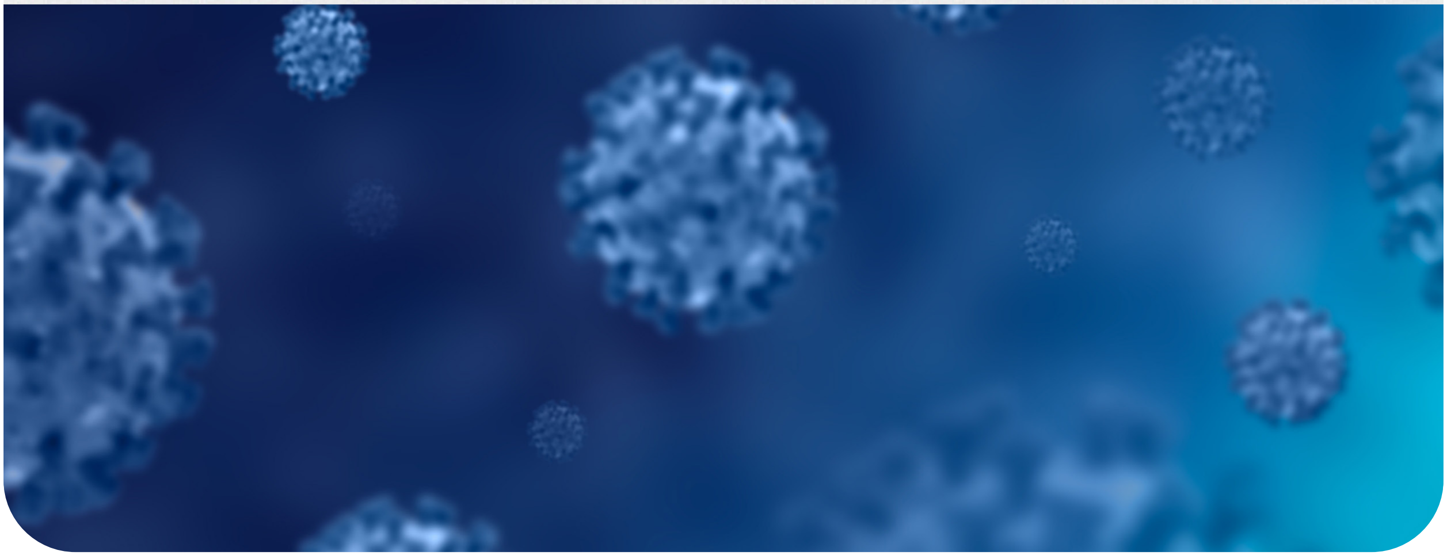
Spectroscopy for Trace-level Virus Detection

Application Note



KEYWORDS

- Viruses
- Fluorophores
- Testing and screening

TECHNIQUES

- Fluorescence
- Raman/SERS
- PCR

APPLICATIONS

- Trace-level virus detection
- Antibody detection

In this overview, we explore the optical sensing tools and techniques available from Ocean Optics for virus detection. Our focus? Rapid testing and screening for viruses including COVID-19.

COVID-19 has placed us all in a unique fight, not against a physical army or intangible idea, but against a novel virus that attacks people of all nations, especially our most vulnerable citizens. But we have multiple avenues to fight back, including:

- **Distancing**. By minimizing person-to-person interaction, we also minimize potential transmissions.
- **Vaccines**. With a well-designed vaccine, even if someone inoculated is exposed to the virus their chances of it turning into a notable infection can be greatly reduced.
- **Treatments**. If someone is exposed to the virus and it does indeed turn into an infection, an effective menu of treatments can help minimize mortality rates and overall severity.
- **Detection and tracing.** These are our eyes in the battle against an invisible foe, and the key tools we'll be examining here.

Virus Detection and Tracing

Detection and tracing are critical in understanding how virus spread occurs historically so that future spreading can be minimized. This allows us to consider what activities and scenarios carry the greatest risk, and who among us may be

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most vulnerable. We can calibrate our policies and actions when we know how and where transmission is occurring.

But while slow detection methods can serve this purpose to a reasonable extent, fast detection techniques bring us even closer to a return to normal routines. A rapid testing system deployed at the entrance of a stadium, school, airport, or nursing home could instantly prevent a super-spreader scenario that we hear about all too often.

Familiar and Newer Viral Detection Techniques

The tried-and-true method of viral detection leans on revolutionary PCR, or polymerase chain reaction, technology. This approach uses polymerase enzymes to replicate or amplify a specific region of genetic material, if it is present. Templates can be designed that specifically target parts of the COVID-19 genetic code; if those code segments are present, they will be amplified. This amplification requires thermal cycling for roughly 30-40 cycles, which is typically the most time-consuming part of the PCR technique.

Once thermal cycling is complete there are several methods to observe if the targeted genetic material is present. This is where applied spectral knowledge can help shape virus detection.

Common fluorophores such as fluorescein and its derivatives can be further complexed so they become fluorescent only when bound to the targeted COVID-19 genetic segment. With these unique fluorescent tools in hand, the next hurdle we face in our effort to decrease test time and increase test sensitivity is optimizing that fluorescence detection.

Figure 1. Ocean HDX is a compact, high-sensitivity spectrometer suitable for fluorescence measurements.

The most common approach for this type of trace-level fluorescence is steady-state broadband spectroscopy, which is well-served by the Ocean HDX spectrometer (**Figure 1**) and LSM LED kits. The Ocean HDX sets a new bar for low-light performance in an amazingly compact footprint. Proprietary internal baffling and other optical design triumphs in the Ocean HDX allow fluorescence detection at levels previously attainable only with much larger and more costly systems. Driving that trace fluorescence is one of Ocean Optics's LSM LED options, providing high-power and stable excitations for clean and coherent emission signals (**Figure 2**).

The traditional broadband spectroscopy approach brings with it a range of advantages, including the ability to observe multiple fluorescent species at the same time with one device, and the ability to develop intricate numerical methods to deconvolute desired signals from the broadband trends.

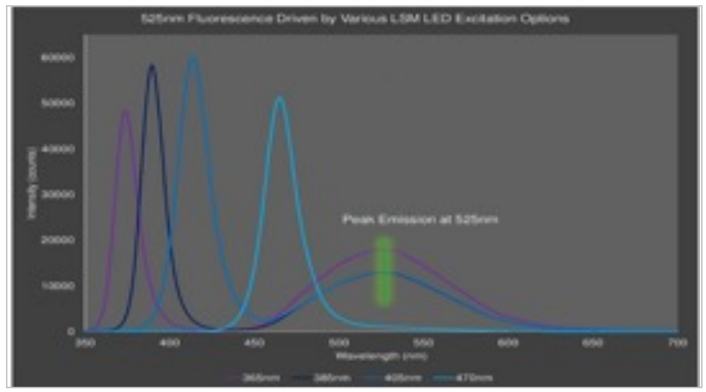

Figure 2. By adjusting LED wavelength excitation, different fluorescence response can be measured.

But there is another way to observe this fluores- cence signal, by using an approach that exploits the fast decay properties of fluorescent dyes in a time-resolved manner. Ocean Optics typically provides the NeoFox phase fluorimetry system as an optical oxygen sensor platform (**Figure 3**), since we also develop the oxygen-responsive sensor chemistries and the supporting probe and patch components that comprise the platform.

Figure 3. Although conceived for detection of oxygen-sensitive fluorescence chemistries, the NeoFox phase fluorimeter can measure the fast decay properties of fluorescent dyes used in medical diagnostics.

But the NeoFox is also popular for embedding into other devices, with modifications in LEDs, filters, and internal settings to optimize the system into a customized detection platform. By strobing the LED as a square wave at kHz speeds, the NeoFox ultra-sensitive avalanche photodiode detector sees the fluorescence signal grow during LED on-time but also decay during LED off-time. This decay time is observed on the micro-to-nanosecond scale and can be tightly correlated to the concentration of fluorophore in the test fluid, such as a small PCR sample. Benefits of this approach include simplified hardware, since the NeoFox contains all its optics and processing electronics in a single casing, and provides good interference immunity to variables like sample color and ambient light.

Raman and Trace Level Detection

While PCR has done wonders in the world of genetic advancement, there are still time constraints from thermal cycling to consider. Ocean Optics provides yet another approach, with the potential to offer immediate viral detection answers in seconds without any complex sample pre-processing. This approach exploits the Raman technique, which uses a laser to drive observable Raman scattering phenomena.

Raman is a fast, powerful identification technique based on the rare interaction of photons with the molecular structure of the sample, specifically looking at the increase or decrease in photon energy level at quantized amounts. These sharp emission signals are inherent 'fingerprints' for an analyte and can quickly tell you when a certain species is present. Ocean Optics has offered high-performance Raman systems for over a decade at multiple wavelength options, such as the highly popular QE-Pro Raman+ platform offered in 785 nm, 638 nm and 532 nm configurations. Adding the wavelength-appropriate laser and probe is all you need for basic Raman measurements.

Figure 4. SERS substrates can amplify Raman emissions and enable trace level detection of analytes.

For trace level detection, Raman emissions can be further amplified by utilizing certain metals that are 'in-tune' with the laser frequency being used, leaning on an effect called SPR, or Surface Plasmon Resonance. By using nanoparticles or nanostructures of a metal such as gold or silver, analytes may come in proper proximity to this SPR effect and lead to a dramatic amplification of Raman emission photons, which is a technique called SERS, or Surface Enhanced Raman Spectroscopy. Ocean Optics has been a leading commercial SERS provider since 2014 and offers low-cost, consumable substrates in an easy-to-use form factor (**Figure 4**). These convenient 5-packs have a proprietary nanoparticle formulation embedded into a quartz matrix and mounted onto a standard glass microscope slide. The user can simply add a few microliters of sample to the nanoparticle-doped region and place the sample under the Raman probe for rapid detection of trace-level analytes.

Figure 5. With high-sensitivity Raman techniques, detection of even small amounts of viruses and antibodies is possible.

Ocean Optics has worked with several developers for rapid COVID-19 detection. Even the preliminary scans with off-the-shelf components have shown repeatable Raman activities for both direct viral fragments and the respective antibodies (**Figure 5**). While these measurements were done in rather clean sample fluids versus patient-obtained clinical

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samples, the research establishes the regions of Raman activity to look for when checking a "dirtier" real-world fluid. When analyzed using advanced algorithms, scans of complex bio-fluids can be thoroughly and rapidly deconvoluted to provide a positive/negative result with high statistical confidence.

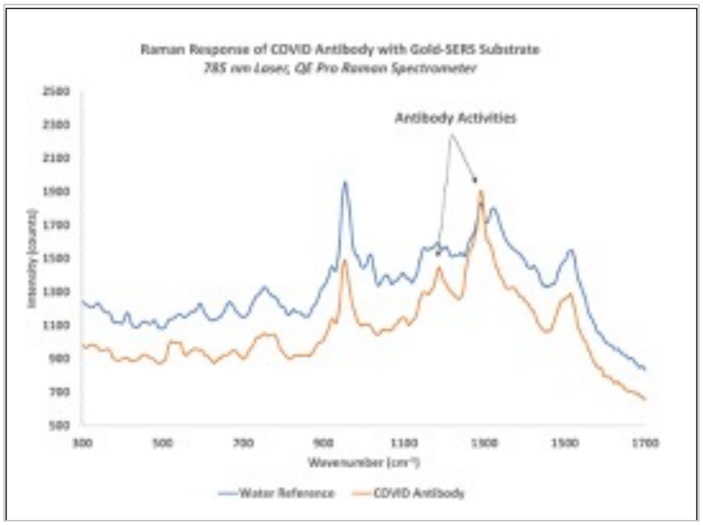

Figure 6. With SERS techniques, we observe peak activity from the introduction of COVID-19 antibodies.

As with any development, your progress is only as good as the partners you find and the resources you make available. Ocean Optics brings a unique level of expertise in spectral hardware, the proper techniques to use with that hardware, and the insight to achieve what has not been done before. If you're in the fight to dramatically advance viral detection to help the world subdue the COVID-19 pandemic, we are eager to learn about your vision and how our applied spectral knowledge can help you unlock the possible.