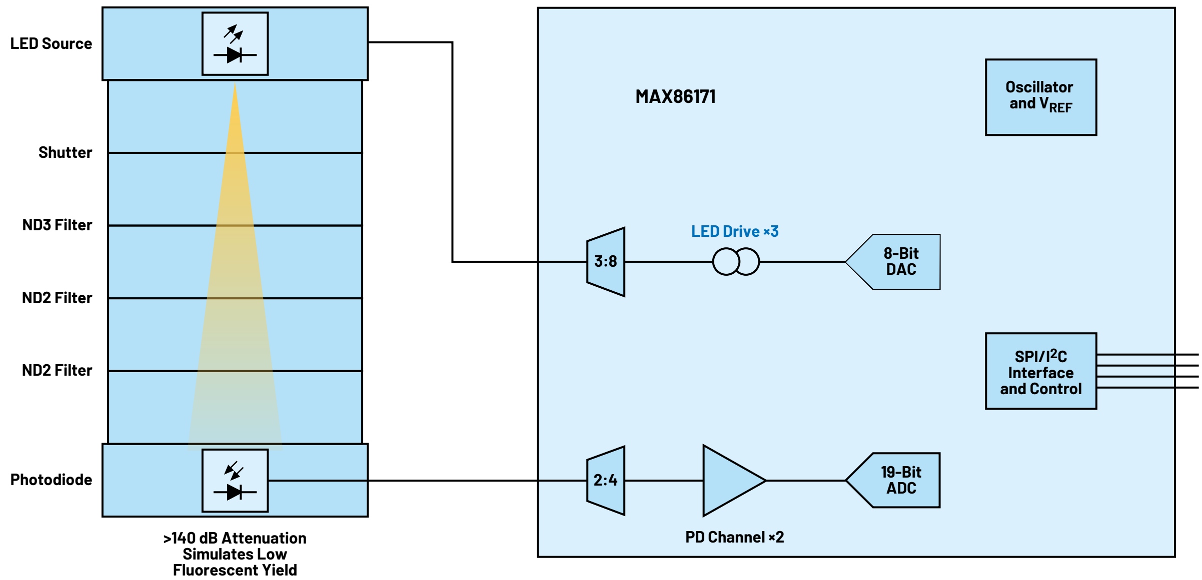

Figure 5. A low light detector measurement with the MAX86171.

new hardware being developed. This type of configurability is critical when trying to adapt a platform over time to operate with new or modified assays. As new variants and diseases are frequently added to testing menus, creating a receiver platform that can be modified to accommodate new assays, without the need for hardware modifications, is highly advantageous.

Integrated optical front ends have clear advantages, however, determining the performance of an optical front end in low light fluorescent applications is not a trivial task. Comparing signal-to-noise ratio (SNR) figures between integrated optical front ends does not give a true sense of the real-life performance of an optical receiver. As the levels of light are typically low, the absolute noise floor of the optical front ends is the critical parameter, rather than the SNR. With the timescale associated with fluorescent measurements, averaging can be employed to reduce this noise floor, though the 1/f noise component places a practical limit on what improvements can be achieved through averaging. Therefore, absolute dark current noise, particularly flicker noise, is the dominant factor. The dark current noise of a full system including PD is not characterized in the data sheet of many integrated optical AFEs and must be measured separately.

Integrated Front Ends from Analog Devices

ADI's integrated optical front ends such as the MAX86171 are ideally suited for PoC fluorescence applications. The integration of the analog signal chain alongside the digital controller enables a single IC solution for implementing an optical receiver. The MAX86171 contains signal-conditioned photodiode inputs, a 19-bit charge integrating ADC, low noise LED drivers, and a FIFO-buffered serial interface.

With nine LED channels and four PD channels, the AFE supports multiassay testing and adequate channels for future testing expansion without hardware upgrades. Programming over SPI or I^{2}C allows the fine tuning of parameters to a given assay, such as integration time, averaging, and dynamic range. A FIFO enables MCUs to remain in sleep mode while measurements are taken, extending battery life in handheld PoC systems.

Most importantly, the high performance and low noise nature of the device enable a high sensitivity detection system. Averaging and low 1/f noise allow a dark current noise of just 11 pA rms for the whole optical signal chain with a photodiode area of 7.5 mm^2. This allows for reliable detection of low photodiode currents in the range of 1 pA to 10 pA, typical for low yield fluorescence applications. In addition, excellent PSRR and ambient light rejection ease the system engineer's burden while designing the power supply unit and mechanical enclosure.

To validate the performance of the MAX86171, an LED driven by the MAX86171 was passed through varying levels of neutral density (ND) optical filters and received via a photodiode by the MAX86171 as shown in Figure 5. By increasing the density of the ND filters, the optical attenuation can be varied from 40 dB (ND2) to 140 dB (ND7), simulating reducing fluorescent yields in a PCR or LAMP-based detection system. Under 140 dB of attenuation, the MAX86171 can reliably detect the increased photodiode current of <10 pA above the dark current floor. This high sensitivity is due to the low dark current noise of 11 pA rms, measured with the photodiode connected to the optical front end.

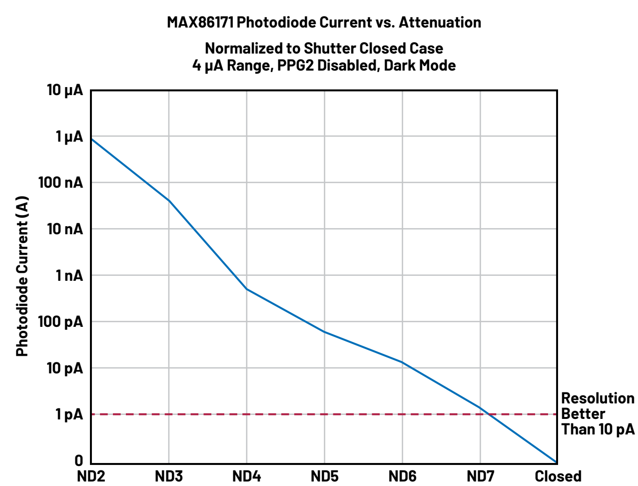

Figure 6. The MAX86171's performance results.

This level of performance exceeds what is typically required in PoC instruments and allows the full potential of the biosensor or chemistry to be showcased. The internal registers of the MAX86171 enable parameters such as pulse width, pulse intensity, photodiode gain, and photodiode biasing to be programmed via firmware. Signal filtering, averaging, and ambient light rejection options are also available to optimize optical detection. Together, this provides a solution with maximum flexibility to adapt to new assays without the need for hardware rework.

Conclusion

Designing a circuit for an IVD system requires careful attention in both the electronic section and system design to ensure that high sensitivity detection is achieved without sacrificing selectivity. Identifying the weak electronic signal is critical when creating a system that can showcase the full potential of the biosensor or chemistry, and ultimately results in a device with accurate diagnostic results.

In the rapidly advancing PoC market, flexibility and future-proofing are crucial as receivers and must be adaptable to the growing and changing menu of tests. The MAX86171 integrated optical front end from ADI meets these stringent performance needs while providing software programmability, taking the risk out of the electronic receiver design, and providing a future-proofed solution.

About the Authors

Wassim Bassalee joined Analog Devices in 2004 where he held system software, application engineering, and system engineering roles. As a field applications engineer, Wassim applies extensive system-level expertise toward enabling and supporting customer innovations. Wassim holds an M.S. degree in electrical engineering from Northeastern University and an M.S. degree in system design and management from MIT.

Aileen Cleary is the marketing manager of the Medical Instrumentation and Life Sciences Business Group at Analog Devices. She focuses on driving business and innovation through customer-centric engagements. Aileen has over 17 years of experience in the semiconductor industry, holding various technical and business roles in both the energy and healthcare markets. Aileen holds a master's degree in electronic and electrical engineering from the University of Edinburgh, Scotland.

Robert Finnerty is a systems applications engineer working in the Digital Healthcare Group based in Limerick, Ireland. Rob joined the Precision Converters Group within ADI in 2012 and since then has focused on precision measurement. He holds a bachelor's degree in electronic and electrical engineering (B.E.E.E) from National University of Ireland Galway (NUIG).

Neil Quinn is a systems applications engineer with Analog Devices working in the Medical Life Science and Instrumentation Team. Neil received a bachelor's degree in electronic engineering from the National University of Maynooth in 2013, and a specialist diploma in embedded systems engineering in 2021. He has experience in optical and impedance instrumentation, industrial and high speed communication interfaces, and ADI's *i*Coupler® digital isolation technology.