# Review: Current Applications and Future Prospects of Spectroscopy With Focus on Point of Need Usage.

**Abstract**

In many different applications Optical Spectroscopy has proven itself as a rapid and non-invasive measurement method which allows its users to generate useful information in terms of atomic composition or the molecular structure of analytes. In recent years new developments in fields of data processing and microfabrication led to a boom of handheld spectroscopic devices for quick measurements directly at the point of action. With more and more scientific recognitions about the capabilities of spectroscopic measurements especially in the clinical sector, spectroscopy should be considered as a fitting measurement method for the integration within Point of Care- Devices. Point of Care or Point of Need Tests are capable to deliver quick results with low to none further sample preparation and no special expertise needed. With the possibility to check certain parameters e.g. of patients, water quality or material composition directly at the place of action. A lot of time can be saved because no transport times to centralized laboratories become obsolete. Especially in the case of a medical emergency every minute counts, the earlier the treating doctor receives health related values the earlier individual treatment can be started and the chances of a successful treatment can be maximized.

## 1 Introduction

Over the years Optical Spectroscopy has established itself as a reliable analyzing technique in many different application fields. The interaction between solid matter and electromagnetic Radiation offers a wide variety of information regarding characterization, purity, quality and concentration of substances.[1] Since the development of the Laser in 1960 and continuous technical progress in fields of optic components and optical image processing, Spectroscopic methods has experienced an enormous leap.[2] There are many advantages against other analytical techniques like rapid and non-invasive measurement, low to no sample preparation and an ultra-low limit of detection that make Spectroscopy well suited for analytical purposes regarding molecular and cellular questioning. [3] This allows Spectroscopy to flourish in a big number of applications within various sectors ranging from a simple purity check of receipt goods to a 2D imaging scan of human body parts. Today there is a huge number of spectroscopic measurement techniques that are used for very different purposes. This paper gives an overlook over current fields of applications for spectroscopic analysis in benchtop systems and the integration of spectroscopic measurements in Point of Need devices. Furthermore, it evaluates if there will be special needs in the Point of Need sector in the near future which can be addressed due to the advantages of a spectroscopic measurement technique.

## 2 Light and Matter

Within this specific paper regarding the use of spectroscopic measurements there will not be any deep explanation of the mostly complicated theoretical background. This chapter simply gives an overview over the spectroscopic properties of atoms and molecules which are used to determine specific data of known and unknown substances.

If a sample is irradiated by light, four basic phenomena occur; a part of the light is reflected on the sample's surface, another part is scattered and a third part is absorbed by the sample itself. The rest passes through the sample unchanged. These effects lead to a difference between the input light intensity and the intensity behind the sample. Spectroscopic analysis measure at least one of those phenomena to generate a spectrum of the measured sample. [4]

To keep it simple, Spectroscopy can examine two different properties; first it can investigate the interaction of electromagnetic waves and atoms and on the other hand the interaction between electromagnetic waves and chemical bonds of molecules. [5]

Atomic Spectroscopy mainly focuses on the absorption and emission of electro-magnetic waves. Within a flame of 2000-8000 K the analyte breaks down into atoms. If an atom is hit by light with a specific wavelength out of the ultraviolet or visible section, electrons jump into a higher energy level. After the excitation the prior absorbed energy is released by emitting an electro-magnetic wave. Every element hereby releases different wavelengths by which they can be identified. [6] Atomic Absorption Spectroscopy (AAS) uses this principle to quantify metal ions within aquatic samples, by detecting the difference of light intensity after an absorption process for each characteristic wavelength.

If two or more atoms form a molecule, the bonds are not stiff, they vibrate with a specific frequency. If the molecule is excited with a specific wavelength within the infrared section, the energy of the light is absorbed by altering the molecule's vibrational mode, therefore this principle is called Vibrational Spectroscopy. Like atoms, every organic functional group requires a specific wavelength to get excited. With that it is possible to determine the functional groups contained in the sample and furthermore derive its chemical structure. If the sample is irradiated by wavelengths bigger than ~ 6000 nm or 1500 $cm^{-1}$ the Absorption pattern is called "Finger-Print section" where every molecule has a unique signal composition by which it can be surely identified like a human by his/her fingerprint.[7] This principle is mostly used to identify unknown substances or for purity checks.

The other basic principle of molecular Spectroscopy is Transmission-Spectroscopy by which a sample is irradiated by UV or visible light. The energy contained in the light is absorbed by the electronic system of the molecule. By measuring the amount of absorbed light can be used to determine the concentration of a specific substance in a diluted sample via Lambert- Beer's law.[8] Furthermore, some mostly organic molecules emit a less energetic light if irradiated by a specific wavelength. This phenomenon is called Fluorescence and is also a widely spread spectroscopic method. [9]

There is a huge variety of other more specialized spectroscopic techniques all based on optic phenomena that are measuring atomic composition or resonances of functional groups. Even a coarse summary of them would go beyond the scope of this report.

## 3 Point of Need Testing

In the case of a medical emergency every minute and every information about the patient counts. Unfortunately, not every emergency occurs within a clinical laboratory, which has the personnel capacity and equipment to determine valuable parameters regarding the patient's condition. Therefore, more and more tasks of a clinical Laboratory are substituted by small, portable and easy-to-use devices which can be used without complicated sample preparations right next to the patient or at home. Point of Care (POC) or Point of Care testing (POCT) delivers rapid and accurate test results directly at the place of action and allows its' operators to react to measured properties immediately. [10] This is for example why the Troponin 1 rapid test kits were introduced in the early 90s to allow a quick bedside check for a heart attacks if patients suffer from Thorax pain.[11]


*The prime example of POCT: A mobile blood sugar measuring device, which allows diabetic patients to check their sugar- level easily anywhere and within minutes.[44]*

But POC isn't limited to the clinical environment, the idea of on-site, real-time testing is transferable to many other sectors of human life under the more general term Point of Need (PON). PON Applications allow various analysis at the point of action and in field use, ranging from simple pH-Test strips to highly technological devices which can identify unknown substances. The main reason for POC/PON Testing is to generate valuable data quick, accurate and everywhere.

## 4 Established Applications

Spectroscopic measurement techniques are very well suited for an integration in a portable PON device because of their earlier mentioned properties of a rapid and none invasive measurements. The following chapters give an overview about the usages of spectroscopic measurements and their implementation in PON devices in various sectors.

### 4.1 Industrial

With handheld Raman or Near-Infrared (NIR) devices, incoming supplier materials or produced goods are tested to ensure minimum contamination and the fulfillment of quality- and purity standards. These are often used because of their non-invasive, quick and easy to use properties and usually don't have any requirements for measurement preparation. [12] In (bio-)chemical production processes, spectroscopic In-Line sensors deliver real-time information about the status of the ongoing reactions like fermentation processes. [13]

Furthermore, in the material manufacturing industry on-line Spectroscopic sensors are used to check the composition of surfaces of produced medical components to accomplish similar products within every manufacturing step.[14] This Application is also shared within the food industry: In-Line Near Infrared sensors are constantly monitoring the production lines to ensure the absence of contaminations. In Addition, NIR sensors are also capable of monitoring the presence of critical process parameters like vitamin- or protein contents of consumables. The real time overview allows immediate detection and reaction to a sudden change of error caused changes of process parameters, this saves the manufacturer a lot of avoidable extra work, time and money.[15] To stay in the food industry Fluorescence-Spectroscopy is often used and widely spread in quality management for many natural products like milk, fruits and vegetables. Apples for example are checked of their phenol content, which play as secondary plant substances a role in look, scent and taste. In the manufacturing of milk products Fluorescence- Spectroscopy is used to check the somatic cell content for example leucocytes, who are an indicator for the cow's health.[16] Due to this ability to detect microorganisms FL is also much used in clinical detection but this will be further addressed in chapter 4.3.

In steel factoring and recycling companies use handheld Laser Induced Breakdown Spectroscopy (LIBS) or X-ray Fluorescence-Spectroscopy (XRF) devices to determine the chemical composition and alloy grade of metal which makes further processing more easy and more efficient. Due to the spectroscopic properties to determine the atomic composition of products those devices are also used to determine the presence of toxic heavy metals in toys, clothes or accessories to ensure that the products fulfill the security guidelines for heavy metal contents. [17]

There are many more specified usages of spectrometric detection in the industrial sector that are simply impossible to sum up evenly.


*A handheld Raman-Spectrometer of the manufacturer Metrohm is used to perform a quality check of incoming goods [45]*

### 4.2 Environmental and agricultural

Spectroscopic tools do also have a high value for environmental analysis and due to the Climate Change the whole sector experiences a big jump in importance. Soil- and water analysis have always been monitored by the local authorities to keep track of environmental development and pollution. UV/Vis- and Atom Absorption Spectroscopy are often used in these sectors due to their properties to analyze aqueous solutions in regards of dissolved metal ions. With that the Water hardness can be determined and samples are checked of the containment of hazardous heavy metals, like lead or mercury. Furthermore, Fluorescence-Spectroscopy is used to analyze Oil contamination on Waters and localize the source of pollution. [18]

Another big problem of current times is the huge amount of pollution caused by microplastics. This problem can also be remedied by spectroscopic measurements. Currently Raman- and near infrared methods are tested in research to detect and identify microplastics in aqueous samples.[19]

With the ongoing carbon crisis emissions control has become an essential tool to reduce Carbon emissions. Here by spectroscopic measurement methods possess a high sensitivity and selectivity to determine trace gasses with very low concentrations.

One way to detect emission is with Photoacoustic Spectroscopy, with this method it's possible to detect various greenhouse gases, volatile organic compounds like Formaldehyde and Anesthetics. The measurement range of Photoacoustic Spectroscopy reaches sub-ppb concentrations.[20] $CO_2$ for example can be measured via non-dispersive Infrared sensors, that are also the spectroscopic sensors used in the $CO_2$ "traffic lights" which were installed in nearly every work environment during the Covid Pandemic.

As mentioned before soil and crop analysis are important parts of the agricultural industry. Soil must be analyzed to ensure proper prop grow. With the measurement of various concentrations farmers can adjust their fertilizer and watering strategies to optimize agricultural processes. This is performed via Near- and Middle- IR-Spectroscopy to detect the composition of bio fertilizers or to analyze harvested crops.[21]

Handheld spectrometers are also used to determine the photosynthetic pigments within the plants' leaves. Photosynthetically active Radiation (PAR) devices check the photon usage of those pigments for photosynthesis. This delivers valuable data over the growing process of the plants. Furthermore, this allows famers to optimize their artificial lightening to increase the plants yield in greenhouses.[22] Laser induced Fluorescence- spectrometers are used in fields as well to judge growth state and nutrient condition of the crops.

Spectroscopic identification is also used in archeology and geology. Portable Raman spectrometers are used to identify minerals, used pigments and antique materials directly at the place of action and deliver valuable data regarding the user's examination.[23]

### 4.3 Medical

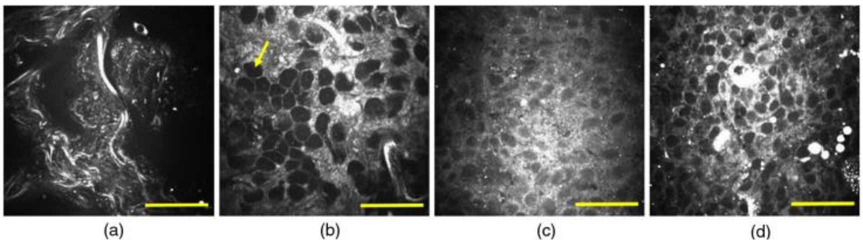
In the clinical environment spectroscopic methods are widely spread. They can be used in pathologic and oncologic diagnostics and 2D imaging. [24] Magnetic resonance imaging is one of the most used imaging techniques today. It is based on nuclear magnetic resonance Spectroscopy which measures the influence from radio waves to a nucleus in a strong magnetic field. After excitation the nucleus responds with an electromagnetic signal displaying their chemical surroundings, which is a very useful property for structural elucidation or validation in nearly any field of use. For MRI the hydrogen nuclei $H^1$ are measured which are abundant in the human organisms through water and fat. Since organic tissues defer through their water and fat shares, they can be distinguished and imaged based on their magnetic resonance. In comparison to other imaging techniques the patient isn't exposed to x-rays or ionizing radiation. [25]

Currently cancer diagnosis is a long and subjective process which requires a big amount of experience.[26] Because of that Oncologist are searching for a new, much faster diagnostic method to determine cancer earlier and easier. Their hopes lie mainly in Fluorescence- and Raman- Spectroscopic determination and imaging techniques. [27] Fluorescence-Spectroscopy is used in photodynamic therapy, in which the patient is administered a light sensitive drug, which is withheld by the tumor. Afterwards the fluorescence can be generated by the excitation of a certain wavelength. With this real-time information it's possible to determine if the patient is suffering from cancer in the first place. In comparison to Fluorescence- Spectroscopy, Raman scattering do not require any light sensitive medication. It fully relies on the different molecular composition of cancerous cells and healthy cells. With coherent anti-Stokes Raman-Spectroscopy (CARS) and the paring with microscopy it's possible to create accurate tissue images which indicates the boundaries between healthy and cancerous tissue. This can ensure that during an operational removal no healthy tissue is unnecessarily removed.[28] Clinical Research also showed that it is possible to recognize if a patient is suffering from a cancerous infection by a surface enhanced Raman- spectroscopic analysis (SERS) of the patients' blood serum. Due to the previously mentioned cell differences the serums' Raman spectrum of a cancerous patients slightly differs from a healthy control group. There are several papers about this usage of Raman-Spectroscopy reporting promising results in the diagnosis of glioma, chest, and cervical cancer. [28][29][30]

Raman- and Fluorescence- Spectroscopy are also used in pathogenic diagnostics. Today a pathogenic diagnosis is a very time-consuming process which is very problematic because a bacterial infection could trigger a dangerous septic shock. The chances of a survival of a sepsis are exponentially bigger if the treatment of the infection starts in the earlier stages. Therefore, quick and easy determination methods are needed to ensure a quick and specific treatment for the patient.[31] Current research shows that multiple bacteria caused sicknesses can be recognized through the Raman-spectroscopic analysis of body fluids like blood serum or saliva. [32]

Within clinical and biological research UV/VIS- and Fluorescence- Spectroscopy are commonly used for the quantification of DNA. Besides, Raman- and IR- Spectroscopy find a proper use in the analyzation of antigens and proteins. They are not capable of completely decoding macromolecules like other analyzation methods could but deliver a relative high amount of information in comparison to the low work input required.[33]

The clinical and medical environment have the biggest interest to integrate spectroscopic PON-devices in their all-day use. Non-invasive analysis, almost no sample preparation with quick and reliable results are the key properties why spectroscopic PON analysis starts to replace currently established techniques.[34] More and more medical devices are introduced e.g., blood sugar-analysis or the determination of cardiac markers are just some of the




*Representitive CARS images of a healty lung tissue (a ) and three different carcinoms: adenocarcioma(b), squamous cell carcinoma(c) and small cell carcinoma(d) [46]* established uses. As previously mentioned, the introduction of spectroscopic based PON devices for oncologic- and pathogenic Diagnostics would significantly improve human healthcare.

### 4.4 Forensics and Law-enforcement

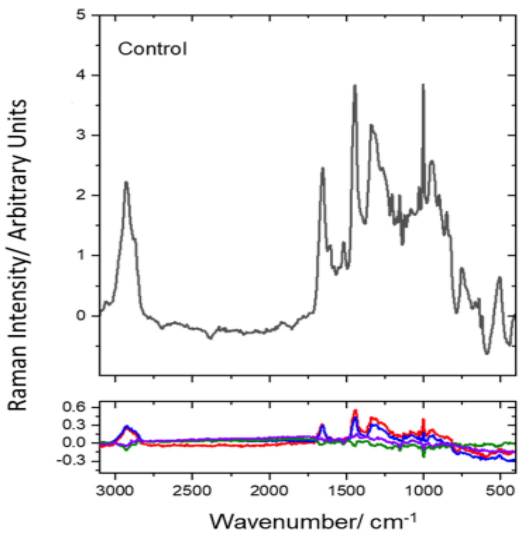
The capability to identify unknown substances within seconds is a very useful property finding appliance in law enforcement and border control. Forensic Analysis is mainly carried out by spectroscopic measurements. Confiscated substances can be identified and quantified via Raman- or IR- Spectroscopy due to their structure elucidating properties.[35] Furthermore, Raman Imaging is used to determine unknown residues on fingerprints to check if the suspicious person had contact with narcotics or explosives. Besides drug profiling, Spectroscopy is used to provide evidence in fraud or forgery of documents with analyzing the ink of used ballpoint pens.[36]

Border control units and other are also able to differ between original products and counterfeits by NMR- IR-, or Raman techniques.[37][43]

In hazardous environments handheld Raman devices can be used to scan the surroundings and identify unknown obstacles from a safe distance. Some Raman devices can safely identify substances from a range of over 1,5 meters and can measure through blister packaging. This guarantees safety for otherwise dangerous in-field deployments. Due to that Raman spectroscopic Handheld device found their way into military units and special forces.[38]

## 5 Prospects

Many clinical investigations have shown the potential inherited by spectroscopic measurement. Raman-Spectroscopy has proven to be a very useful tool in much different clinical research. As mentioned, Raman-Spectroscopy delivered reliable results in the field of oncologic diagnostics of various cancerous diseases. Some studies have also shown that a Raman-Spectroscopy analysis of blood serum can validly detect psychological limitations like schizophrenia and bipolar disorder as well as Alzheimer's decease.[39][40] With new progress in chemometrics and data alignment it could be possible that an PON-device can someday precisely determine your state of health by a simple scan of your blood serum.




*Above: A Raman blood serum spectra of a heathy control group. Underneath: spectral differences between three types of Bipolar disorder (Blue, green, purple), schizophrenia (red) and the healthy control group [40]*

Because of the many advantages PON devices have, a lot of research is performed by scientists of many sectors to search for technologies which can lead to the replacement complex and time-consuming lab analysis. Research in the sectors of microfluidics and lab-on-a-chip-systems (LOS) are tightly bound to the progress in field of PON usage. The paring of microfluidic chips and Spectroscopy opens new possibilities in fields of body fluid analysis, which is currently limited by the superstition of many signals due to the complex compositions of blood or salvia.[41]

With the rapid advances in microfabrication, and nanofabrication are continuously pushing the development of communication technologies like tablet computers or smartphones. Today smartphones go way beyond their original purpose and possess a variety of different sensors and communication channels like WIFI and near field communication (NFC). [42]

Together with the possibility to manufacture analyzing platforms in the micrometer range, complete laboratory processes can be shrunken down to chip size. With the combination of all three technologies PON devices could leap up to a completely new level. Biosensors or LOC devices paired with a spectroscopic detector are measuring or monitoring specific biomarkers while the chemometrics and imaging is performed by smartphones. This would revolutionize the field of personal diagnostics and would supply significant medical information anytime, anywhere to anyone. But unfortunately humankind needs some more time for a sustainable production and far more research has to be done before spectroscopic biosensors or PON-Devices reach everyday Maturity. [42]

Furthermore, this could improve environmental analysis as well. This technology could lead to the creation of useful PON devices, that for example could tell you within minutes if water is drinkable or not, what would require a quantitative measurement of dissolved metal ions, containment of micro bacteria and a scan for microplastics. In some time and after a lot more research in different areas we might be able to reach state of medicine , which seems science- fictional. One Simple Device which can diagnose any abnormalities of a humas body in seconds.

## 6 Conclusion

The miniaturization and technical implementation of scientific proven biomedical analysis performed by spectroscopic measurement method could lead to a big improvement in medical diagnostics and personalized treatment. If the implementation into medical PON devices is successful, medical personnel can help patients much faster and more individually. Spectroscopy paired with other technical progress would also a allow a rapid, accurate and quantitative analysis of any specific tasks in handheld devices relatively cost-efficient. In Spectroscopy we have found a powerful Analyzing-Method, which can generate a huge amount of information regarding specific questioning, which is shown in many clinical, biochemical and environmental studies. Now the current challenge is the transfer of academic research into broadly usable devices.

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