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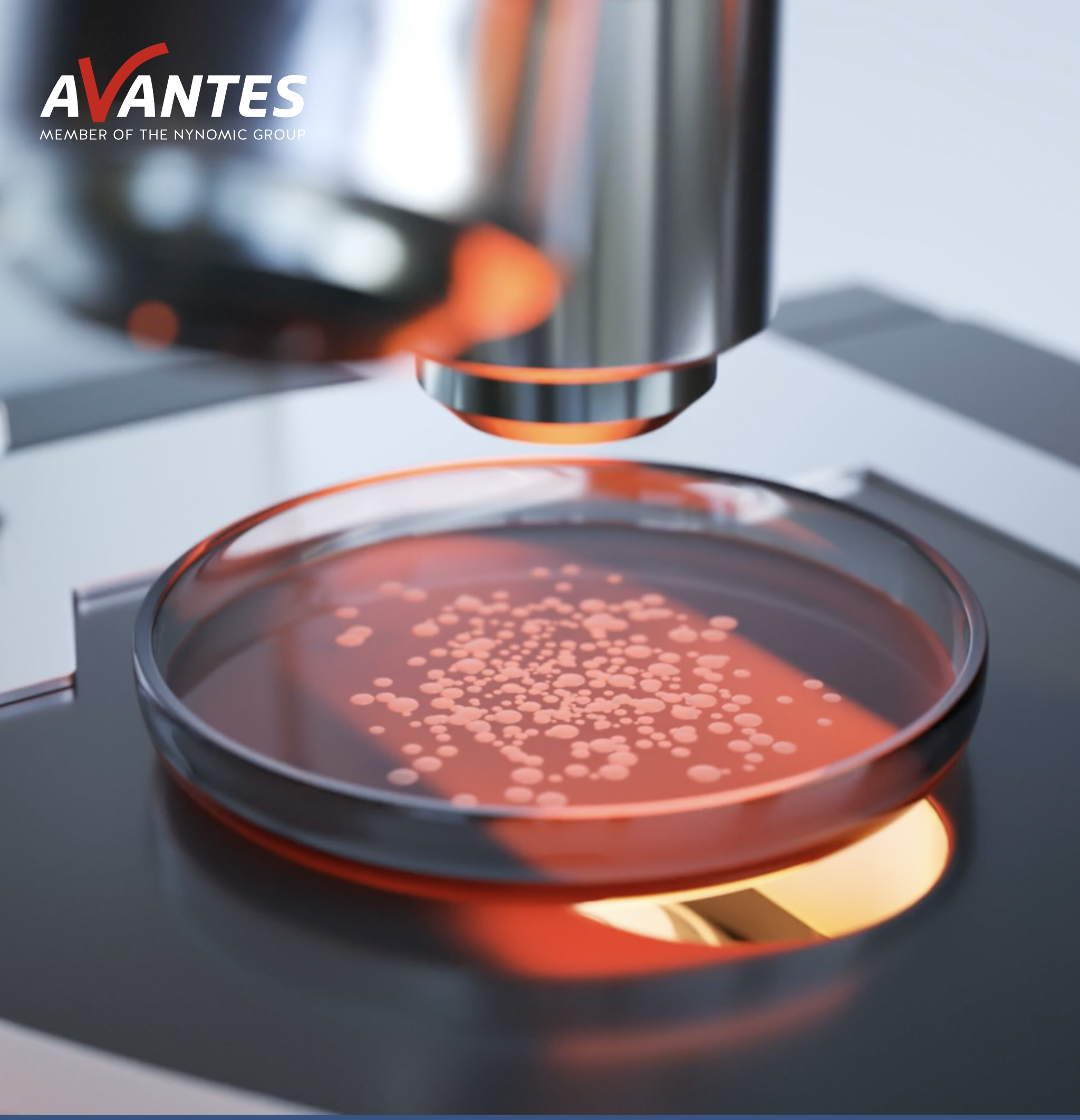

EBOOK

BIOMEDICAL APPLICATIONS AND SPECTROSCOPY

WELCOME

A key part of Avantes mission statement refers to provide state-of-the-art, innovating measuring equipment that helps humankind live longer and healthier. By providing our enabling spectroscopy solutions to (bio) medical researchers, pharmaceutical manufacturers and Original Equipment Manufacturers, we can contribute to that mission and help them achieve their measurement challenges.

With almost 30 years of experience, Avantes is a equipped partner to guide customers to a spectroscopic solution, tailored to their application and research needs.

Curious how spectroscopy can help you reveal answers by measuring all kind of materials in-line at your production facility, in a lab or in the field? Please contact one of our technical experts, we are happy to help!

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SPECTROSCOPY IN THE BIOMEDICAL & LIFE SCIENCE INDUSTRY

Medical and biomedical researchers, as well as Original Equipment Manufacturers (OEM), frequently utilize spectroscopy techniques for clinical and research processes. Ultraviolet, visible and near-infrared wavelength ranges are measured for a variety of medical and biomedical applications.

Fibre-optic based spectrometers offer a great value to the industry due to their ability to facilitate in-situ (in vivo) measurements within clinical settings. The fibre-optic interface is often exploited for low-cost, disposable testing procedures. Low-cost instruments also present the opportunity to bring the lab to the patient. Biomedical analysis can benefit from the superior price to performance ratio realized with using fibre-optic spectrometers in place of traditional, higher-priced instruments and detectors.

Our instruments are utilized in various medical and biomedical applications such as blood analysis (co-oximetry), endoscopy, tissue fluorescence, capillary electrophoresis, phototherapy, and for many other purposes. Avantes' experiences in these industries range from OEM component supplier to research system configurator.

In this eBook we dive into multiple biomedical and life science applications in which spectroscopy is applied to give you a better understanding of all the opportunities spectroscopy has to offer in this market.

SECTION 1

1 CLINICAL CARE OPTICAL SPECTROSCOPY

In 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, the advent of wearable diagnostic systems, and an 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 fibre-optic technologies which provide for micro scale sampling on tissues, bodily fluids, and synthesized matrices used in life sciences cannot be understated.

1.1 Weapons to Fight Cancer

Spectroscopy has proven to be invaluable in the fight against cancers. The standards for lung cancer detection is the use of autofluorescence bronchoscopy in which a narrow probe is inserted through the patient's mouth into the upper bronchial tree. Autofluorescence has been shown to be far more sensitive than white light bronchoscopy in the detection of Carcinomas or dysplastic lesions; however, it also has a high rate of returning false positives. Researchers at the Department of Respiratory Diseases in Rotterdam, the Netherlands have investigated the use of absorbance/ reflection optical spectroscopy to improve specificity without losing sensitivity.

The team used a specially designed probe to feed through the 2.8mm bronchoscope channel with fibre light sources The mucosa tissue was irradiated with a tungsten/halogen broadband white-light (predecessor to the AvaLight-HAL-S-Mini) and a blue laser calibrated to 407 nm introduced via fibre-optics. The emission peak wavelength for autofluorescence of healthy tissue was 500nm. The resulting reflectance and fluorescence emissions were collected via a multichannel Avantes spectrometer installation equivalent to two AvaSpec-ULS2048CL-EVOs in parallel.

An area that displays an abnormal fluorescence profile can be rapidly targeted for additional spectral measurements which can be acquired in <1 second. Diseased tissue displayed drastically lower emission intensity at shorter wavelengths compared to healthy tissues. The combined autofluorescence imagine and optical reflectance spectroscopy significantly improved the positive predictive value compared with autofluorescence alone without sacrificing sensitivity.

Both the excitation and fluorescence wavelengths at 407 and 500 nm respectively are within the 360-600 nm range in which blood is a primary absorber. This does create a challenge for this application, but not an insurmountable one. Researchers were confident that the modified bronchoscope with additional fibres was feasible to deploy during a standard bronchoscopy procedure.

Reference:

Bard, Martin PL, et al. 'Improving the specificity of fluorescence bronchoscopy for the analysis of neoplastic lesions of the bronchial tree by combination with optical spectroscopy: preliminary communication.' Lung Cancer 47.1 (2005): 41-47.

1.2 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. Smart biopsies and endoscopies may combine tissue reflection or fluorescence measurements within the hardware used to perform these procedures.

Fibre 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 that facilitate sample acquisition in just a few milliseconds.

1.3 Real-world Application Development for Smart Biopsy Technology

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 have led to reduced fatality 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 to low- and middle-income countries having disproportionately high mortality rates for these cancers due to a 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 fruition. 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 of clinical deployment. (Yu et al. 2014)

The system designed for this research consisted of the smart fibre-optic probe with a pressure sensor that integrates a tissue-sensing channel and self-calibration channel, coupled to 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 a resolution of 1.8 nm are coupled to the white LED and used for diffuse reflection spectroscopy (DRS) and self-calibration (SC). Channel C, covering 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 historical 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 cellular 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 the concentration of malignant tissues. The ideal system designed for this research application was the AvaSpec-2048 (which has since been 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-EVO 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 (since replaced by the AvaSpec-ULS2048CL-EVO) spectrometer with the AvaLight-Hal-S halogen light source to perform single fibre reflectance spectroscopy to identify cervical premalignancy. This non-invasive methodology has the potential to reduce the number of unnecessary biopsies (Tabrizi 2013).

References:

Horak, L., et al. "Auto-fluorescence spectroscopy of colorec- tal 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).

Tabrizi, Sanaz Hariri, et al. "Single fiber reflectance spec- troscopy 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 epithe- lial tissue with a smart fiber-optic probe." Biomedical optics express 5.3 (2014): 675-689

1.4 Blood Perfusion

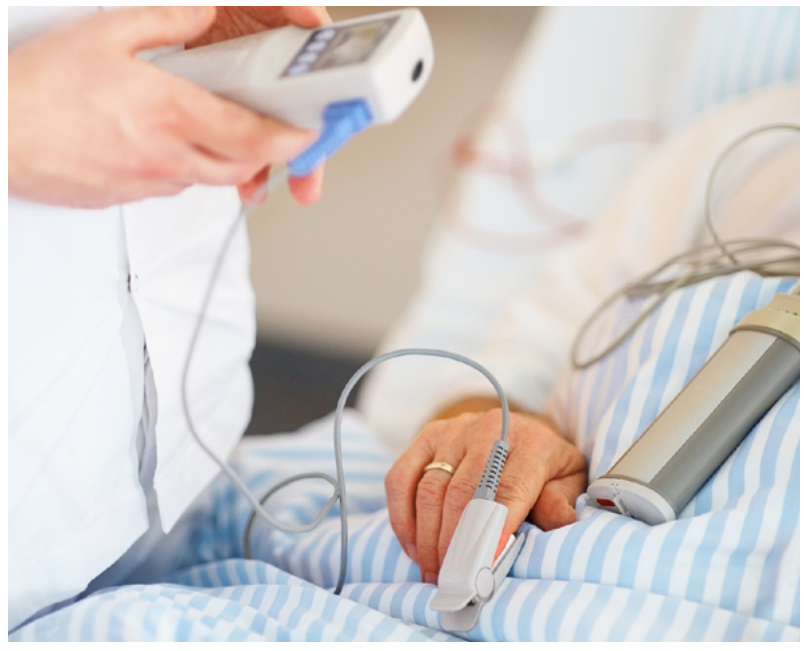
Blood perfusion is defined as the blood volume flow through a given volume or mass of tissue. It can be measured in units of ml/ml/sec or ml/100 g/min), which represents the amount of local blood flow through the capillary network and extracellular spaces in the tissue. This parameter is an important 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 that provide real-time monitoring of tissue health. The AvaSpec-Mini2048CL is the ideal candidate for such a system.

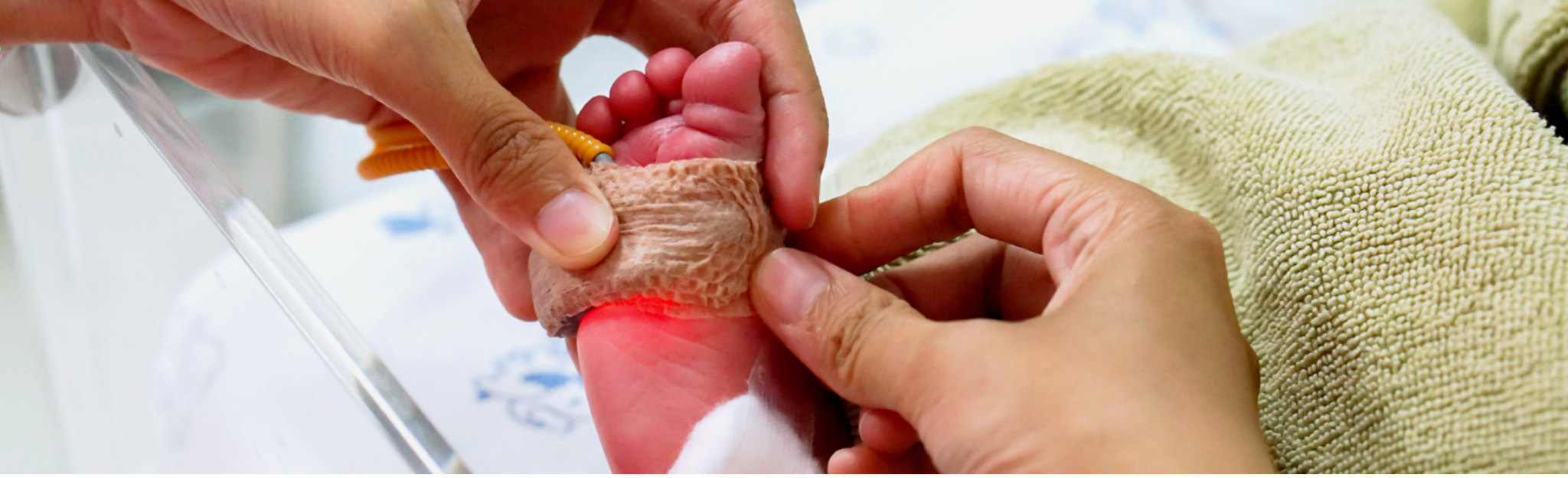
Reference:

Bi, Renzhe, et al. "Optical methods for blood perfusion mea- surement—theoretical comparison among four different modalities." JOSA A 32.5 (2015): 860-866.

1.5 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 deoxyhemoglobin. While full spectroscopic sampling and analysis are 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 AvaSpec-ULS2048CL-EVO is ideally suited to the application with its 30-microsecond integration times and 2kHz sampling rates.





1.6 Blood Gas Analysis, Co-Oximetry

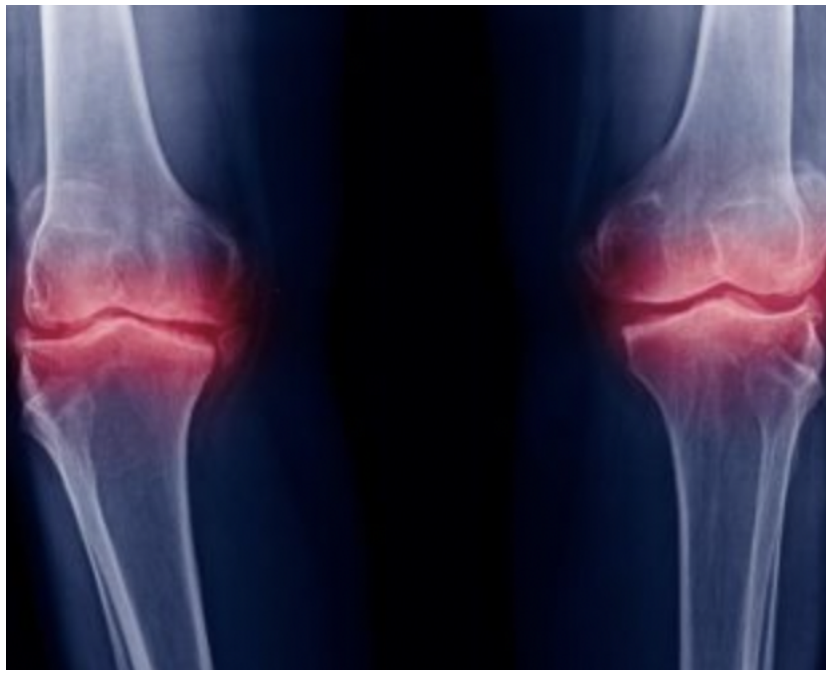
Co-oximetry refers to the spectroscopic technique which enables the quantitative measurement of blood parameters: oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxy-Hb), carboxyhemoglobin (COHb), and methoxyhemoglobin (MetHb) as a percentage of the total hemoglobin concentration in a blood 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 AvaSpec-Mini2048CL is also an ideal candidate for this application because of its small size.

1.7 The Role of NIR Spectroscopy in the Treatment of Osteoarthritis

Medical researchers studying osteoarthritis are exploring the use of near-infrared reflection spectroscopy to characterize bone tissue and improve standards of care for arthroscopic surgeries. There are a large number of uses for near-infrared spectroscopy in the field of biomedical research including non-invasive monitoring, blood testing, protein identification, and more. The near-infrared range is so important because it offers the best quality of reflection spectra measurements, with the least scattering and absorption between 650 nm and 1900 nm. Spectral measurements in the near-infrared are non-invasive and non-destructive, making this particularly attractive for the potential development of clinical applications.

The Avantes family of NIR instruments offers the best mix of sensitivity and resolution for medical applications with NIR spectroscopy.

Our next-generation EVO electronics provide lower noise and offer the latest high-speed communications options for fast data when working in vivo.



What is Osteoarthritis?

Osteoarthritis is a common degenerative condition characterized by the depletion of cartilage in the joints, causing pain and loss of mobility. A common cause of osteoarthritis is simply age; however, traumatic joint injury can cause joint degeneration in people of any age. The progression of osteoarthritis can be slowed and symptoms managed, but there is no way to reverse the underlying causes that lead to the development of this condition.

Recent research in osteoarthritis has suggested that changes to the subchondral (below the cartilage) bone structures, such as a thickening of the subchondral plate, are discernible before lesions or other symptoms become detectable in the cartilage itself.

Current standards for the diagnosis and treatment of osteoarthritis rely on radiographic imaging to detect hardening of the subchondral layer or a decrease in joint space and visual and tactile inspection during arthroscopic surgery. In recent years, advances in imaging and computing power for analysis has led to an increased interest in the use of NIR to quantify the progression of joint damage and evaluate treatment during in vivo arthroscopies.

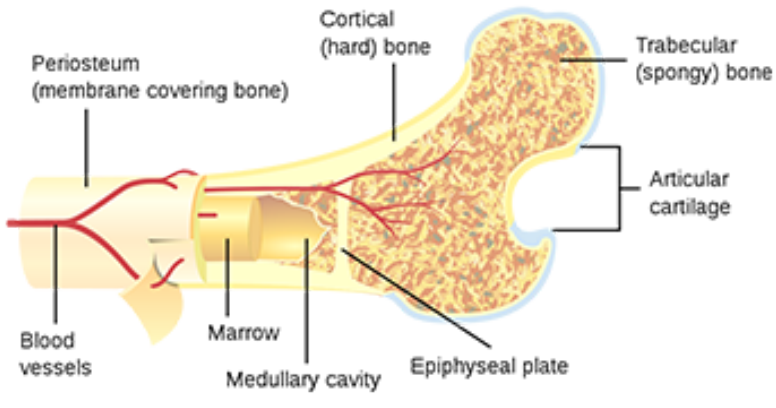


Fig. 1: Bone cross-section

Evaluating the Biomechanical Properties of Bone In Vitro

Research from the University of Eastern Finland published in June 2018 in the journal Nature investigated the potential for near-infrared spectroscopy for use in characterizing human subchondral bone properties and sought a wavelength range capable of estimating human bone properties in a clinical setting.

This experiment examined several key parameters of bone integrity in bone samples harvested from human cadavers, including subchondral bone plate thickness, bone mineral density, and structural model index using near-infrared spectroscopy.

The NIR spectral data was collected using a dual-channel Avantes system that paired the AvaSpec-ULS2048L-EVO with the high-sensitivity AvaSpec-NIR256/512-2.5-HSC-EVO (the 256 pixel version). Spectra were collected across three wavelength ranges already identified for the ability to penetrate living tissue, called the biologic or therapeutic optical window. The first window covered the range 650-950 nm, the next from 1100-1350 nm, and the third biologic window examined was 1600-1870 nm. This data was correlated against micro-computed tomography results of the same bone samples using partial least squares regression multivariate technique.

This work showed that wavelength-dependent penetration of light into osteochondral samples plays a significant role in the relationship between optical response and subchondral bone properties. The first optical window, λ 650-950 nm, showed the strongest correlation and lowest error rate against the tomography results and shows the greatest potential for adaptation into arthroscopy standards of care.

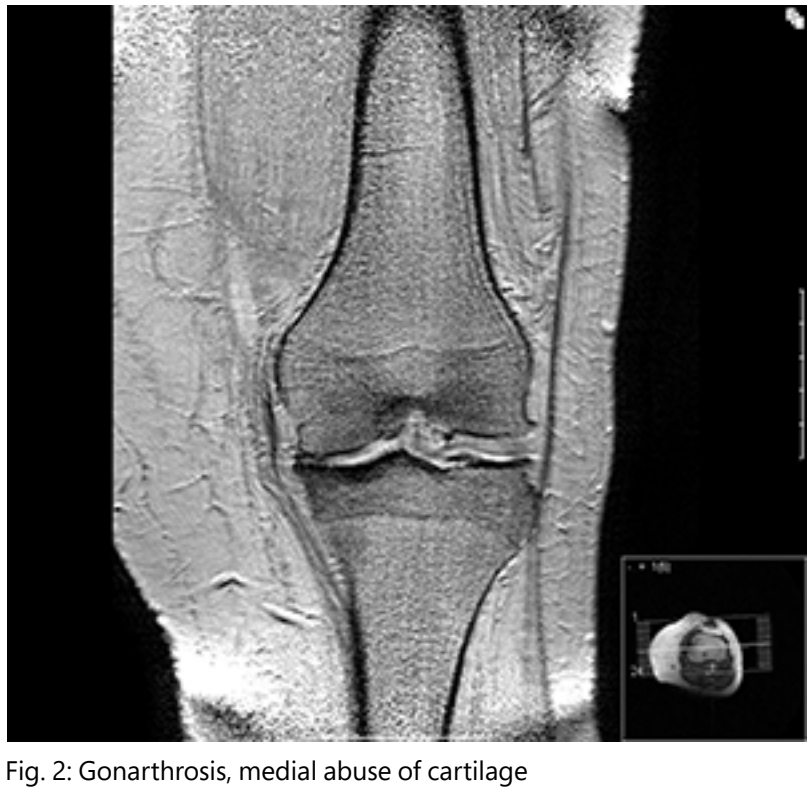


Fig. 2: Gonarthrosis, medial abuse of cartilage

Developing Clinical Applications for NIRS Arthroscopy

A second group of researchers from Utrecht University in the Netherlands and the University of Eastern Finland published research in the journal Nature in September 2018 that sought to prove the reliability of NIR spectroscopy to simultaneously evaluate both articular cartilage and subchondral bone in vivo with the assistance of an artificial neural network (ANN).

Currently, there are no quantitative arthroscopic tools to evaluate both cartilage and subchondral bone. Orthopaedic surgeons use radiographic imaging and subjective scoring of injury severity relying on visual inspection and tactile probing with a metal hook during arthroscopic surgeries. While some clinical tools exist for evaluating cartilage, their use is limited by practical issues, and no clinical tool currently exists for the evaluation of the subchondral bone morphology.

Using the AvaSpec-ULS2048XL-EVO, this study first collected NIR spectral data arthroscopically from ponies 12 months after receiving experimental joint repair procedures, then collected samples from the same ponies for in vitro spectral measurements. Additional spectral data was collected in vitro from samples harvested from unaffected ponies as a control. These samples also underwent optical coherence tomography (OCT) for the complete analysis of bone morphology to serve as a reference for prediction modelling with the assistance of a shallow Artificial Neural Network (ANN).

This experiment collected spectra from a broad wavelength range covering the visible from 450nm through 2500 nm in the near-infrared but discounted wavelengths over 1900 nm due to water's high NIR absorption properties. Additionally, the visible range between 450 and 750 nm saw interference from conventional arthroscopic light and therefore was only be used for probe orientation and positioning, but was excluded from modelling. The wavelength range between 750 and 1900 nm, which nearly spans all three therapeutic optical windows, was determined to be the optimal range for prediction of cartilage biomechanical properties including subchondral bone plate thickness, bone volume fraction and bone mineral density.

The results of the partial least squares analysis produced a prediction model capable of predicting bone integrity parameters with a 95% confidence rate. The measurements performed in vitro showed fewer prediction errors, unsurprisingly, likely because of inherent complications in achieving optimal probe placement while performing arthroscopy. There were also fewer prediction errors for analyzing the biomechanical properties of cartilage compared to analysis of the subchondral bone due to the tissue depth. Nevertheless, the researchers concluded that NIR spectroscopy was capable of simultaneous characterization of articular cartilage and subchondral bone integrity in humans with potential for augmenting conventional arthroscopy techniques in the clinical assessment of defective joints.

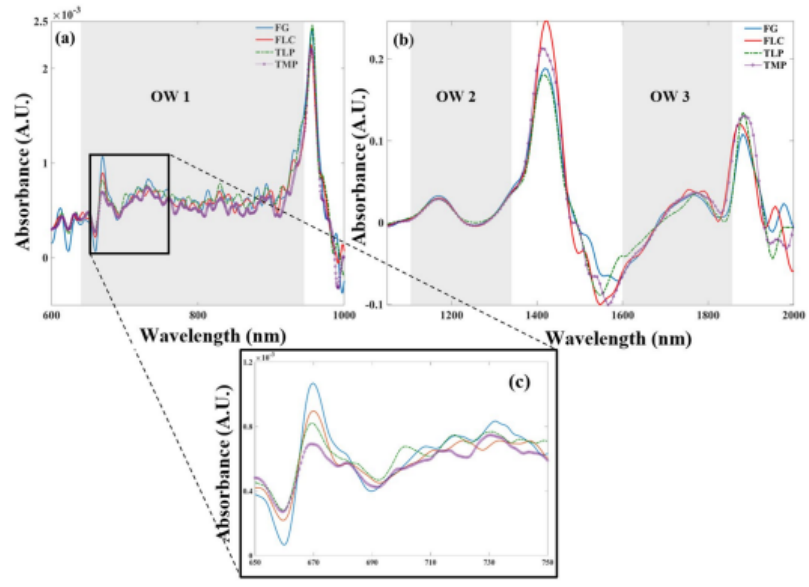


Figure 2. Representative 1st derivative NIR spectra of samples from the different anatomical locations highlighting the (**a**) 1st (OW 1), (**b**) 2nd (OW 2) and 3rd (OW 3) optical windows. The close-up view of a region of OW 1 (**c**) shows spectral variation with anatomical location consistent with the trend of differences in subchondral bone properties between FLC, TLP and TMP. [FG = femoral grove; FLC = femoral lateral condyle; TLP = tibial lateral plateau; TMP = tibial medial plateau].

Representative NIR Spectra Bone Samples

References:

Afara, Isaac O., et al. 'Characterizing human subchondral bone properties using near-infrared (NIR) spectroscopy.' Scientific reports 8.1 (2018): 9733. https://www.nature.com/articles/s41598-018-27786-3.pdf

Sarin, Jaakko K., et al. 'Arthroscopic near-infrared spectroscopy enables simultaneous quantitative evaluation of articular cartilage and subchondral bone in vivo.' Scientific reports 8.1 (2018): 13409. https://www.nature.com/articles/s41598-018-31670-5.pdf

'Osteoarthritis – Symptoms, and Causes – Mayo Clinic', 14 Nov. 2018. https://www.mayoclinic.org/diseases-conditions/osteoarthritis symptoms-causes/syc-20351925

1.8 Seeking the Key to Non-Invasive Diabetes Diagnoses & Monitoring

Diabetes is a chronic disease that affects more than 420 million people worldwide, roughly 8.5% of the population. Rates of diabetes have nearly doubled in the last three decades as more developing countries face increased urbanization and adopt Western eating habits. Treating diabetes requires constant monitoring and maintenance, which poses a significant burden for the afflicted, their families, and their communities. Additionally, increases in the rates of diabetes is taxing on healthcare systems and national economies.

Current diagnostic standards and therapies for diabetes are invasive and burdensome, but recent advances in medical sensing technology has put non-invasive diabetes testing and blood glucose monitoring within the reach of medical researchers. Avantes is proud to be on the forefront of the exciting breakthroughs emerging in the field of biomedical sensing.

Current Standards for the Diagnosis and Treatment of Diabetes

The diagnosis and ongoing management of diabetes currently requires direct measurement of blood glucose or glycated haemoglobin levels. There are a few methods used by medical professionals, including glucose tolerance tests and random or fasting blood sugar tests. These methods are primarily known as amperometric detection tests because the reaction of blood sugar to a reagent generates a small electrical charge proportional to the levels of sugar in the sample. This method can be very accurate when performed in a laboratory setting and is also standardized and well understood.

Current testing methods, while well established, still pose numerous problems for patients and medical professionals around the world. In some cultures, there may be taboos or societal strictures regarding the drawing of blood that makes it difficult to secure patient compliance. Blood samples are also unstable and require refrigeration. This can be a significant issue in developing nations, especially rural areas where electricity and refrigeration might not be readily available.

The chronic nature of managing diabetes requires those afflicted to monitor their glucose levels frequently on a daily basis. This involves collecting a tiny sample of blood, usually with a lancet prick to a finger. This procedure can be painful and can create additional complications if a diabetic has suppressed healing abilities, and they must be performed repeatedly on a daily basis.

While handheld blood glucose monitors are becoming more readily available around the world (accounting for roughly 85% of all biomedical sensors sold to consumers today), the monitoring of glucose is still a manual process requiring test strips. Combined with environmental factors that could affect the test such as temperature and humidity, these blood-testing meters might not provide accurate measurements under all conditions.

The Search for Non-Invasive Glucose Monitoring

Because of the invasive and repetitive nature of glucose testing, and the difficulties associated with blood testing around the world, researchers are eagerly seeking non-invasive alternatives to standard amperometric detection tests. Researchers have investigated many alternatives including electrochemical testing and carbon nanotube-based methods. Recently, the focus has shifted to optical methods of detection using NIR absorbance and Raman spectroscopy.

Two of the most promising methods under investigation include the use of near-infrared light to measure blood glucose directly through the skin, with much the same functional design as a pulse oximeter. Another method under investigation involves the use of fingernails as a testing sample.

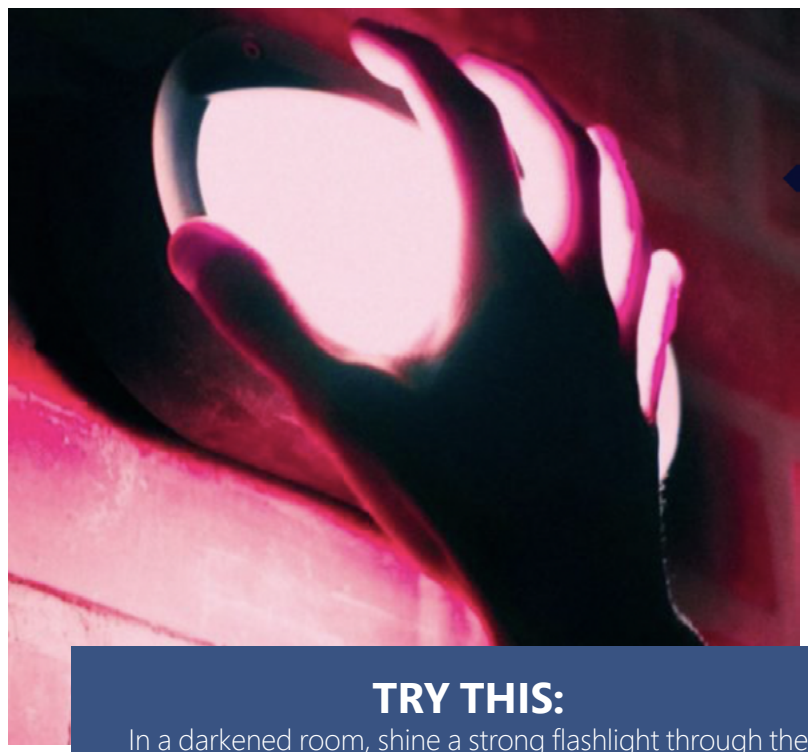
The largest hurdle researchers face when developing a new non-invasive testing protocol for diabetes is the creation of standardized models for interpreting results. Measurement parameters must account for absorption patterns, linear uptake rates, and countless other factors that doctors and scientist must understand to develop a repeatable and standardized model for interpreting and predicting spectra response. There are also variations across human characteristics and these variations must also be neutralized to allow for standardization of a new protocol.

Near-Infrared and the Diagnostic Window

Much of the optical sensing technology for biomedical applications centres around the near-infrared due to a peculiar phenomenon researchers refer to as the diagnostic window, or the optical window.

Light absorption by human tissues is wavelength-specific. Proteins and DNA absorb the ultraviolet (UV) spectrum, visible light is absorbed by hemoglobin in the blood, and the infrared range is highly absorbed by water. At the very end of the visible spectrum, however, and into the near infrared (NIR) range between 650 nm and 1100 nm, there is little absorption by water or haemoglobin and less scattering than in the UV and visible ranges. And, most importantly, it is possible to use light in this range on living subjects without causing tissue damage.

This optical diagnostic window allows doctors and researchers a view into the body. Dr Frans F. Jöbsis at Duke University demonstrated in his landmark 1977 study that oxygenated and deoxygenated tissues show distinct absorption properties in the NIR. Since then, NIR spectroscopy has been used in the study of metabolic diseases like diabetes, cancers, cardiovascular diseases, neurological disorders, and many other conditions afflicting our societies.

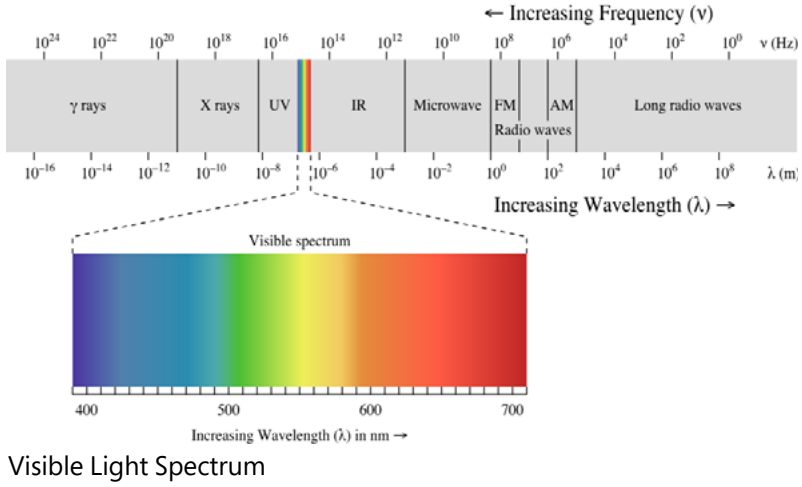


TRY THIS:

In a darkened room, shine a strong flashlight through the palm of your hand. Looking at the back of your hand, you will see a red spot of light on the back of the hand. What you see is the tail end of the spectrum of visible light, the red light between 650-750 nm, which falls within the optical diagnostic window of 650-1100 nm

NIR Raman Spectroscopy

Recent experiments in the development of optical biosensors couple the optical window available in the Vis/NIR range with the molecular fingerprinting specificity of Raman spectroscopy. The potential of this technique is very promising, but the added complexity of Raman analysis increases the barriers to developing standardized diagnostic models.



Visible Light Spectrum

Glycated Nail Protein Suitability for Diabetes Testing

Because glucose testing is of vital importance to a growing diabetic population, and because the demand for glucose sensors represents 85% of the biosensors market, Biomedical device developers are in a race to present the next wave advancement in blood monitoring technology.

One line of investigation involves the assay of glycated keratin proteins. Keratin, the protein that makes up our fingernails and hair, can bond with glucose. This glycation has a linear relationship to blood glucose levels over time. Researchers seeking a spectral model for diagnosing diabetes choose fingernails due to observable differences in nail characteristics of diabetics. For the purposes of developing a standardized model, fingernails are also preferable because there is less growth-rate variation than for hair. The use of fingernail clippings has the potential to improve testing for initial diagnosis of diabetes, especially in developing nations. Fingernail clippings can be collected without pain and without requiring special training. Additionally, psychological and cultural attitudes regarding fingernail clippings are relaxed compared to bodily fluids like blood; and since they are stable, fingernails can be stored without refrigeration without loss of sample viability.

For testing, fingernail samples are ground and mixed with a reactive agent. Because nails are not very permeable to these reactive agents, the samples require preparation time and possibly further processing. This method, while minimally invasive, does still require expert sample preparation that should be done in a lab by trained personnel and, unfortunately, will not be suitable for home glucose monitoring.

Transmittance via Earlobe for Home Use

The transmittance measurement technique is another one that researchers are developing, and one that would be suitable for home monitoring applications. Lobe transmittance measurements actually require a combination of wavelengths applied to the ear lobe simultaneously. The attenuated light is caught by sensors on either side of the earlobe. First, the reflectance of green visible light is used to determine skin parameters such as tissue thickness. Next, red light transmittance/absorption is used to determine blood volume, and finally the NIR wavelength is used to determine glucose concentrations.

This method shows a great deal of promise, as it is a simple design involving a clip for the earlobe which connects to a spectrometer with fibre cables making it relatively easy for anyone without special training. Additionally, the lack of sample preparation and easy design mean that it will not require laboratory oversight and can be performed by anyone.

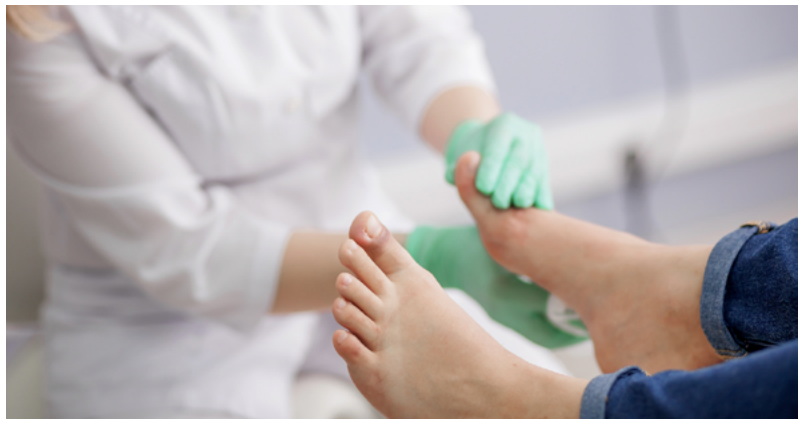
Overcoming Barriers to Optical Glucose Monitoring

For many diagnostic methods being investigated today, the main barrier to full testing validation is researchers' ability to reconcile individual variation to create a standardized model for analysis of the results. The work of these scientists and experts bring us closer every day to the reality of non-invasive, inexpensive and accurate blood glucose monitoring alternatives. While it is impossible to predict when a new method or technology will win approval of the Federal Drug Administration (FDA) or relevant medical certifying bodies, it is becoming increasingly likely. In the near future, diabetes patients will no longer need to suffer through

painful blood testing and it will be thanks to the work of dedicated scientists, doctors, and researchers working today on these exciting optical testing methods.

At the Forefront of Medical Research

Dr Angelika M. Domschke, previously with the University of Hamburg, is researching ophthalmic glucose monitoring using the AvaSpec-ULS2048 to test and monitor the development of a contact lens that sits in the eye and provides continuous monitoring. The ULS2048 provided Dr. Domschke and her team with exceptional response speed and a signal-to-noise ratio of 200:1. This is the reliable workhorse of the Avantes StarLine spectrometers.



Researchers at Groningen University in the Netherlands are studying skin fluorescence to monitor vascular damage. Diabetes patients are susceptible to vascular damage, poor circulation and slow healing in their extremities, this team aims to make treating diabetic foot complications easier. These researchers used an older model from Avantes, but our AvaSpec-Hero offers the highest sensitivity due to the 0.13 numerical aperture of the optical bench and thermo-electrically cooled, back-thinned detector. This instrument is ideally suited for the demands of high-sensitivity measurements in the NIR.

Dr Ishan Barman, in his doctoral thesis in the MIT Department of Mechanical Engineering, studied the challenge of developing accurate diagnostic models with NIR Raman spectroscopy. In his work 'Unraveling the puzzles of spectroscopy-based non-invasive blood glucose detection,' his system recommendations for a spectrometer describe an instrument that matches the system specs of the AvaSpec-Hero. This instrument offers optimal sensitivity with a 0.13 numerical aperture which collects nearly the full light carried by a fibre optic. The Hero offers the optimal balance between high sensitivity and high resolution, with a TE Cooled back-thinned detector. It is capable of facilitating longer integration times in low-light applications, making this your optimal choice in Raman systems.

Researchers around the world trust Avantes instruments for biomedical research. The Avantes SensLine of spectrometers offer several models tailored for applications with low light levels with standard or thermoelectrically cooled options. Another great solution is the Avantes CompactLine of miniature spectrometers. The AvaSpec-Mini packs a lot of power into a compact size. At about the size of a deck of cards, this unit performs on par with many of our the larger form factor instruments.

References:

https://www.cdc.gov/diabetes/data/statistics/2014statisticsreport.html
https://www.cdc.gov/diabetes/data/index.html
https://professional.diabetes.org/content/fast-facts-data-and-statistics-about-diabetes
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3500977/
https://www.researchgate.net/publication/7882853_Home_blood_glucose_biosensors_A_commercial_perspective
http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf
http://www.edn.com/design/systems-design/4422840/Non-invasive-blood-glucose-monitoring-using-near-infrared-spectroscopy

1.9 Dermal Reflection

Reflection measurements on skin an internal tissues can reveal a great deal of information which can aid in the diagnosis of conditions. One example of such measurement is the detection of advanced glycogen end products (AGEs) in patients using a dermal autofluorescence measurement. Deep tissue reflection may also be measured in the near infrared (800-1100 nm) to determine the effectiveness of radiation therapy at reducing cancerous masses. Ultra violet and visible fluorescence may also be used in the detection of cancerous tissues. Avantes offers a number of high sensitivity, low stray light instruments for medical and biomedical detection. The AvaSpec-HS2048XL-EVO back-thinned CCD operates over the range from 200-1100 nm features a 0.22 numerical aperture and back-thinned CCD detector for optimal sensitivity. Fibre-optic sampling facilitates the non-invasive measurement of small areas.

2

SECTION 2

MEDICAL RESEARCH AND SPECTROSCOPY

Many biomedical research applications exploit the natural fluorescence response of amino acids, the essential building blocks of all proteins. These protein fluorescence responses to light have been used for everything from pharmaceutical manufacturing to cancer treatments, and even biowarfare defence. Exploring this biomedical spectroscopy niche is a dive into the deep end of cutting-edge science. Spectroscopy is an essential technology that makes these biomedical applications, and so many others, possible. Avantes, a leader in the development of high-sensitivity, high-resolution spectrometers, is the trusted choice for hundreds of researchers and original equipment manufacturers in biomedical applications.

2.1 Protein Detection and Identification

Proteins and Amino Acids

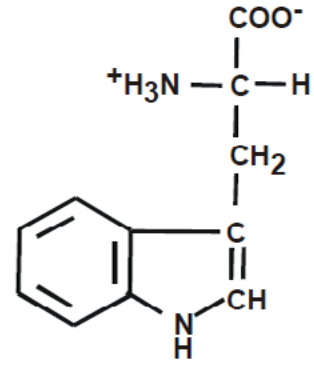
Proteins, the complex organic compounds made of chains of amino acids, are the most abundant organic molecule in all living things on Earth. These molecules play many roles within cells and organisms. They act as catalysts in biochemical reactions, as hormones, regulate physiological processes, and defend the body against disease. Many of these proteins have a weak intrinsic fluorescent response to UV excitation, with different proteins reacting to excitation at specific wavelengths and fluorescing at different wavelengths depending on the species.

Molecular Structure

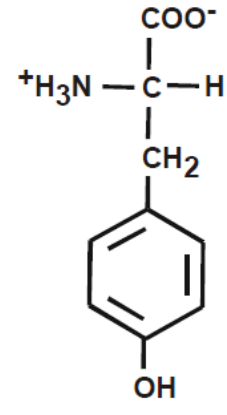
Three common amino acids – tryptophan, tyrosine, and albumin, which are responsible for the majority of inherent fluorescence – have a common structure consisting of hydrogen-based ring structures. These ring structures, called aromatic hydroxyl groups, absorb UV radiation and emit a weak fluorescent signal at varying wavelengths.

Interactions

The amino acid compounds have distinct absorption and emission profiles, and different quantum yields. They can also react to each other, changing the spectral profile; the presence of tryptophan, for example, will quench the fluorescent signal of tyrosine due to resonant energy transfer of a similar excitation wavelength. Tryptophan can be excited at 280 nm, while tyrosine can be excited at 274 nm. The fluorescence response is significantly different, however; tryptophan fluoresces at 348 nm, while tyrosine's response can be detected at 303 nm. Albumin, on the other hand, when excited at 257 nm, will fluoresce at 282 nm. Because these amino acids are prevalent in all life on earth and are the common building blocks of many more complicated proteins, the reactions of these amino acids are often used as a representative sample for these complex proteins in research applications. Changes in the reaction can also be monitored as a process control function.



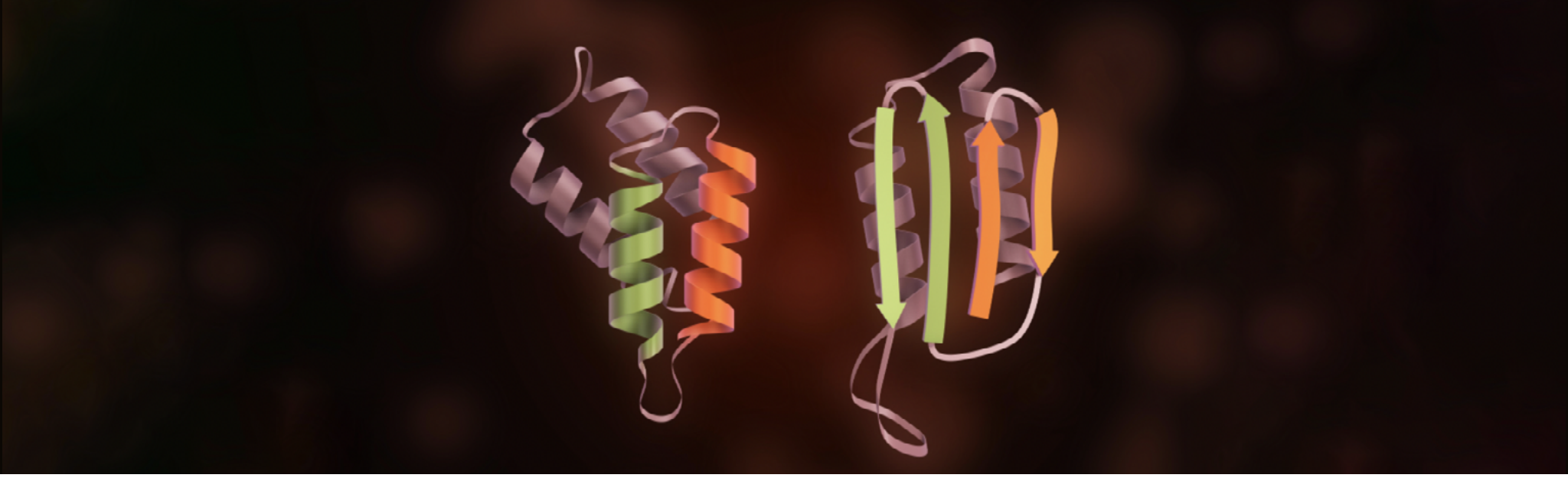
Tryptophan



Tyrosine

Reference:

Held, P. 'Quantitation of peptides and amino acids with a Synergy™ HT using UV fluorescence.' B.-T. Instruments, Winooski, VT (2003).



2.2 Protein Contamination Detection on Surfaces

Research has demonstrated that conventional methods of sterilization, including thermal and chemical processes, are not sufficient to guarantee complete inactivation of all pathogenic biomolecules, especially proteins. It's a grave concern in surgical settings where the decontamination of reusable medical instruments can directly impact patient care.

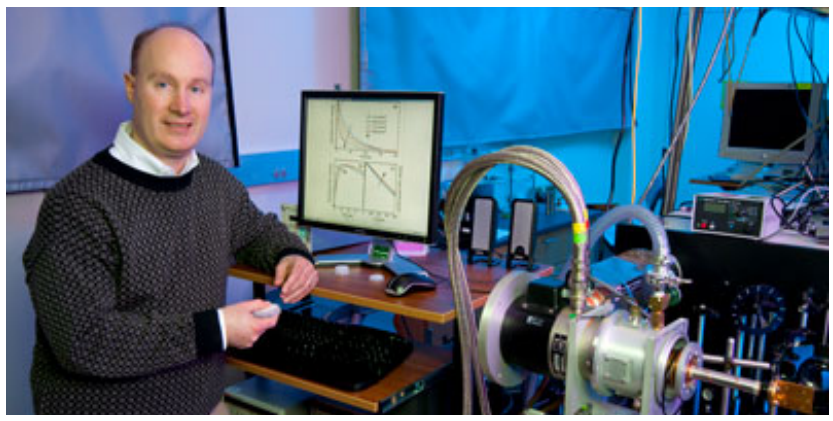
One class of proteins is of particular concern, Prions are proteins that are folded 'wrong' manifesting in fatal neurological degenerative diseases like the human variant of mad cow disease called Creutzfeldt-Jakob disease, Kuru, and Fatal Familial Insomnia. While rare, these diseases are caused by infectious proteins that transmit their incorrect folding patterns to new proteins in a manner epidemiologically similar to a viral infection. Because proteins are the compound most resistant to current methods of decontamination, transmission of these 'contagious' neurological diseases present a serious danger. A new method of decontamination being investigated requires a low-pressure, inductively coupled plasma discharge. Spectroscopic instruments are used for process control and monitoring test results.

Reference:
Kylián, Ondřej, et al. 'Elimination of Homo▫polypeptides of Amino Acids from Surfaces by means of Low Pressure Inductively Coupled Plasma Discharge.' Plasma Processes and Polymers 6.12 (2009): 848-854.

2.3 Detection of Dangerous Biological Compounds

Researchers at the Swedish Defence Research Agency (FOI) are investigating the use of fluorescence spectroscopy as the first line of detection in bioaerosol detection systems. Due to the dangerous nature of biological warfare agents (BWAs) themselves, tyrosine and tryptophan – amino acids likely to be a part of any biological agent – are used in testing in the place of these BWAs. An ideal system would be able to monitor minute particle concentrations in real time and identify compounds present with a high degree of specificity.

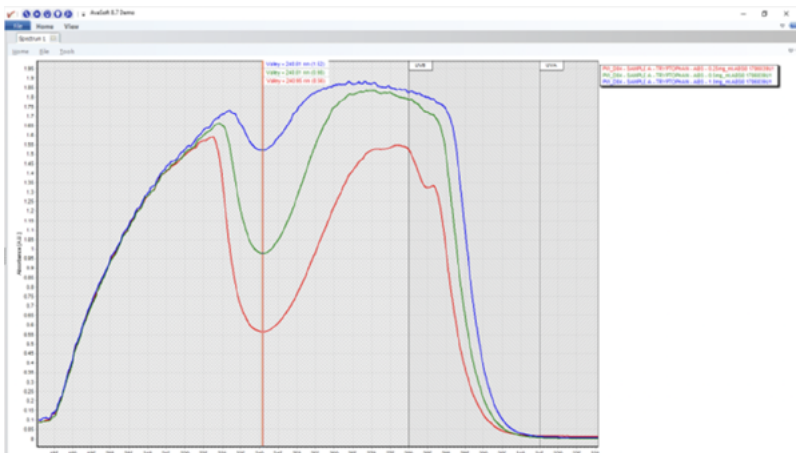
The system in testing with the Swedish researchers forces ambient air through a nozzle to be confined to a single particle beam and passed through the optical chamber. The use of a continuous wave blue laser at 404 nm, received by an Avantes spectrometer, acts as a trigger. At this stage, fluorescence and scattering are analyzed. When a compound is present at pre-determined detection levels, it triggers a pulsed UV laser at 263 nm. The resultant laser-induced fluorescence can be further analyzed to classify individual aerosol particles.



Reference:
Jonsson, Per, et al. 'Bioaerosol detection and classification using dual excitation wavelength laser-induced fluorescence.' Chemical, Biological, Radiological, Nuclear, and Explosives (CBRNE) Sensing XVI. Vol. 9455. International Society for Optics and Photonics, 2015.

2.4 Experimental Design

Avantes US Engineers reproduced a series of experiments conducted with samples of tryptophan, tyrosine, and bovine serum albumin recently to demonstrate our protein- detection capabilities. The team used conventional absorbance techniques with a continuous wave (CW) illumination source (AvaLight-DHc) and an AvaSpec-ULS4096CL-EVO spectrometer configured for UV (190-400 nm). Absorption measurements, recorded between 190- 320 nm, correlated changes in concentration to changes in absorption. Fluorescence was not measured during this experiment.



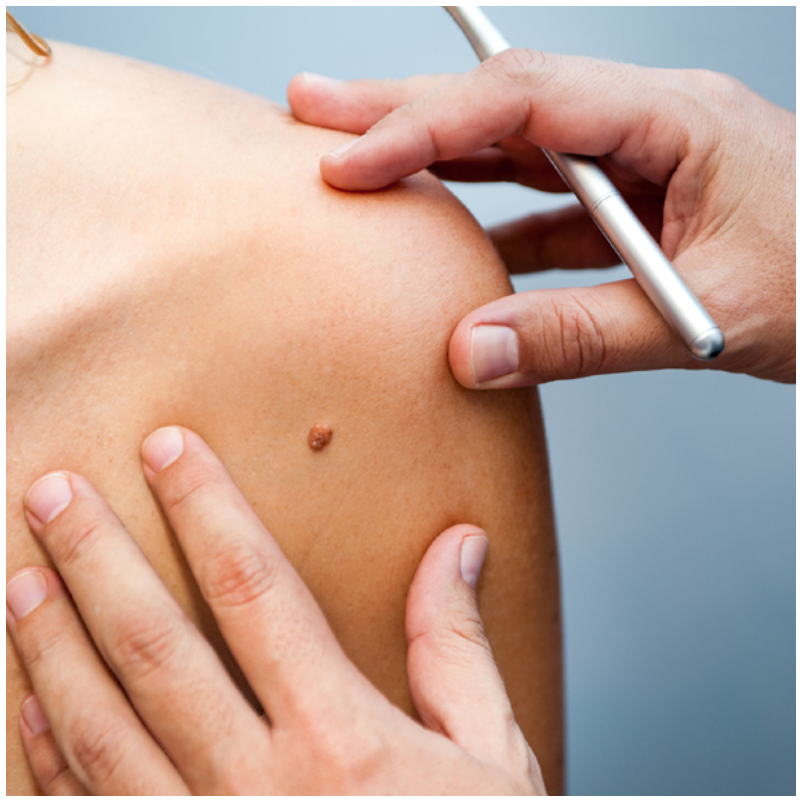
Spectral absorption response of tryptophan at different concentrations

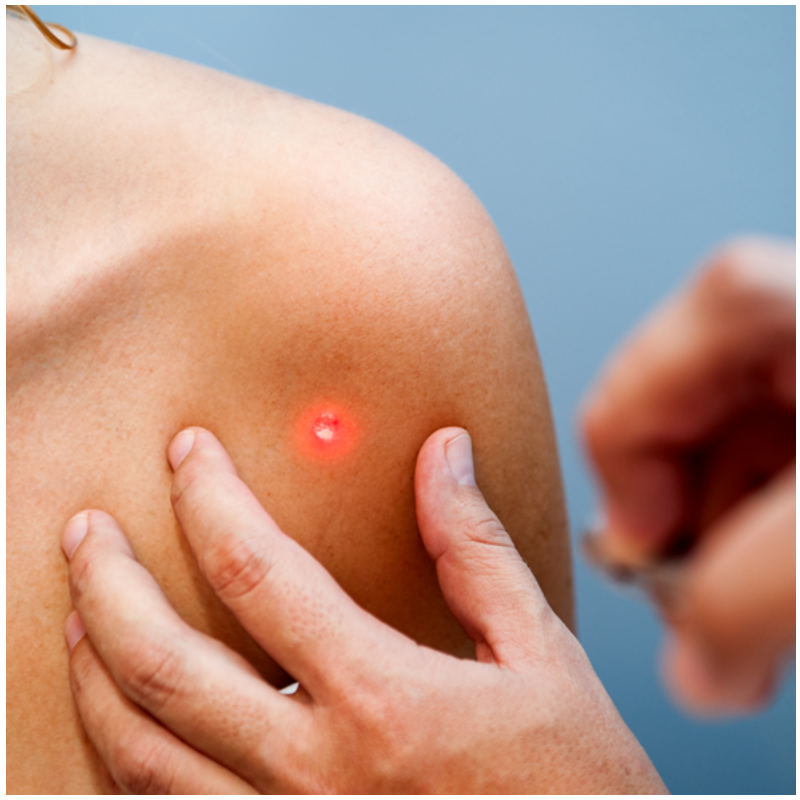
Results

The absorption profiles of the amino acids correlated directly with the amino acid concentration in solution. As fluorescence is a function of absorbance and quantum yield, the fluorescence can be estimated and would be expected to also correlate with concentration.

2.5 Diffuse Reflection

Researchers at Irvine Beckman Laser Institute (located on the campus of the University of California at Irvine) have used near-infrared spectroscopy not only to identify and monitor cancer mass reduction during chemotherapy treatments but also 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 the full collection of the light received by a fibre optic of the same NA.





NIR Diffuse Reflection

Reference:

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.

2.6 Exploration of Fluorescence Theory and System Design

Fluorescence spectroscopy is a powerful tool for identifying the presence of both organic and inorganic molecules in complex systems. This can be accomplished by either utilizing the inherent fluorescence properties of the molecule – a process also referred to as 'autofluorescence' – or by introducing a molecular tag into the system which has a known fluorescence spectrum and an affinity for the molecule of interest. These fluorescent tags, also known as 'fluorophores', can be engineered with specific absorption and emission bands enabling the use of multiplexing to detect a wide variety of species in a single analyte.

This technique is widely utilized in many biological and biomedical applications including DNA sequencing, and when used in tandem with confocal microscopy, provides multispectral images of cells and other small objects. Another typical application of fluorescence spectroscopy comes from the field of anti-counterfeiting, where fluorescent tags are added to the ink of currency. When illuminated by the proper excitation wavelength, these tags emit a unique fluorescence spectrum known only to the manufacturer.

Theory of Fluorescence Spectroscopy

To fully understand just how powerful fluorescence spectroscopy is, it is useful to briefly explore the fundamental physics involved. Before the fluorescence process can occur, a molecule must first absorb a photon with enough energy to excite the system from the ground state (S_o) to the next electronic energy level (S_1). Once the molecule is in the excited state, it releases this excess energy as quickly as possible to relax back down to the more stable ground state. This excess energy must be converted into a combination of phonons and photons called non-radiative or radiative decay. As shown in Figure 1, in the case of fluorescence emission, the molecule will first drop to a lower vibrational state non-radiatively in the S1 band before radiatively decaying to the S0 band. This process results in the emitted photon having less energy than the absorbed photon, therefore 'shifting' to a longer wavelength compared to the absorbed photon, this shift in wavelength is referred to as a 'Stokes shift' and is demonstrated in the Jablonski diagram of electronic states.

The intraband vibrational mode structure and the energy differential between S_0 and S_1 are highly dependent on the molecular bond structure, particularly the presence of double and triple bonds which exploit loosely bound p-electrons. As a result, complex organic and biological molecules tend to exhibit high autofluorescence. This response is why the life sciences were among the earliest adaptors of fluorescence spectroscopy and allows for the design of large organic molecules known as fluorophores with specific absorption and emission properties tailored for specific applications. Furthermore, these fluorophores can be designed to bond with specific molecules of interest, creating chemically sensitive fluorescence tags such as those mentioned previously for DNA sequencing. In recent years,

quantum dots have also become popular in fluorescence applications. In this case, the emission spectra are not related as much to the molecular structure of the material but instead are dependent on the size of the quantum dot itself. As the cost and complexity of nanofabrication technology have come down over the past decade, quantum dots are increasingly used for a wide range of fluorescence applications including anti-counterfeiting.

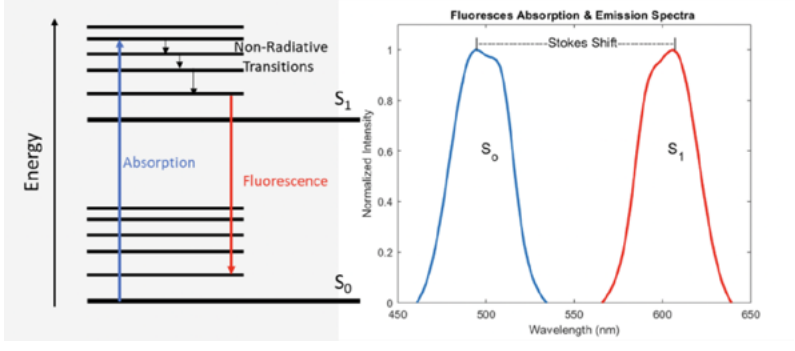


Fig. 1: Jablonski Diagram and the fluorescence absorption/emission spectra of a typical fluorescent molecule

Typical Measurement Configurations

Because fluorescence spectroscopy can be used in such a wide variety of applications, the instrumentational configurations also vary widely depending on the application. For this reason, most researchers prefer to use configurable components which can be easily swapped in and out depending on the needs of the specific application. Avantes has worked closely with many researchers and process engineers to facilitate fluorescence measurements in the laboratory, clinical, and industrial environments using our fibre-coupled miniature spectrometers, light sources, and accessories. Over this period, we have developed a full suite of fluorescence spectroscopy configurations, which researchers have been able to use in both laboratory and translational research. Many of these configurations have also served as the basis for a wide range of commercial products which utilize Avantes' OEM spectrometers as their measurement tool.

Due to the relatively low-energy levels associated with fluorescence spectroscopy compared to other methods such as UV/Vis spectroscopy, it is generally preferable to select a high-sensitivity spectrometer such as the AvaSpec-HERO or the AvaSpec-HS2048XL-EVO. Higher-sensitivity spectrometers such as these are particularly useful in more demanding applications such as the measurement of autofluorescence in tissues or the detection of low-concentration fluorophores in a sample matrix. Fortunately, when compared to other low-light spectroscopy applications, such as Raman spectroscopy and diffuse reflection spectroscopy, fluorescence has the advantage of relatively broad emission bands allowing for spectroscopists working with stronger fluorescing samples to alternatively consider a less sensitive spectrometer such as the AvaSpec-ULS2048CL-EVO or the AvaSpec-Mini2048CL with a wide entrance slit to accept more light into the spectrometer. Nearly all Avantes spectrometers come with the option of replaceable entrance slits, which allow the user to experimentally determine the optimal entrance slit width for each specific fluorescence application, further enhancing the flexibility afforded by fibre- coupled miniature spectrometers.

Cuvette-Based Measurements

The simplest of all fluorescence spectroscopy set-ups utilizes a fibre-coupled cuvette holder with orthogonal connection ports to collect spectra from a sample in solution in a standard 10ml cuvette. This approach is possible because most small molecule solvents, such as water, alcohol, and cyclohexane, have virtually no autofluorescence signal, allowing for the sample and fluorophore to be dissolved in a solution for easy handling.

While similar to typical UV/VIS measurements, in a fluorescence measurement configuration, the excitation port, and the collection port must be orthogonal (at 90-degree angles) to each other, as shown in Figure 2 below, to prevent transmitted light from the excitation source from overpowering the fluorescence single. When utilizing this fluorescence measurement configuration, the port in line with the excitation source might be left open to prevent the transmitted light from reflecting around inside of the cuvette holder. It may also be capped with a mirror to create a double pass cell, or connected to a second spectrometer in order to simultaneously measure the UV/VIS absorption spectrum. The dual UV/VIS and fluorescence capability of this simple component set-up is particularly useful for performing quality control during the manufacturing of fluorescent

dyes and quantum dots as it allows for the simultaneous determination of the excitation and emission properties of the molecule.

Additionally, a thermoelectrically controlled cuvette holder like the CUV-UV/VIS-TC (displayed in Figure 2) allows the operator to precisely control the temperature of the sample between -30°C and +105°C with an accuracy of 0.05°C. This type of cuvette holder not only provides the ability to stabilize the temperature of the sample during the measurement but also allows for the sample temperature to be varied in real time, allowing for the quantification of temperature effects on the emission spectra.

Figure 2: CUV-UV/VIS-TC-Temperature controlled cuvette cell holder from Avantes

Probe-Based Measurements

While cuvettes work well for many applications, it's not always desirable to remove a sample for testing purposes. When testing liquid or powder samples, one alternative is to utilize a fibre-optic fluorescence probe like the one shown in Figure 3. These probes use a bifurcated design allowing the excitation source to be coupled to one leg and the spectrometer to the other leg. While these probes can utilize many different internal fibre configurations, for example, twelve 200-micron core fibres surrounding one 600-micron core fibre as shown in Figure 3, they all have one thing in common: the excitation and collection paths at the sample are both colinear. This geometry dramatically simplifies the probe design allowing for a compact form factor, but it does result in increased excitation signal collection compared to the orthogonal approach utilized by a cuvette holder.

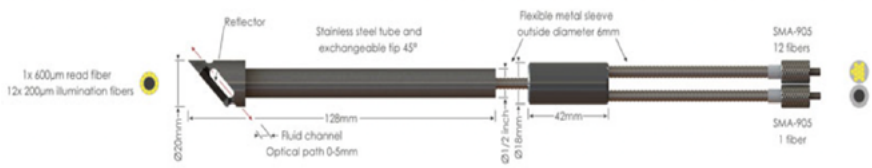


Figure 3: FCR-UV200/600-2-IND – Fluorescence probe from Avantes

To mitigate the collection issues associated with this fluorescence system configuration, it becomes necessary to add additional filtration steps along the collection path. Avantes offers both inline and direct attached filter holders which allow the user to filter the signal on both the excitation and collection paths. Typically, placing a bandpass filter in the excitation line, and only allowing light in the excitation band into the probe will accomplish this. Since there is no such thing as a perfect filter, however, it is often necessary to add a long pass filter on the collection path to further reduce the excess light from the excitation source. Figure 4 (on next page) shows an example set-up where the FH-DA direct attach filter holder is attached to the excitation light source, and an FH-INL inline filter holder is inserted between the collection leg of the bifurcated fibre and a patch cord connected to the spectrometer.

In addition to standard immersion measurements, fluorescence probes are also ideal for in situ testing in a wide variety of fields ranging from biomedical diagnostics to archaeological research. For each of these applications, the probe fibre configuration may be slightly different from the example shown in Figure 2, but the overall principle remains the same. One unique application of fluorescence probes are in dental curing, where the ultraviolet light source can serve both as the catalyst for curing and as the excitation source for the fluorescence measurement itself.

Another interesting utilization of these probes is in art authentication, where the fluorescence spectra can provide insight into pigments used in the production of a painting, allowing investigators to determine if the paint used matches the period when that work of art was allegedly produced. However, overexposure to ultraviolet light can also damage the pigments themselves, so ensuring the integrity of the work requires additional care.

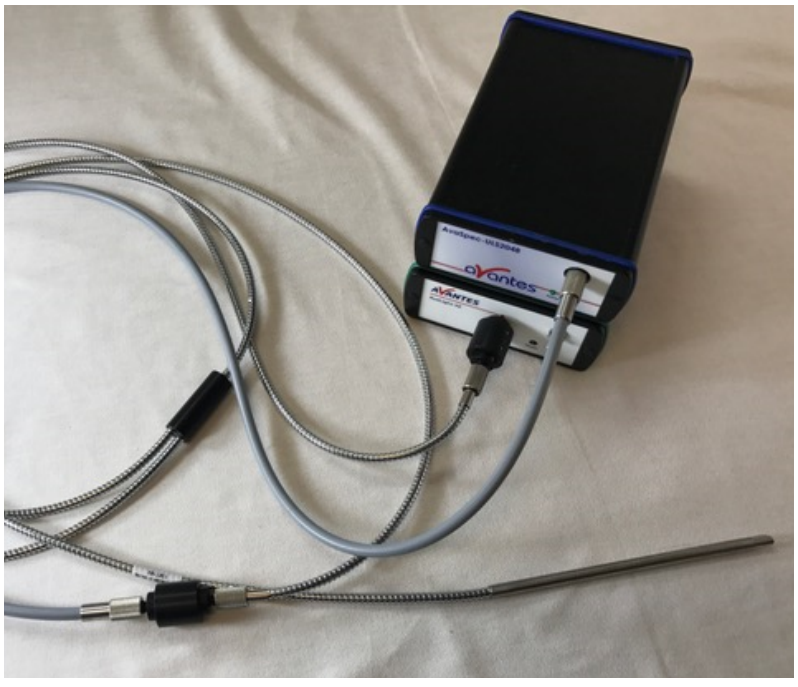


Fig. 4: Typical set-up fluorescence probe configuration

Fluorescence Microscopy

Fluorescence microscopy dates to the early 20th-century, coinciding with the invention of the ultraviolet microscope in 1911. Early researchers in the field quickly realized that ultraviolet excitation – which was originally chosen in an attempt to increase spatial resolution of the images – was inducing autofluorescence in their samples, and by 1914 they had demonstrated that fluorophores could be created to bind to living cells which allowed molecular information to be ascertained on the microscopic level for the first time.

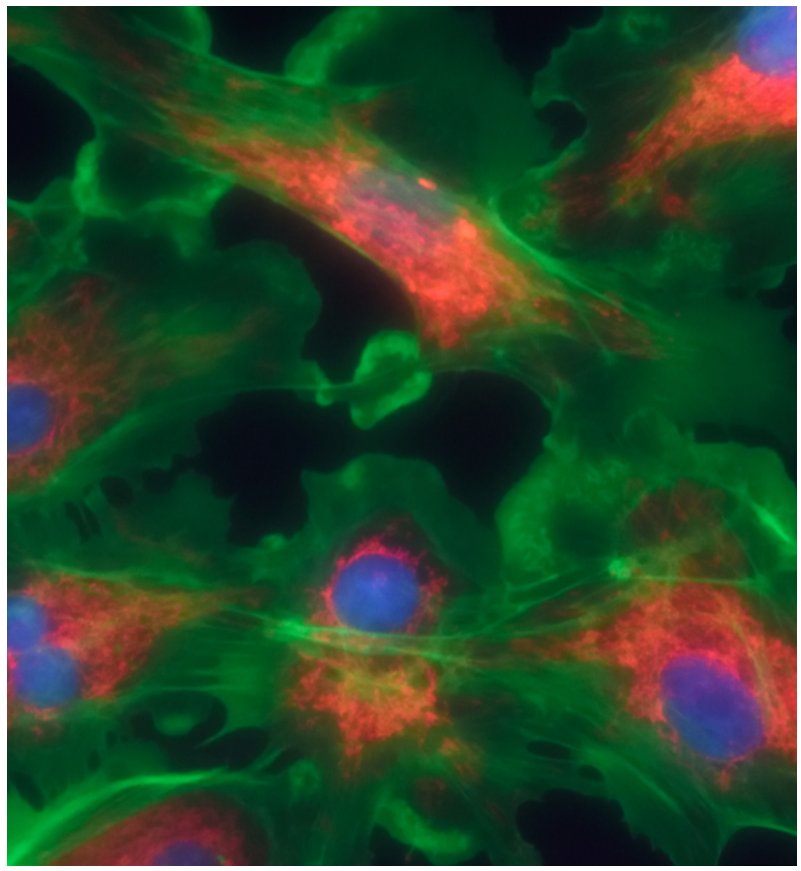
Since then, fluorescence microscopy has become one of the most widely utilized techniques in biological sciences, providing high-resolution hyperspectral imaging of living cells and other biological samples. While in most cases, the excitation source is a single mode laser to allow for diffraction limited imaging, the spectrometer requirements are otherwise virtually the same as the other configuration discussed earlier.

Avantes offers three standard microscope adaptors which allow the user to easily connect a miniature spectrometer to any standard microscope port via a fibre-optic patch cord.

Final Thoughts

Avantes offers a wide range of spectrometers and accessories that are ideal for both laboratory and OEM fluorescence spectroscopy applications including the AvaSpec-HS2048XL-EVO, AvaSpec-HSC1024X58-TEC (AvaSpec-Hero), and AvaSpec-ULS2048XL-EVO. Each of these spectrometers is available as either a standalone unit, OEM module, or can be integrated into a multichannel rack mount system that combines excitation source and spectrometer(s) in a single housing, making them ideal for custom-designed laboratory or inline systems. The AvaSpec instrument line communicates via USB3.0, Ethernet, RS-232 and allows active digital & analogue input/output capabilities providing a multitude of interface options with other devices.

Additionally, the Avantes AvaSpec DLL software development application, with sample programs in Labview, MatLab, Delphi, Visual Basic, C#, C++, and many other programming environments, enables users to develop their own code for fluorescence applications.



2.7 Effects of Light on the Biological Clock

Most organisms have a biological clock which has evolved as a consequence of the rotation of the Earth around its axis. The biological clock generates rhythms of about 24 hours and adapts to daily changes in its environment.

Light is the main synchronizer of the biological clock to the external light-dark cycle, and is detected by photoreceptors in the eye. To determine the effects of light on the biological clock in mice, in vivo electrophysiological recordings of neurons of the biological clock were performed. Mice were exposed to various wavelengths of light using monochromatic LEDs.

Principles of the Biological Clock

Most organisms have a circadian clock, which has evolved as a consequence of the rotation of the earth around its axis. The circadian clock resides in the suprachiasmatic nucleus and generates rhythms of about 24 hours.

The suprachiasmatic nucleus adapts to daily changes in its environment. Light is the main synchronizer of the biological clock to the external light-dark cycle and is detected by ocular photoreceptors in the retina. Light information is then sent to the suprachiasmatic nucleus via the optic tract. In the suprachiasmatic nucleus, light information leads to an enhancement in electrical activity of the neurons.

Experimental Conditions

To determine the effects of light on the biological clock in mice, in vivo electrophysiological recordings of neurons were performed.. Mice were exposed to three different wavelengths of light using monochromatic LEDs. The wavelengths of light used were UV (max 365 nm), blue (max 467 nm) and green (max 505 nm).

During light exposure, the extracellular activity of a group of neurons of the suprachiasmatic nucleus were recorded.

The spectrometer used in these experiments is an AvaSpec-2048. We have since released its successor: the AvaSpec-ULS2048CL-EVO. This spectrometer was used to determine the exact wavelength of light, including the bandwidth and to determine the light intensity and amount of photons per wavelength light.

Results

Exposure to all three wavelengths of light led to an enhancement in electrical activity of neurons of the suprachiasmatic nucleus. The effects of light on electrical activity of the neurons were dependent on the wavelength, duration and intensity of light.

Similar to behavioural effects of light, the effects of light on electrical activity of the neurons were time dependent. Light exposure during the night led to a large enhancement in neuronal activity, while light exposure during the day led to a minimal increase.

3

SECTION 3

FIND YOUR IDEAL MEASUREMENT SETUP

In this section you'll find the instruments used in the applications displayed in this eBook. If you need help finding your most ideal measurement setup, feel free to let us know. We offer the free option to perform a feasibility study or you can try a setup through our free Demo Program.

Either way, we strive to offer you the best measurement solution that matches your application needs.
We're happy to help!

3.1 Demo Program

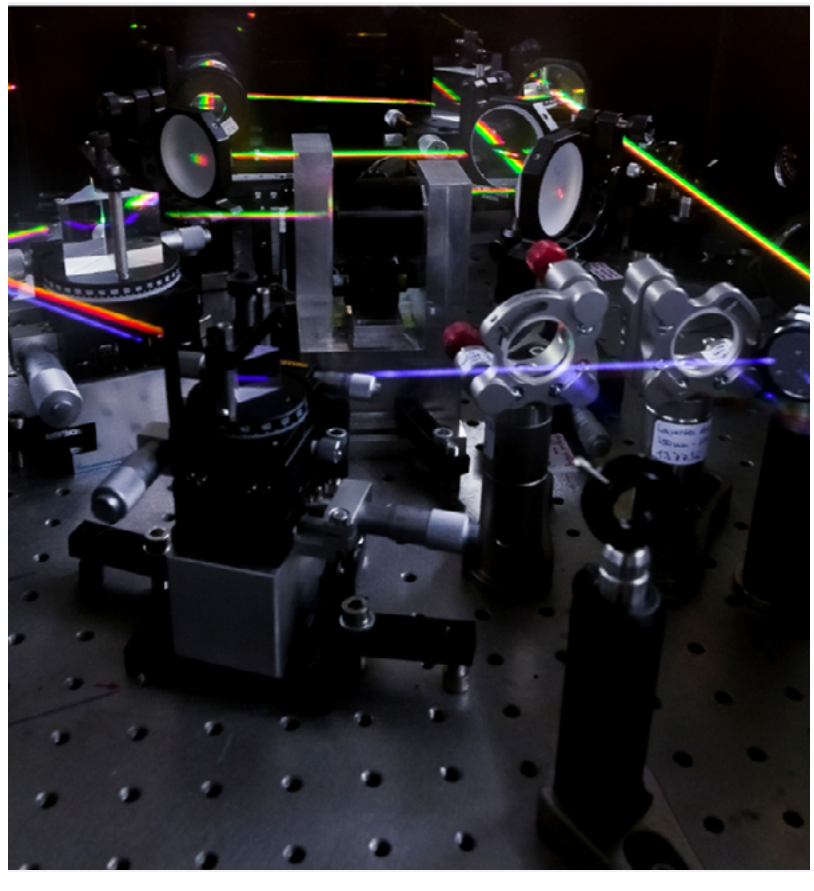
We understand the importance of getting it right when making an instrument purchase decision. Sometimes applications have special needs that are not known in advance. The Avantes demo program allows you to test an Avantes spectrometer, light source, and even some accessories in your experiment or operation to validate functionality and fine tune specifications. Vetting our instruments in your applications ensures you will be successful after you make a purchase. In the rare event we don't meet or exceed your measurement demands, we eliminate the need for costly returns and reworks.

Compare with an Existing Instrument

Often our customers have experienced a competitive or different class of instrument and would like to have a comparison to see if their measurements can be improved or cost optimized. Demanding applications such as fluorescence and Raman are often performed with high cost instrumentation which may be overkill for the needs of the applications. Avantes instruments raise the bar of performance such that our more affordable technology can replace higher cost, slower systems.

Fine Tune Software Integration and Control

The Avantes demo program allows you to familiarize yourself with our software or take a closer look at our software development kit (SDK) and sample programs. Avantes instruments can be controlled using our proprietary software AvaSoft or via your own software written in Labview, Matlab, C#, C++, Visual Studio, Python or any of a variety of Linux environments.



3.2 Products used in this eBook

On the coming pages the used spectrometers in the eBook are categorized by productline. More information and specifications of each product can be find when clicking the button below each spectrometer.

CompactLine
200 - 1750 nm

AvaSpec-Mini2048CL

- Symmetrical Czerny-Turner, 75 mm focal length
- Wavelength range of 200-1100 nm
- HAM S11639, CMOS linear array, 2048 pixels (14 x 200 µm)
- Sensitivity of 337,500 counts/µW per ms integration time
- 30 µs-40 sec integration time
- Interface: USB 2.0 (480 Mbps), pigtailed (40 cm) USB-A
- Data transfer speed is: 4.6 ms/scan

Click for more product information

AvaSpec-Mini4096CL

- Symmetrical Czerny-Turner, 75 mm focal length
- Wavelength range of 200-1100 nm
- HAM S13496, CMOS linear array, 4096 pixels (7 x 200 µm)
- Sensitivity of 261,000 counts/µW per ms integration time
- 30 µs-40 sec integration time
- Interface: USB 2.0 (480 Mbps), pigtailed (40 cm) USB-A
- Data transfer speed is: 4.6 ms/scan

Click for more product information

StarLine

200 - 1100 nm

AvaSpec-ULS2048CL-EVO

- Ultra-low stray light (ULS), 75 mm focal length
- Wavelength range: 200-1100 nm
- Resolution: of 0.06-20 nm, depending on configuration
- Stray light is 0.19-1.0%, depending on grating
- Sensitivity in counts/µW per ms integration time 375,000
- Signal to noise is 300:1
- 9 µs-59 sec seconds integration time
- Sample speed of 0.38 ms/scan with store to RAM
- HD-26 connector, 2 Analog in, 2 Analog out, 13 Digital bidirectional, trigger, sync., strobe, laser
- Data Transfer speed: 0.38 ms/scan (USB3), 1.0 ms(ETH)

Click for more product information

AvaSpec-ULS4096CL-EVO

- Ultra-low stray light (ULS), 75 mm focal length
- Wavelength range: 200-1100 nm
- Resolution: of 0.05-20 nm, depending on configuration
- Stray light is 0.19-1.0%, depending on grating
- Sensitivity in counts/µW per ms integration time 218,000
- Signal to noise is 335:1
- 9 µs-40 sec seconds integration time
- Sample speed of 0.70 ms/scan with store to RAM
- HD-26 connector, 2 Analog in, 2 Analog out, 13 Digital bidirectional, trigger, sync., strobe, laser
- Data Transfer speed: 0.70 ms/scan (USB3), 1.31 ms(ETH)

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SensLine

200 - 1160 nm

AvaSpec-HERO

- High-sensitivity symmetrical Czerny-Turner, 100 mm focal length optical bench; NA - 0.13
- CCD array image sensor with one stage TE cooled, 1024 pixel detector
- Wavelength range: 200-1160 nm
- Resolution of 0.2-7 nm, depending on configuration
- Sensitivity of 445,000 counts/µW per ms integration time
- Integration time of 5,2 ms - 180 sec
- USB 3.0 high speed, 5 Gbps, Gigabit Ethernet 1 Gbps interface
- 5.2 ms/scan sample speed with store to RAM

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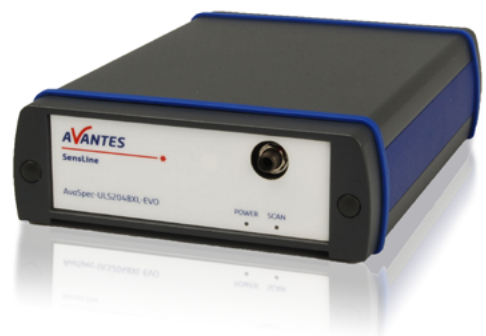

AvaSpec-ULS2048XL-EVO

- Ultra-low stray light (ULS) symmetrical Czerny-Turner, 75 mm focal length optical bench
- Back-thinned CCD, 2048 pixel detector
- Wavelength range: 200-1160 nm
- Resolution of 0.09-20 nm, depending on configuration
- Sensitivity of 460,000 counts/µW per ms integration time
- Integration time of 2 µs-20 sec
- USB 3.0 high speed, 5 Gbps, Gigabit Ethernet 1 Gbps interface
- 2.44 ms/scan sample speed with store to RAM

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SensLine

200 - 1160 nm

AvaSpec-HS2048XL-EVO

- High-sensitivity (HS), asymmetrical design, 37.5 mm focal length; NA – 0.22, f/2.27
- Back-thinned CCD image sensor, 2048 pixels
- Wavelength range: 200-1160 nm
- Resolution of 1-20 nm, depending on configuration
- Sensitivity of 1,250,000 counts/µW per ms integration time
- Integration time of 2 µs-600 sec
- USB 3.0 high speed, 5 Gbps, Gigabit Ethernet, 1 Gbps
- 2.44 ms/scan sample speed with on-board averaging

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NIRLine

up to 2500 nm

AvaSpec-NIR256-2.5-HSC-EVO

- TE-cooled symmetrical Czerny-Turner, 100 mm focal length optical bench
- InGaAs linear array detector with 2 stage TE-cooling, 256 pixels
- Wavelength range: 1000 – 2500 nm
- 4.4-85.0 nm resolution, grating and slit dependent
- Dual gain mode, switch between high sensitivity (HS) and low noise (LN) settings
- LN Sensitivity of 55,000 counts/µW per ms integration time
- HS Sensitivity of 990,000 counts/µW per ms integration time
- 10 µs – 5 ms integration time
- Sample speed of 0.54 ms/scan with onboard averaging

AvaSpec-NIR512-2.5-HSC-EVO

- TE-cooled symmetrical Czerny-Turner, 100 mm focal length optical bench
- InGaAs linear array detector with 2 stage TE-cooling, 512 pixels
- Wavelength range: 1000 – 2500 nm
- 2.6-85.0 nm resolution, grating and slit dependent
- Dual gain mode, switch between high sensitivity (HS) and low noise (LN) settings
- LN Sensitivity of 26,600 counts/µW per ms integration time
- HS Sensitivity of 480,000 counts/µW per ms integration time
- 10 µs – 5 ms integration time
- Sample speed of 0.54 ms/scan with onboard averaging

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Curious how spectroscopy can help you reveal answers by measuring all kind of materials, in-line, at your production facility, in a lab or even in the field? Please visit our website or contact one of our technical experts, we're happy to help you.

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