

Achieving Reagent-Free Blood Analysis With Optical Spectroscopy

A Q&A with Olga Pawluczyk, President and CEO, P&P Optica

P&P Optica Inc. (Waterloo, ON, Canada) burst onto the optical spectroscopy scene earlier this year after receiving a major technology development award from the Canadian government. The company is using the funding to fast-track its capabilities in designing and building VPH (volume phase holographic) spectrometers into a new family of high-resolution optical analyzers.

Olga Pawluczyk, president of P&P Optica, is one of the key innovators involved in the success of the company's technology. An engineer by training, Pawluczyk became the third employee of P&P Optica in 2001, following completion of her master's degree in medical biophysics. The company was then focused on optical consulting and fiber optics for spectroscopy. By 2004, the company had doubled in size and spun off its optical cabling business into an independent entity. Pawluczyk assumed majority ownership of P&P Optica and repositioned the firm as a supplier of high-performance, gel grating-based, dispersive optical spectrometers.



P&P Optica has developed a sensitive non-scanning optical spectrometer that enables users to determine the chemical composition of substances that were previously detectable only through mass spectrometry. The firm's instruments are capable of measuring both broadband and Raman spectra, and they enable researchers to use multichannel or high-throughput modes to detect signals previously undetectable by non-scanning optical systems.

In this Q&A, Pawluczyk introduces us to a new spectroscopy-based approach to reagent-free blood analysis that her company is in the final stages of developing. She explains how the technology works, discusses the impact it will have on the blood analysis market, and explores future applications for it in the biomedical arena.

I understand P&P Optica has been developing a new spectroscopy-based technology for reagent-free blood analysis. Can you tell us about it?

We recently started a project to develop a second-generation reagent-free blood analysis instrument that will measure the most commonly analyzed elements in blood (such as cholesterol, iron, and albumin) within minutes, without a dedicated laboratory, expensive chemicals, or costly reagents. We envision the device being installed in doctor's offices, clinics, and emergency rooms — any situation where near-instant blood analysis is an advantage or a necessity. We anticipate that the second-generation prototype will be completed and ready for initial trials by the first quarter of 2011.

Currently, conventional blood-assay generally requires the use of one or more chemical reagents, test strips, or reagent trays that significantly increase the cost of blood analysis. Depending upon the lab and jurisdiction, this basic suite of blood analysis costs between \$35 and \$85 in North America. Comparatively, our blood analysis device will not require any time- or temperature-sensitive consumables (other than the anticoagulant-coated vial that holds the blood), and the results will be available in minutes, not days. Not only does this reduce the cost of each test to pennies, it also saves hours for both the patient and the physician.

How exactly does the device work?

The three key components that make our spectrometer such a success seem simple, but they are actually the result of an entire career devoted to holography and spectroscopy — that of our chief scientific officer, Dr. Romuald Pawluczyk, who also happens to be my father.

The first requirement was to design and build a high-performance spectrometer that was capable of distinguishing between very small differences in spectra. This was achieved through the development and production of spectroscopy-specific, low-noise volume phase holographic gratings designed to operate within our patented transmission-based spectrometer. These “gel gratings,” as we call them at P&P Optica, offer terrific performance advantages over competing gratings. Together, the gratings, custom optics, and transmission-based design were all designed to operate at, or very near, the theoretical limits of efficiency for each of our components.

Secondly, and of equal importance, was the development of sample collection and preparation techniques. Our early discoveries demonstrated the importance of understanding just how the light interacts with the samples and how to best couple that light into a spectrometer. Thus, to ensure proper sample handling, custom-designed sample holders were built to allow consistent measurement of chemicals within the complex physiological fluids.

Finally, it was necessary to develop software that could extract the required information from the spectral information while compensating for changes in the sample and variability of the instrument.

All three areas of achievement were made possible through the labors of Dr. Pawluczyk, myself, and our fantastic researchers here at P&P Optica.

What are the biggest challenges you've had to overcome to bring this technology to market?

Like many small tech companies, our primary issue during the first few years was the day-to-day bootstrapping/struggle of cash flow versus R&D. We knew we had a product that was significantly better than any other dispersive spectrometer out there — the only problem was how to get it to market without starving. We have succeeded in overcoming that initial barrier, and we are now working to expand our stable of proven applications.

Recently, we achieved extraordinary success in a LIBS (laser-induced breakdown spectroscopy) application where the customer tested our spectrometer against one of the “market leaders.” Not to brag too much, but our spectrometer had 14x higher throughput. To put this into perspective, in food analysis, for example, we could detect a 14x smaller *E. coli* bacteria colony than other spectrometers!

As we developed new spectroscopic applications, it became imperative to form key partnerships to enhance our product offerings. Perhaps the most crucial of such partnerships is our production agreement with Raytheon ELCAN Optical Technologies (Midland, ON, Canada), a division of Raytheon Canada Limited. Not only did this free us up to intensify our research efforts as our partnership grew, thanks to ELCAN's engineers, it also resulted in significant design refinements that both reduced the hours required for assembly and generated improved spectrometer performance. An additional complimentary benefit that ELCAN brought to the table is their ISO 13485 medical device manufacturing certification. This certification delivers confidence to our customers and to us.

What initially motivated P&P Optica to develop this technology?

We grew alongside our biomedical researcher clients, and together we developed the spectrometers to meet the demands of the researchers' applications. This resulted in the development of new abilities to acquire increasingly precise results, which furthered research and spurred even more ambitious projects. The outcome of these partnerships is both ground-breaking research and great proof-of-concept applications that have since evolved into product lines. Consequently, after eight years of development, we arrived at a place where our abilities in limits of detection and throughput were eliminating the molecular-level guesswork from their research.

In the past, it was always a case of the spectrometer's performance being limited by the abilities of the cameras and detectors. Over time, however, as lasers and detectors improved, our unique gel gratings and optical design gave our spectrometers an additional edge — unlike most other spectrometers, P&P's systems are detector-limited, even when using EMCCDs (electron multiplying charge coupled devices). This means we were increasingly able to quickly acquire the information in a large volume and dynamic range without introducing artifacts, ghosting, or errors. The net result was that we were able to improve the dynamic range, which gave us the ability to measure minute quantities within complex backgrounds. This, in turn, led to other

markets, such as in biohazard and remote threat detection, as well as extremely accurate sample measurement in active biological samples.

What differentiates this instrument from other approaches to blood analysis?

The critical differentiator is that no time-sensitive or temperature-sensitive materials are required to perform the tests. An additional advantage is that the high-quality spectra we obtain using our spectrometers inherently hold information about everything in the measured sample. This means that the cost of measuring one analyte is the same as measuring dozens. Furthermore, the device is designed to operate independently of an operator, which is to say it will function automatically without the need for a skilled technician. Of course the actual sampling of the blood from the patient will still require the gentle skills of a trained nurse or phlebotomist, as the case may be.

What are your future plans for this technology? Are you exploring other application areas?

From our own research, it is becoming increasingly apparent that in terms of blood analysis techniques, spectroscopic applications are moving rapidly towards biomarker detection. This is a particularly exciting avenue to explore, as it massively expands the potential biomedical applications of spectroscopy.

One of my own personal interests is the use of spectroscopic techniques to assess the risk for a given disease. Our first systems were made for exactly that application: breast cancer risk prediction at the Ontario Cancer Institute. Imagine using a spectrometer — non-invasive, non-ionizing, inexpensive technology — to see if we need to change our behavior to reduce the risk of such a disease. What if this same technique could be applied to Alzheimer's, depression, or diabetes?

We have certainly noticed an explosion of interest in biomedical spectroscopy applications, and the success of one project has led many others in the field. For example, we have had considerable success over the last few years providing spectrometers for microscopy and the detection of autofluorescence in biological samples. The sensitivity of the system completely removed need to apply contrast agents, which typically change the functioning of cells. The success of this endeavor led to other biomedical applications, such as integrating our spectrometer into custom-designed OCT (optical coherence tomography) imaging systems. The outcome of that project has resulted in over 12 published papers after only a few years of research.

What is fascinating about working with newly developing, easy-to-adapt, easy-to-optimize platform technologies such as dispersive optical spectroscopy is the wide array of possible applications. In some industrial areas, such as pharmaceutical production facilities, spectrometers have a well-established hold. But in my opinion, they are underutilized and could rapidly be deployed into new applications to solve the myriad of problems underlying most pharmaceutical product recalls. Furthermore, spectrometers are ideally suited to helping

pharmaceutical companies meet new FDA regulatory initiatives, both in terms of processing and verification stages of production.

Determining the exact chemical composition of products is becoming increasingly important. Our food supply is now so varied and comes from so many sources that testing for pathogens, nutritional value, and contaminants is becoming crucial. There is just no other nondestructive, easy-to-use technology that is positioned to do this other than spectroscopy. How about optimization of production and processing of materials from paper to metal? What industry *wouldn't* benefit from advances in spectroscopy?