APPLICATION NOTE:
DEVELOPMENTS IN SMART BIOPSY, BIOMEDICAL SENSING

MEMBER OF THE NYNOMIC GROUP

Techniques

- Diffuse Reflection
- Autofluorescence

Keywords

- Diffuse Reflectance
- Pulse Oximetry
- Co-Oximetry
- Blood Gas Analysis
- Blood Perfusion
- Cancer Detection

Introduction

n the realm of life science research and clinical instrumentation, optical spectroscopy, and sensing play critical roles in a variety of areas. Optical spectroscopy provides an ideal means for non-destructive sampling and real time analysis in vivo or in the lab. The instrumentation needs of these applications have evolved rapidly in recent years with the evolution of point of care devices, advent of wearable diagnostic systems, and increase in demand for lower and lower detection-limit systems. The size, performance, and cost of instruments is of considerable importance for these applications, often with mutually exclusive specifications. The importance of the enabling fiber optic technologies which provide for micro scale sampling on tissues, bodily fluids, and synthesized matrices used in life sciences cannot be understated.

This application note focuses on human life science applications for optical spectroscopy with emphasis on clinical care, research, and biotechnology.

Clinical Care Optical Spectroscopy

Smart Biopsy/Endoscopy

Today, the concept of a Smart biopsy or endoscopy may refer to the use of a biopsy or endoscopy procedure to extract deeper information from these invasive procedures which may aid in diagnostic processes. The smart biopsy of the future seeks to develop a rapid, and minimally-invasive diagnostic tool that, when deployed in a clinical setting, can reduce the number of unnecessary traditional invasive biopsies and improve early detection and treatment of a variety of diseases in the developing world.

Endoscope

Smart biopsies and endoscopies may combine tissue reflection or fluorescence measurements within the hardware used to perform these procedures. Fiber optics are critical to the extraction of the spectroscopic information during the procedure.

Typically requiring both high speed and high sensitivity sampling, this application's demands are challenging. Avantes has successfully used our AvaSpec-HS2048XL-EVO to support these applications. This instrument offers high sensitivity detection with high speed sampling capabilities. The high sensitivity 0.22 numerical aperture optical bench of this instrument is combined with sophisticated electronics which facilitates sample acquisition in as little as a few milliseconds.

Real-world Application Development for Smart Biopsy Technology

Avantes USA
500 S. Arthur Ave., Unit 500
Louisville, CO 80027
Tel. +1 (303)-410-8668
www.avantesusa.com

infousa@avantes.com | www.avantesusa.com

Avantes BV
Oude Apeldoornseweg 28
7333 NS Apeldoorn
The Netherlands
Tel. +31 313 670 170
www.avantes.com


Endoscope

Worldwide, cancer treatment outcomes are often connected to early detection and treatment. Cancers such as, prostate, colorectal cancer, cervical cancer, and oral cancers have all been targets of research into the use of diffuse reflectance spectroscopy (DRS) for rapid and accurate detection of cancer.

In the developed world, early detection and treatment has led to reduced fatality


AvaSpec-ULS2048CL-EVO

rates for epithelial cancers, but existing diagnostic equipment for performing DRS is expensive, bulky and demands high power output. It also requires highly-trained personnel. These obstacles lead low- and middle-income countries to have disproportionately high mortality rates for these cancers due to lack of diagnostic equipment. The development of a portable, low-cost, easy-to-use, and most importantly, accurate diagnostic tool for the detection of epithelial cancers would save lives around the globe.

Research in the last few years has focused on overcoming the challenges inherent in bringing a reliable portable DRS system to reality. Two of those challenges are the inability to standardize the pressure applied to the probe when performing tests manually, and the lack of a reliable way to perform a real-time calibration in the field, two potential sources for significant user error with the potential to vary test results widely. One potential solution integrated a self-calibrating channel with a novel probe design that adds an optical pressure sensor to the probe tip that only allows data capture when probe pressure falls within a predefined range. The pressure sensor and self-calibration features reduce the need for advanced operator training and improve the accuracy and efficacy for clinical deployment. (Yu et al. 2014)

The system designed for this research consisted of the smart fiber optic probe with pressure sensor that integrates a tissue-sensing channel and self-calibration channel, coupled to a high-powered white LED and 850 nm LED light sources, and a three channel AvaSpec-2048 series array spectrometer and computer with LabView and Matlab software programs for analysis. Two visible channels (A & B) covering wavelength range 400-635 nm with resolution of 1.8 nm are coupled to the white LED and used for Diffuse Reflection Spectroscopy (DRS) and selfcalibration (SC). Channel C, cover the NIR range from 750-932 nm range and 0.23 nm resolution was coupled to the 850 nm LED and used for the optical pressure sensor.

The historic method of detecting and identifying colorectal cancer is visual inspection through endoscopy using white light. Colorectal carcinoma typically develops along predictable stages of neoplastic transformation which, in turn, results in changes to the optical characteristics of transformed cells. Early stages of celular defects in mucosal linings are undetectable under traditional white light endoscopy, while fluorescence spectroscopy offers a uniquely sensitive tool to detect early changes to the physical properties of abnormal cells (Horak 2006). Depending on the cellular environment, spectral features may exhibit an autofluorescence response shifting from 510-560 nm in healthy cells toward the red at 630-690 nm relative to concentration of malignant tissues. The ideal system designed for this research application was the AvaSpec-2048 (now replaced by the AvaSpec-ULS2048CL-EVO) measuring 560-800 nm with a direct attach filter holder.

Further studies apply NIR spectroscopy using a dual channel spectrometer system consisting of the AvaSpec-ULS2048L and AvaSpec-NIR256-2.5-HSC NIRLine spectrometers to identify oral cancer biomarkers in saliva (Hurskainen 2019). And, in another study, research partners in Iran and the Netherlands employed the AvaSpec-2048-USB2 (now replaced by the AvaSpec-ULS2048CL-EVO) spectrometer with the AvaLight-Hal-S halogen light

AvaSpec-Mini2048CL

source to perform single fiber reflectance spectroscopy to identify cervical premalignancies. This non-invasive methodology has the potential to reduce the number of unnecessary biopsies (Tabrizi 2013).

Blood Perfusion

Blood perfusion is defined as the blood volume flow through a given volume or mass of tissue. It can be measured in units of ml/ml/sec or ml/100 g/min) which represents the amount of local blood flow through the capillary network and extracellular spaces in the tissue. This parameter is an important medical diagnostic procedure for determining normal and pathological physiologies. For example, the viability of a tissue transplant demands satisfactory post-operative blood perfusion. Using a technique called Diffuse Correlation Spectroscopy (DCS), blood perfusion is measured by treating scatter of emitted photons as a function of the motion of cells within a target volume (Bi et al. 2015). This approach offers promise for wearable spectroscopy systems which provide real time monitoring of tissue health. The AvaSpec-Mini2048CL is the ideal candidate for such a system.

Pulse Oximetry

Anyone visiting a medical facility has benefitted from pulse oximetry technology which provides for a painless, accurate, real-time measurement of pulsatile arterial blood levels from a fingertip measurement. Most devices of this type consist of two LEDS, one at 650 nm (visible) and the other at 950 nm (near infrared), and two sensors which together measure the oxygen absorbance (SPO2) from the ratios of oxyhemoglobin and deoxyhemoblin. While full spectroscopic sampling and analysis is not required, spectrometers are frequently used in the validation and qualification of these devices and their subcomponents. Given the high-speed sampling requirements of this measurement, the Avantes AvaSpec-ULS2048Cl-EVO is ideally suited to the application with its 30 microsecond integration times and 2kHz sampling rates.

Co-Oximetry in Neonatal care

Blood Gas Analysis – Co-Oximetry

Co-oximetry refers to the spectroscopic technique which enables the quantitative measurement of blood parameters: oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb), carboxyhemoglobin (COHb), and methemoglobin (MetHb) as a percentage of the total hemoglobin concentration in a blood sample. While pulse oximetry is a measure of oxygenated hemoglobin as a percentage of total hemoglobin, Co-oximetry separates and quantifies all of the types of hemoglobin. These blood gas parameters are traditionally measured using a spectrometer via transmission/absorbance from 380 to 780 nm. This application also requires exceptionally low stray light and thermal stability specifications in the instrumentation. Avantes has successfully implemented the AvaSpec-ULS2048CL-EVO and its subcomponent optical bench, the Avabench-75-ULS2048CL-U3, into clinical devices for this application. The new AvaSpec-Mini2048CL is also an ideal candidate for this application.

NIR Diffuse Reflection

Medical Research

Diffuse Reflection

Researchers at the University of CA at Irvine Beckman Laser Institute have used near infrared spectroscopy not only to identify and monitor cancer mass reduction during chemotherapy treatments, but to characterize specific histological features in order to predict response to treatment. Diffuse reflection spectroscopy measurements are inherently demanding of sensitivity and Avantes developed the AvaSpec-HS2048XL-EVO high sensitivity spectrometer specifically for these types of applications. This instrument features a 0.22 numerical aperture (NA) optical bench and large pixel detector providing for full collection of the light received by a fiber optic of the same NA.

For more information about these or any other medical or biomedical applications, please contact a Sales Application Engineer at infousa@avantes.com or info@avantes.com or visit our websites at www.avantes.com and www.avantesusa.com

References

- Bi, Renzhe, et al. "Optical methods for blood perfusion measurement—theoretical comparison among four different modalities." JOSA A 32.5 (2015): 860-866.
- Horak, L., et al. "Auto-fluorescence spectroscopy of colorectal carcinoma: ex vivo study." Journal of Optoelectronics and Advanced Materials 8.1 (2006): 396.
- Hurskainen, Miia. "Attempt to Reliably Identify Oral Cancer Salivary Biomarkers Using Near-Infrared Spectroscopy and Savitzky-Golay Algorithm." DEStech Transactions on Engineering and Technology Research icicr (2019).
- Santoro, Ylenia, et al. "Breast cancer spatial heterogeneity in near-infrared spectra and the prediction of neoadjuvant chemotherapy response." Journal of biomedical optics 16.9 (2011): 097007.
- Tabrizi, Sanaz Hariri, et al. "Single fiber reflectance spectroscopy on cervical premalignancies: the potential for reduction of the number of unnecessary biopsies." Journal of biomedical optics 18.1 (2013): 017002.
- Yu, Bing, et al. "Diffuse reflectance spectroscopy of epithelial tissue with a smart fiber-optic probe." Biomedical optics express 5.3 (2014): 675-689