SPECTROSCOPY FOR REAL-TIME DETECTION OF VIRAL PATHOGENS

INTRODUCTION

To the leading voices that have studied the threat of zoonotic spillover, the transmission of pathogens from animals to humans, the coronavirus outbreak was predictable. The current outbreak stemmed from a virus inherent in bats, as did the SARS and Ebola viruses. Since we're penetrating deeper into ecozones where humans have been absent, future threats, which already exist and are circulating in wildlife, can be expected to cause new outbreaks every 3-4 years.

There is an intensive worldwide effort underway to deal with the current pandemic, including development of rapid testing, which is key to getting the spreading of the virus under control.

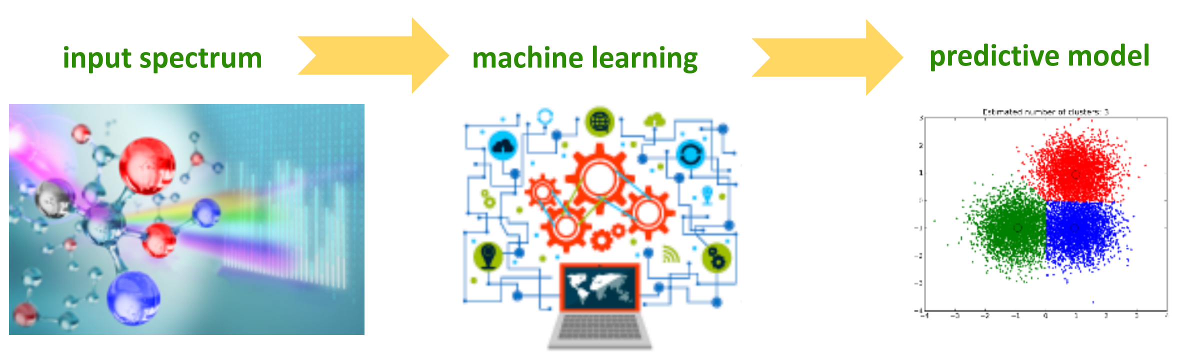
Spectrometers using light from the UV to the infrared (IR) region of the spectrum have been used to detect and identify both bacterial and viral pathogens under specific circumstances. Identification and quantification of pathogens [such as the coronavirus] presents challenges that are currently addressed with various chemical-based technologies, such as PCR or antibody test. These technologies require obtaining physical samples, saliva or blood, and delivering these samples to another location where trained personnel and laboratory equipment reside. Optical detection methods provide reliable platforms for detection of pathogens, but single spectroscopic processes have been used which limit sensitivity and specificity. In particular, Fourier transform infrared spectroscopic [FT-IR] and Raman spectroscopic processes have been used to detect pathogens and their susceptibility to an antibiotic in a culture-free environment. Efforts to date have utilized laboratory-class instruments so that the process and total time required is generally similar to the chemical-based methods in that delivering a sample to the lab is required.

There is a critical need for portable, rapid, on-site, real-time and low-cost detection of viral pathogens by measuring directly on surfaces or in bodily fluids such as mucus and saliva.

LIGHTSENSE TECHNOLOGY PLATFORM

Spectroscopy is the study of the interaction between matter and types of radiation, or light. Spectrometers are used to determine the composition of chemical substances, generating spectra that are unique for the substance being analyzed, providing a "spectral fingerprint". Spectra contain large amounts of data and Artificial Intelligence can be used to detect patterns and predict outcomes. This is illustrated in the figure below.

Lightsense is developing a new generation of miniaturized handheld spectrometers that can be used in a wide range of materials analysis applications with performance comparable to that of laboratory instruments but at dramatically lower



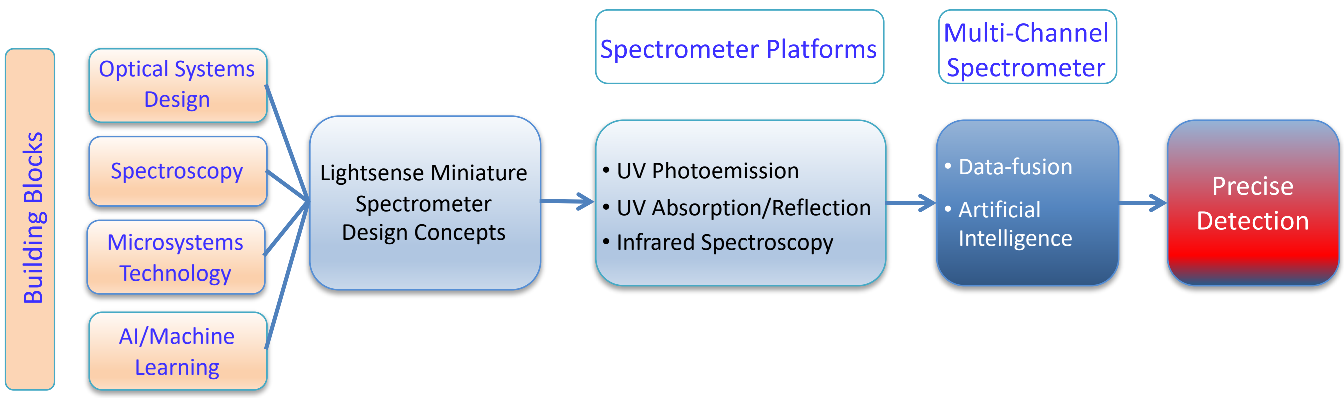
Spectral "fingerprints" of molecules provided by a spectrometer contain large amounts of data characteristic of the substance being analyzed. The left figure illustrates a digitized spectrum generated by light interacting with complex molecules. Artificial Intelligence (machine learning) can discern changes and subtle features undetected by the eye or standard analytical techniques and recognize the substance being measured by a learning process without detailed deconvolution of the spectrum into its constituent components.

cost. The first product has recently been launched, a smartphone-sized low cost detector of illicit drugs as shown in the figure (www.lightsensetechnology.com).

DrugDetect-M1, first product based on Lightsense spectrometer platform. The dimensions are similar to that of a smartphone.

Lightsense has developed a radical new architecture consisting of a combination of spectral processes, fully integrated, with data fusion and embedded Artificial Intelligence (AI) that will be capable of quantifying the substance accurately. Prototypes of such a multi-spectral, data-fusion instrument, *Enhanced Photoemission Spectrometer (EPS),* has been constructed and demonstrated to accurately measure the composition of drug mixtures at low concentration.

The Lightsense platforms based on single and multiple spectroscopic processes can measure molecular structures and their concentrations, including bacteria and viruses, with high sensitivity and precision. Our patented process is referred to as "EPS" [Enhanced Photoemission Spectroscopy]. These platforms include 1) Fourier Transform Infrared (FTIR) spectroscopy (with Raman, Stokes-based, as an alternative for certain applications); 2) Ultraviolet fluorescence (UVF) in the range of 270nm to 550nm; and 3) a combination of FTIR (or Raman), UVF, and UV reflection/absorption. Each process has strengths and weaknesses with regard to specificity and quantification, with the overwhelmingly most promising results so far having been obtained from IR (Raman) + UV absorbance + UVF combination measurements. A schematic illustration of the multi-spectral architecture is show below. The integrated unit will be a compact handheld spectrometer.



Current development efforts at Lightsense include a compact, inexpensive Fourier Transform Infrared spectrometer that will be integrated into the EPS system for maximum sensitivity and reliable detection, particularly for viruses. Data fusion and advanced artificial intelligence [AI] make appropriate combinations of these processes superior to current systems in both sensitivity and speed.

Applications for this measurement architecture are numerous and include detection of pathogens (including on foodstuffs), industrial chemical compounds, environmentally non-friendly pollutants, medical compound verification and narcotics diversion control in hospitals, rapid substance identification/quantification at airports, and chem-bio warfare agents.

A key element of the EPS architecture is AI-based learning where the instrument is "trained" to recognize the signature of the substance being detected. AI/machine-learning has been demonstrated to be able to discern subtle features in spectra not easily detected otherwise and dramatically enhance the analytical and detection capability of the system. Artificial intelligence algorithms are key to the accurate determination of the individual pathogen components in the complex saliva mixture, and these algorithms are developed for specific applications of the platform.

An example of the implementation of this process is having a person provide a saliva sample onto an inexpensive disposable UV-transmissive "slide" which is subsequently placed on the EPS platform's window where the properties of the substance are analyzed in real time. In this disposable design, there is no contact between the saliva and the internal components of the platform, eliminating cleaning between samples. This process allows a rapid turnover of samples, with the operator wearing a mask and disposable gloves for personal protection.

PROOF-OF-PRINCIPLE

The current test setup uses a separate probe for each spectral process. A marketable system will require a single probe designed for these specific processes, since no commercial product of that kind is available.

As an example of the power of just 2 spectroscopies, measurement of pharmaceuticals using the EPS platform show extremely favorable results. Comparison of the S/N ratio for the prominent Gentamicin feature in the EPS data with typical Raman data show that actual substance identification is statistically improved by 30x using the EPS system, even when measuring a concentration 20 times less than the Raman sample. Comparison of these EPS results show a ***6,000x improvement in sensitivity*** for concentration compared, for example, to Raman spectroscopy alone. In this case, fusion of data from 2 EPS processes (UV absorption + Raman) resulted in the following concentration measurement data of components of commercial Gentamicin Substance identification is derived from both the Raman spectrum and UV absorption spectrum, while accurate concentration is determined from the UV absorption data. Fully integrating 3 measurement techniques and utilizing AI for pattern recognition and analysis is expected to increase this enhancement further.

Identification and concentration derived from EPS platform

SUBSTANCE	CONCENTRATION MEASURED	CONCENTRATION PER MFG.
Gentamicin	0.29%	0.3%
Benz. Chloride	14.1%	14.2%
Purified Water	76.0%	76.3%

The dual-process EPS platform have been utilized to detect drugs in urine, early pregnancy [hormonal detection], individual components of compounded pharmaceuticals at extremely low concentrations, illicit drugs at concentrations less than 1% in complex mixtures, and accurate determination of ratios for QC of chemotherapy compounds. A key property of EPS systems is the ability to determine not only the molecules of interest, but also the concentration with very high sensitivity, which may be critical for pathogen detection in human saliva.

While single-process measurements show promise for mass detection of pathogens, the Lightsense EPS platform outperforms any of these studied to date. Furthermore, the EPS platform will be handheld, is estimated to be 10x less costly than tabletop instruments and require 2 minutes or less for each individual determination of pathogen presence. The AI algorithm assures an extremely low false positive rate and no false negatives at all.

The implementation envisioned for the Lightsense EPS spectrometer would be a kit that allows safe and fast testing in crowded environments like airports, customs or border control, etc. It would include inexpensive (proprietary) and disposable test slides and an instrument that can be operated easily without needing trained technicians. The total time for the test is estimated to be no more than 1-2 minutes per person, with the total cost of disposables a few dollars.

INTELLECTUAL PROPERTY

Lightsense has built an extensive R&D network in the US and Europe that will be recruited for this project. In particular, Lightsense is working with several departments at the University of Arizona on both optical design, machine learning, and advanced materials for its MEMS platforms. Lightsense is also seeking partnerships with AI companies for a rapid development of the analytical capability. Lightsense has secured all necessary intellectual property rights to the EPS architecture and its constituent components, including seven issued patent and three recently filed patent applications. Several additional patent applications and continuations-in-part are in preparation, including on the disposable slide design.

TEAM

Lightsense has a seasoned management team with successful experience from multiple startups, large companies (Intel, Perkin Elmer, AMD, LSI Logic, Philips, LG, AMAT), high-impact research institutions, and government service. By employing a multi-disciplinary team of experts in science, technology, and business development, and a team of experienced executives, Lightsense will be able to assist its partners to bring the best products to market in the most profitable ways.

Terje Skotheim, Ph.D. – Founder & CEO World renowned scientist in physics and materials science. For more than 20 years, after a successful academic career, Terje has focused on bringing multiple technologies from the laboratory to the product stage with over 70 patents and more than 300 publications, he is a founder of several start-up companies [B.S. physics MIT, Ph.D. physics UC Berkeley].

Bruce I. Berkoff, - CMO (Chief Marketing Officer) Global experience in the technology industry, key marketing (CMO) positions at several leading technology companies. CMO at CBRITE, CMO/CSO at Applied Materials (AMAT)/AKT, and EVP CMO at LG Philips Display & others [Princeton and UC Berkeley].

Wade Poteet, Ph.D. – VP Technology 30+ years as research physicist/engineer, emphasized system design and manufacturing of advanced instrumentation in optics, electro-optics and detector technology from x-rays to the far infrared spectrum, including ultra-high precision devices and large telescopes and received recognition awards from NASA [Virginia Polytechnic Institute].

John Coates, Ph.D. – Key Partner, Design & Spectroscopy A veteran of the optics and spectroscopy industry with a storied career, including at Perkin-Elmer & Nicolet, with over 30 years of experience in optical spectroscopy, instrumentation & sensor design, responsible for developing over 90 IR spectroscopy systems.

Michael Berman – VP Microsystems and Manufacturing 30+ years' experience in microchip and MEMS (microsystems) development and manufacturing in the US and Asia, covering chip design, process and equipment engineering, maintenance, and production. Engineering and R&D at AMD, LSI Logic and Sematech, and has over 50 patents in chip processing technology.

Joshua Nelson, CFO – Financial at Lightsense, including ongoing financial management, financial & tax strategy, and risk management strategy. Key role in organizing the manufacturing supply chain for Lightsense spectrometers. Provided financial leadership for multi-nationals (Mettler-Toledo Process Analytics) and Tucson-based startups (Sion Power Corporation, Instant Bioscan) [Business Administration from the University of Arizona].

Kevin Harris – Director of Engineering Electronic design and data acquisition & control. 20+ years of experience, including managing large programs in engineering design of optical systems and instruments, including extensive work on telescopes and space optical platforms. Software development using all major protocols of electronic communication [University of Arizona].

Gordon Davidson – Government Business and Relations Formerly Director at EPA and advisor to DOE under Clinton and has subsequently been advising a number of early stage companies, with a focus on energy and environment.

Stephen Whalley – Strategy Advisor Advising Lightsense on MEMS technology and overall strategy; 25 years with Intel Corporation in directing multiple product and technology development programs. Serves on multiple industry association boards in the semiconductor and MEMS/sensors arenas.

Richard Kris, Ph.D. – Advisor Advising Lightsense on diagnostics for medical and pathogen applications and is coordinating collaborative work with academic research laboratories in the US, Canada and the UK. Rick has a long career in diagnostics and biomedical technology, having served on the faculty of NYU School of Medicine.

CONCLUSION

Lightsense has unique capabilities and know-how to build small and sensitive spectroscopy devices capable of chemical and molecular identification and owns or has exclusive patent rights to Enhanced Photoemission Spectroscopy (EPS). This enables a unique, high-performance and cost-effective solution for many problems facing the country, such as fast and simple pathogen detection. It includes a disposable system for sample analysis, allowing simple and fast throughput for crowded lines of test subjects with a handheld and lightweight testing device that can be used by minimally trained personnel.

For more information, contact:

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APPENDIX I

PHOTOELECTRIC PROCESSES

Lightsense has extensive experience with all the of photoelectric processes required for a multi-spectral instrument and associated hardware/software. The Enhanced Photoemission Spectroscopy (EPS) solution involves three or more of these unique processes to identify molecules simultaneously in different ways, thus enormously increasing the accuracy and robustness of the molecular identification and quantification process, including samples of pathogens, drugs, chemicals, and any of these in complex mixtures.

A list of the photoelectric processes employed by Lightsense and a brief explanation of how each one functions follows.

PRIMARY PROCESSES

1. **UV Fluorescence**
   UV Fluorescence is the emission of light of a certain wavelength by a molecule [or group of molecules] that has absorbed light of a certain other shorter wavelength. In most cases, the emitted light has a longer wavelength, and therefore lower energy, than the absorbed radiation. The absorbed and emitted wavelengths are unique to specific molecules, but the background radiation can overwhelm the details of the spectrum, requiring additional processes to deconvolve the spectrum.

2. **FT-IR**
   FT-IR [Fourier Transform Infra-Red] spectroscopy is a high-sensitivity technique used to obtain an infrared spectrum of absorption or emission of a molecule. An *FT-IR* spectrometer simultaneously collects high-spectral-resolution data in the mid-infrared wavelength range. Each data point in the collected spectrum is subjected to Fourier analysis to obtain the actual spectrum. Combining spectra from this process with additional processes enhances the absolute molecular identification process.

3. **Specular Reflection**
   Specular Reflection is the process where broadband energy [many wavelengths] is directed toward a surface, and certain portions (wavelengths) of the incident energy are absorbed, and certain portions are reflected. The reflected energy spectrum is unique to the molecules comprising the surface, but additional spectroscopic process can assist in deconvolving the spectrum from background radiation.

ADDITIONAL PROCESSES FOR CERTAIN APPLICATIONS

4. **Raman Spectroscopy (alternative to FTIR)**
   Raman spectroscopy is the measurement of the wavelength and intensity of inelastically scattered light energy from molecules. The Raman scattered light occurs at wavelengths that are shifted from the incident light by the energies of absorbed molecular vibrations and rotational modes. Raman spectra often require information from supplemental photoelectric processes to determine specific molecules, especially in mixtures.

5. **UV Absorption**
   UV Absorption is similar to specular reflection, but in transmission instead of reflection. As light of many wavelengths passes through a material, some wavelengths are absorbed, and an absorption spectrum for specific molecules can be obtained. As in other photoelectric processes, supplementing the spectra with those from other processes greatly helps identify specific molecules.

6. **Scattering**
   Scattering is used to determine size of molecules in a mixture or individually. Molecules exposed to light absorb light energy and re-emit light in different directions with different intensity such that monitoring that re-emitted light at many points in different directions around the molecule can identify the size of the molecule from the intensity of light detected. This technique is generally useful down to several microns with current techniques. Viruses are generally in the range of 0.1 µm in size or smaller, so this technique is generally not applicable, and is useful only for larger targets, such as (bacterial) food pathogens.