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Note from the CEO

Mike Hennessy Jr.
President & CEO, MJH Life Sciences®

Welcome to the April/May 2024 issue of *Spectroscopy* magazine. We're thrilled to bring you a diverse collection of articles that reflect the vibrant and ever-evolving world of spectroscopy. Let's delve into the content of this exciting issue.

Starting with the "Atomic Perspectives" column, Glenna Thomas presents "The Application of Atomic Spectroscopy Techniques in the Recovery of Critical Raw Materials from Industrial Waste Streams." This piece explores how atomic spectroscopy is key to extracting valuable raw materials from industrial waste streams, aligning with the global trend toward sustainability. Thomas discusses the use of inductively coupled plasma mass spectrometry (ICP-MS), inductively coupled plasma optical emission spectrometry (ICP-OES), and X-ray absorption spectroscopy (XAS) in recovering rare earth elements (REEs) and other critical materials from various industrial byproducts. This column is a must-read for anyone interested in sustainable practices within the industry.

Next, in the "Focus on Quality" column, Mahboubeh Lotfinia and R D McDowall examine a timely topic in their article, "Coming to Screen Near You?" They discuss the FDA's proposed Remote Interactive Evaluation (RIE), a voluntary program designed to assess regulatory compliance and prepare laboratories for future inspections. Lotfinia and McDowall question the impact of RIE on good variable practice (GxP) laboratories and whether this initiative, while voluntary, is an offer that laboratories can't refuse. Their analysis offers valuable insights for those navigating the ever dynamic landscape of regulatory compliance.

In the "IR Spectral Interpretation Workshop" column, Brian C. Smith presents "Infrared Spectral Interpretation: In The Beginning I–The Meaning of Peak Positions, Heights, and Widths." After a decade of writing on infrared spectroscopy, Smith revisits the basics, exploring why different molecules have unique peak positions, heights, and widths in their spectra. This review is a useful primer for those looking to refresh their knowledge before moving on to more advanced topics in future issues.

The Icons of Spectroscopy Laureate Series continues with a tribute to "William F. Meggers: The Dean of American Spectroscopists," whose contributions to spectroscopy and atomic physics were groundbreaking. Senior Technical Editor Jerome Workman highlights Meggers' achievements and his enduring impact on the field, showcasing why he earned the title "Dean of American Spectroscopists."

Finally, our "2024 Review of Spectroscopic Instrumentation" by Ellen Miseo provides a comprehensive overview of the latest products introduced at Pittcon or during the past year, offering a detailed look at the new instruments and technologies shaping the field.

We hope you enjoy this issue and find the content both engaging and informative. Happy reading!

Editorial Advisory Board

The Application of Atomic Spectroscopy Techniques in the Recovery of Critical Raw Materials from Industrial Waste Streams, Part I

Glenna Thomas

This month's column is a contribution from my daughter Glenna, who recently completed her PhD studies in environmental science from the University of Copenhagen in Denmark. Her article explores the current landscape of global critical raw materials (CRM) trends in research and the applications of atomic spectroscopy (AS), including inductively coupled plasma-mass spectrometry (ICP–MS), inductively coupled plasma–optical emission spectrometry (ICP–OES), and X-ray analytical techniques in their identification of diverse industrial and environmental media, which have been essential in method validation and quantification of CRMs in complex matrices presenting high risks of interference. Some important examples that are presented include rare earth elements (REE) in water leaching purification (WLP) residues that co-occur with radioactive materials, REEs and other metals in acid mine drainage (AMD) environments, REEs in coal combustion (fly ash) residues, arsenic (As) from groundwater treatment sediment, and platinum-group elements (PGE) from sewage sludge. In addition, the article classifies the different techniques in use at each stage of the CRM recovery train, investigate present challenges to each analytical method, and discuss the problem-solving tools used.

- Robert Thomas, Column Editor

This column will be presented in two parts. The first part focuses on identifying the different types of raw materials that will be required, including critical minerals and elements, which have an impact on the green economy, transportation, electronics, and defense technology sectors. The second part of the column (appearing in the June/July issue) will address the analytical challenges encountered by researchers in analyzing these types of samples with atomic spectroscopic techniques, and how they can be overcome.

What Are Critical Raw Materials?

There is a growing demand for the sustainable supply of critical raw materials (CRM) that will support our globe's transition toward a green and circular economy. The term *CRMs* (or, as they are sometimes classified, "critical materials," "critical elements," and "critical minerals") refers to a growing list of elements and raw materials that are considered part of a particular economic and strategic interest for key industries and global economies while having a high risk of supply chain disruption (1). Supply chain disruption might occur because of a monopoly of CRM production by a single country, limited global reserves of a CRM, or the rate of consumption exceeding the rate of production. The core industries reliant on CRMs are those related to green energy, transportation, electronics, and defense technology.

The list of CRMs is determined by different governing bodies and often changes. The U.S. Department of Energy most recently compiled a list as of August 2023 with two distinct categories of CRMs—*critical materials for energy* and *critical minerals*—while the European Commission published a single list for critical raw materials in March 2023 along with accompanying legislation in The Critical Raw Materials Act (Tables I and II) (1,2).

The United Nations has also emphasized the importance of aligning CRM objectives with sustainable development, particularly the Paris Agreement, the international treaty on climate change (3). A task force launched in January 2022, entitled "Working Group on Transforming the Extractive Industries for Sustainable Development," is devoted to such discussions on supporting the transition towards green and circular economies (4). The current geopolitical and industrial emphasis on CRMs (and, in particular, the sustainable sourcing of CRMs) relies heavily on scientific expertise to enable the transformation of the supported industries.

Research has turned to various industrial waste streams as secondary sources for CRMs. These waste products (such as acidic mine waters, coal combustion

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TABLE I: List of critical materials for energy published by the United States Department of Energy (U.S. DOE) in July 2023. Materials with an asterisk (*) are also on the list of critical raw materials published by the European Commission in March 2023.

Critical Materials for Energy		
Aluminum	Gallium*	Nickel*
Cobalt*	Iridium*	Platinum*
Copper*	Lithium*	Praseodymium*
Dysprosium*	Magnesium*	Terbium*
Electrical steel	Natural graphite*	Silicon*
Fluorine	Neodymium*	Silicon carbide*

ash, water treatment plant residues, mineral and metal processing plant residues, and mine tailings leachate) show a potential for CRM recovery that can complement waste treatment or remediation. Research and development is underway, but for the large part, most technologies are still at laboratory scale and have yet to be commercialized. With certain threats to CRM supply chains, the upscaling of these innovative technologies is critical for establishing renewable resources. This will require cutting-edge analytical techniques at every step along the way to ensure scientific and economic resources are being efficiently invested. Atomic spectroscopy (AS) has been essential in this journey. Whether it is identifying CRMs in waste streams, understanding phase chemistry, testing solubility, or separating CRMs from co-occurring minerals and compounds, AS is one of the most resorted-to suites of analytical techniques in CRM research and recovery.

Applications of Atomic Spectroscopy for the Analysis of Critical Raw Materials

This part of the article focuses on two important CRM groups—rare earth elements (REE) and platinum group elements (PGE)—as well as arsenic (As), which was recently added as a CRM under European legislation (2).

REEs comprise the lanthanide elements on the periodic table with atomic numbers (Z) 57–71, lanthanum (La) through lutetium (Lu), and sometimes includes scandium (Z = 21) or yttrium (Z = 39) because of their similar chemical characteristics and geological occurrences (5). When including yttrium only, the grouping is referred to as "rare earth elements plus yttrium" (REY). REEs may be further divided into categories of "light" and "heavy" based on their ionic radii and atomic mass, although there can be disagreement in literature of the exact delineations. Light rare earth elements (LREEs) typically include lanthanum (La), cerium (Ce), praseodymium (Pr), neodymium (Nd), samarium (Sm), and europium (Eu), whereas heavy rare earth elements (HREEs) include gadolinium (Gd), terbium (Tb), dysprosium (Dy), holmium (Hm), erbium (Er), thulium (Tm), ytterbium (Yb), and lutetium (Lu). Promethium (Pm) occurs in extremely low concentrations in the earth's crust and is generally neither analyzed nor included in subcategories. Although there are many secondary sources of REEs, current literature focuses largely on acidic mine waters and mine waste material (6) and coal combustion (fly and bottom) ash (7).

The platinum group elements (PGE) comprise ruthenium (Ru) (Z = 44), rhodium (Rh) (Z = 45), palladium (Pd) (Z = 46), osmium (Os) (Z = 76), iridium (Ir) (Z = 77), and platinum (Pt) (Z = 78). They are major components of catalytic converters in cars, and they can be found in concentrated levels along roadsides (in soils and drainage water) (8). Besides primary sourcing from PGE mines, secondary sources include PGE mining wastewater

TABLE II: List of critical minerals published by the United States Department of Energy (U.S. DOE) in July 2023. Minerals with an asterisk (*) are also on the list of critical raw materials published by the European Commission in March 2023, and *italicized mineral names* are only on the list of critical raw materials published by the European Commission (not included in the U.S. DOE List of Critical Minerals).

Critical Minerals						
Aluminum	Cerium*	*Feldspar*	Indium	Niobium*	Samarium*	Tungsten*
Antimony*	Cesium	Fluorspar*	Iridium*	Palladium*	Scandium*	Vanadium*
Arsenic*	Chromium	Gadolinium*	Lanthanum*	*Phosphate rock*	*Strontium*	Ytterbium*
Barite*	Cobalt*	Gallium*	Lithium*	*Phosphorus*	Tantalum*	Yttrium*
Beryllium*	*Coking coal*	Germanium*	Lutetium*	Platinum*	Tellurium	Zinc
Bismuth*	Dysprosium*	Graphite*	Magnesium*	Praseodymium*	Terbium*	Zirconium
Boron	Erbium*	Hafnium*	Manganese*	Rhodium*	Thulium*	
	Europium*	*Helium*	Neodymium*	Rubidium	Tin	
		Holmium*	Nickel*	Ruthenium*	Titanium*	

and waste deposits from a number of other metal-ore mines where PGE co-occur in the geological bedrock (9). PGEs are considered critical because of the potential for socio-economic and geopolitical factors to disrupt their supply chain rather than decreasing reserves (8).

Arsenic (As) is a naturally occurring metalloid (Z = 33) used in electronics, pesticides, pharmaceuticals, and as an alloying agent (10). There are many geogenic and anthropogenic sources of As contamination around the world that threaten public health–most notably from As-contaminated groundwater sources (15). Groundwater treatment plants that remove As produce vast quantities of As-rich residues and sludge that require hazardous waste treatment; however, the recovery and recycling of arsenic from groundwater waste residues is a relatively new concept in research and industry (15).

REEs, PGEs, and As are typically found at parts per billion (ppb), micrograms per liter (µg/L), or micrograms per kilogram (µg/kg) concentration levels in the natural environment, depending on units and sample material. However, they are often significantly higher–parts per million (ppm), milligrams per liter (mg/L), or milligrams per kilogram (mg/kg)–in industrial waste products (residues, deposits, tailings, leachate) due to anthropogenic processes of enrichment (11,12). That being said, determination of these elements in both environmental and industrial samples require analytical techniques with a high degree of sensitivity (low detection limits). Industrial waste products have incredibly complex matrices that necessitate sample dilution for instrument operation. This ends up lowering CRM concentrations back to ppb levels in an analyzed solution.

Although a range of techniques have been and can be employed for determination of REEs, PGEs, and As, mass spectrometry (MS), emission spectrometry, and x-ray spectroscopy are the most preferred. In recent years, research has explored such applications towards a variety of industrial waste products with CRM recovery potential. Amidi and colleagues (2020) used X-ray fluorescence (XRF), inductively coupled plasma–mass spectrometry (ICP–MS), and scanning electron microscopy with energy dispersive X-ray spectroscopy (SEM–EDX) to characterize and quantify (88367 ppm) REEs in water leach purification residues from Malaysai containing high levels of iron (32%) and phosphate (20.8%) (12). Pyrgaki and associates used ICP–MS to characterize REE contents in coal fly ash from Greece, achieving lower detection limits of 0.01 and 0.05 ppm (13). Taylor and associates analyzed the REE contents of iron oxide-apatite deposits (IOA) from magnetite mines in the Adirondack Mountains in the United States through wavelength dispersive X-ray fluorescence spectrometry (WDXRF), ICP–MS, and ICP–OES (14). Wang and colleagues studied the molecular scale solid-phase characteristics of As- and Fe-rich groundwater treatment sludge from treatment plants located in Europe, India, and the United States using Fe and As K-edge X-ray absorption spectroscopy (XAS) (15). Using XRF and ICP–OES, Zheng and colleagues analyzed Pt, Pd, and Rh in leaching residues from spent auto-exhaust catalysts from recycling enterprises in China (16). These are just a few recent examples of the research trend towards the characterization and analysis of more chemically complex and diverse industrially sourced samples, which help decision makers distribute the resources needed for developing these technologies at local and global scales.

The second part of this column addresses the analytical challenges encountered by researchers in measuring these elements by atomic spectroscopic techniques and how they can be overcome, and will be published in the June/July issue.

Glenna Thomas is an environmental research scientist and science illustrator who recently completed her PhD in Environmental Science at the University of Copenhagen in Denmark. Her research focuses on sustainable remediation techniques for soil and water contamination as well as recovery technology for critical materials. She has a background in geology, soil science and pedology and specializes in analytical techniques for the measurement of rare earth elements and heavy metals. Glenna is currently unaffiliated and resides in Christchurch, New Zealand. ●

Coming to a Screen Near You?

Mahboubeh Lotfinia and R.D. McDowall

The United States Food and Drug Administration (FDA) is using Remote Interactive Evaluations (RIE) to assess regulatory compliance, review submission material, or determine the timing of future inspections. Here, we look at some of the impacts of RIE on GxP laboratories. Although RIE is voluntary, is this an offer that you cannot refuse?

Since the pandemic, changes have occurred in the regulatory oversight of GxP laboratories because of travel restrictions or country access. Instead of an inspection (physical entry to a facility) via remote oversight, assessments and/or evaluations have been used by various regulatory authorities. For example, the United States Food and Drug Administration (FDA) has used Remote Interactive Evaluations (RIE) (1) since 2021 and Remote Regulatory Assessments (RRA) since 2022 (2). For RRA, the FDA requests records and documents to be transferred to them for review, with the process being conducted entirely remotely (2). In some cases, the remote review outcome can be a warning letter and/or an import ban for a company (3–7). In 2024, the FDA provided an update to RRA draft guidance to *promote greater consistency in the way RRAs are conducted* (8). The FDA has also issued draft guidance on Alternative Tools for assessing drug facilities (9), which references the RRA draft guidance. There is also an agency web page explaining Remote Oversight Tools (10). *Any interaction with a facility other than inspection or a record request is considered as RIE* (11).

The European Medicines Agency (EMA) has also issued guidance on distant assessments for Good Manufacturing Practices (GMP) (12). These remote assessments and evaluations are not a substitute for inspections, but rather an expansion of regulatory oversight (12).

Recently, the FDA updated the draft guidance for Remote Interactive Evaluations (13), and our focus here is on the interpretation of this document for a regulated spectroscopy laboratory. Where there are gaps in the draft guidance, we have added the experience of the International Coalition of Medicines Regulatory Authorities (ICMRA) on remote regulatory oversight (14). The FDA is a member of and a contributor to ICMRA. In addition, some of our personal experiences of remote audits will also be included where appropriate. Post-pandemic, the FDA are continuing to use RRA and RIE for regulatory oversight in some cases. The various sources cited for remote regulatory oversight are shown in Figure 1, but our focus is on the October 2023 RIE draft guidance, circled in red. In this column, the words "investigator" and "inspector" are equivalent in meaning and relative to a person from a regulatory authority conducting on-site or remote regulatory oversight.

When is the FDA So Close, Yet So Far Away?

In the next pages, we discuss how RIE could be conducted when evaluating a regulated spectroscopy laboratory and how a laboratory should prepare. The key steps of RIE are shown in Figure 2.

Facility Selection for a RIE

Will you consider yourself lucky to be selected for RIE? The RIE planning phase is shown in yellow in Figure 2 and described below:

- **Have you been good boys and girls?** The FDA will not offer RIE to any laboratory with a poor compliance history or data integrity issues. For example, have you received a warning letter or 483 observations for recurrent issues? If so, the FDA does not put your name on the guest list. For the inquisitive, the CDER risk-based site selection model is found in the FDA Manual of Policies and Procedures (MAPP) section 5014.1 (15).
- **Don't call us, we'll call you:** You can't volunteer for a RIE. The FDA decides and initiates a request to an organization with good compliance history. The guidance states the acceptance of RIE is voluntary, **but** is this an offer that can't be refused? If you turn the request down, you could delay a regulatory decision related to the facility inspection or pending drug application. Are you feeling lucky?
- **Agree and plan the RIE:** Ideally, you should consent to the RIE in writing. Afterwards, the FDA runs a brief meeting to generate the virtual agenda which should cover the schedule, logistics, language, and recording. If the laboratory is within the scope of the RIE, you could have a starring role in the RIE. It is helpful to hold rehearsals to get prepared for the conducting phase (14). We discuss this topic later in this column.
- **Schedule:** The FDA and the laboratory will agree on the time for RIE meetings, taking into account any time zone differences. ICMRA notes that a remote evaluation takes longer in comparison to an onsite inspection (14). The time needed for the remote tour and documentation review are important elements that should be discussed during the meeting.
- **Logistics:** The RIE will use FDA video conferencing platforms, and it is important that company IT ensures connection quality and bandwidth. Limitations, sharing methods as livestreaming and/or pre-recorded video, and ways of providing access to the electronic records should be discussed. The RIE guidance briefly outlines the need for direct and encrypted view access to the electronic systems (13); however, per ICMRA experience, if direct access cannot be granted, providing a member of staff to access the system under the direction of the inspector could be a solution (14). For example, how can an investigator view the screen of a standalone spectroscopic system via live streaming? Is there sufficient live streaming resolution to read what is on the screen?
- **Language:** All documents and discussion will be in English; therefore, a translator will need to be available for the RIE if English is not your native language or if you are not fluent. Although it is not stated in RIE guidance, there is a section on this subject in the RRA guidance lines 417–422 (8). Nevertheless, in February 2024,

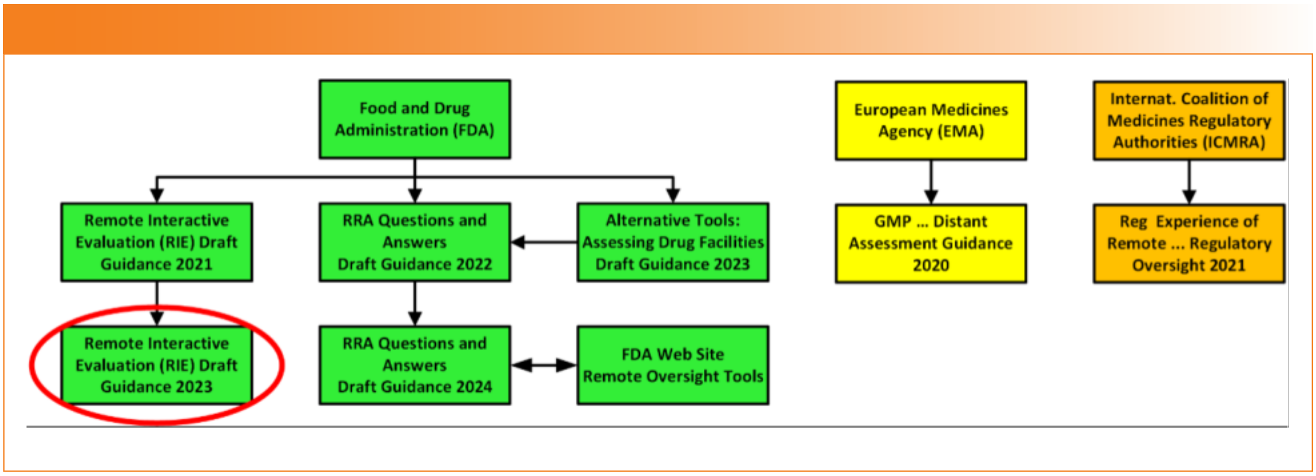


FIGURE 1: Sources of Remote Regulatory Oversight.

TABLE I: Considerations for a livestreaming tour and discussion with SMEs at spectroscopy laboratory control

Points to Consider	What to Do	What Not to Do
• Does the location of the laboratory match the facility plan? • How is access to the laboratory controlled? • Does the location of major instruments match the shared floor plan? • Show the journey from sample receipt to the reportable result: o Sample Management o Sample Preparation e.g. Walk-in sample rooms where technology allows o Analysis e.g. Point the questions at the equipment room where technology allows o Data acquisition, processing and reporting o Traceability of standards, measurement and data	• Conduct dry runs to ensure that there is sufficient Wi-Fi signal throughout the laboratory • Mock rehearse of the livestreaming with the possible questions • Make slow camera movement including zooming to allow the investigators time to assess what they are looking at • Engage in conversation and listen to what the investigators ask for • Using the camera device with adequate resolution and focus • Manage the background noise (e.g. keep away from noisy equipment and staff talking in the background) • Listen to the investigator's requests of what to see	• Don't use a mobile phone, camera, or WhatsApp • Don't stand next to the noisy equipment • Don't restrict what investigators want to see • Don't talk in the background • Don't shake the camera specially if when walking (motion sickness can result!) • Don't position the camera to only show the areas that you want to present • Don't remove timestamps from video • Don't turn the camera upside down (yes, really!)

the US Government Audit Office (GAO) voiced concerns with the FDA's practice of *relying on interpreters provided by the foreign establishment being inspected raises serious concerns about the accuracy of information being gathered* (16).

Conducting the RIE

This process is shown in orange in Figure 2. The RIE starts with a virtual opening meeting, and the investigator will work through the agenda. Traditionally, an inspection will start with an investigator presenting a Form 482 Notice of Inspection; however, this does not happen in a RIE (13). Live streaming a remote video tour of a laboratory and record and information review is discussed in the next sections.

Personnel and records are the two fundamental elements that need to be synchronized to build transparency and trust with the investigator. This is the same approach that you would take for an inspection.

- **Personnel:** Having the right SMEs at the right time, in the right environment, with the right technology. They also need to be trained to handle inspector questions and cooperate fully.
- **Records:** Availability of the scanned searchable documents and secure access to the electronic files under direction of the investigator. Timely online access to systems and documents needs to be ensured. In terms of the extensive paper-based systems, the ICMRA has found them to be a significant limiting factor for running remote inspection (14).

Lights, Camera, Action?

Are you the next Steven Spielberg? One of the most important portions of a RIE is a virtual video laboratory tour. Based on our experience, a video tour must be interactive and filmed with adequate camera resolution. A pre-recorded slide show is unaccept-

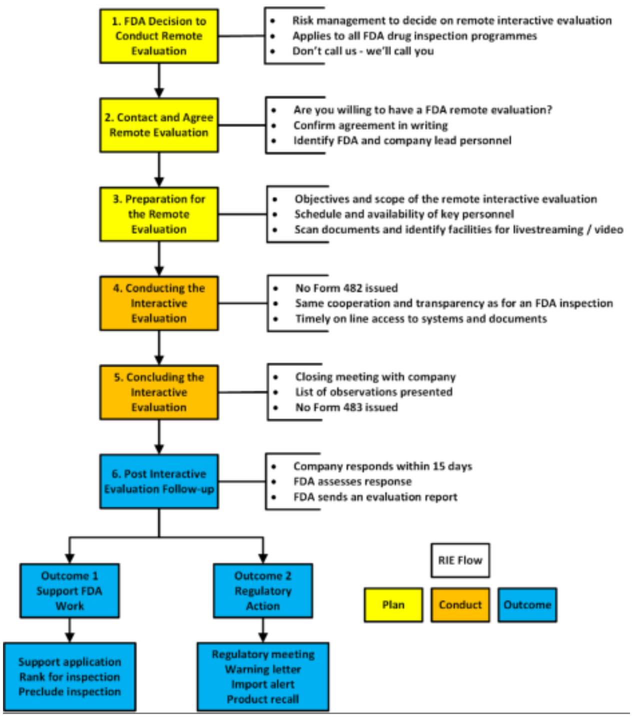


FIGURE 2: FDA Remote Interactive Evaluation Workflow (13).

able because it only gives the laboratory's perspective and may not be what an inspector wants to see. RIE mentions pre-recorded videos (13) may be used, but these suffer from a lack of investigators' direction. Table I presents our dos and don'ts for livestreaming. One key point is to rehearse the live streaming laboratory tour and to ensure that there is enough bandwidth throughout the laboratory to handle any requests from the investigator. If there is signal drop out, manage an inspector's expectations at the opening meeting or, better still, set up a WiFi repeater to extend signal coverage. One problem with a remote tour is that an inspector cannot look into wastepaper bins and desk drawers easily.

An Oscar-Winning Performance?

The organization needs to identify laboratory SMEs and appoint trained and experienced staff who know the procedures, spectroscopy instruments, and application software. The assigned team needs to be aware of laboratory processes such as sample receipt and storage, sample preparation, instrument analysis, data generation, retention, and integrity and back-up processes. Additionally, they should be trained in handling inspection questions: if you cannot answer, refer to your supervisor or someone who can. There needs to be an individual documenting what the inspector asks for and if the request has been fulfilled.

Table II presents the points that should be considered when the laboratory is sharing documents; again, this is not exhaustive. Preparation is essential so that you don't end up with a Golden Raspberry instead of an Oscar-winning performance.

Spectroscopists should be skilled in handling the request for remote document reviews because turnaround time is needed and the review process could take longer in comparison to the inspection, as shared by the ICMRA (14).

A review of spectroscopic records could find that IR identity testing is a subjective process, with analysts making a manual comparison rather than using the instrument's application's compare function or a spectral library. This could result in a video replay back in the laboratory looking at the electronic records in the application software. Inexperienced use of application software has been seen in remote audits and is an indication of a laboratory failing to keep current (18,19). Just remember Cahn's Axiom: when all else fails, read the manual.

Closing Meeting

Will you get a form 483? No, but management gets a list of observations at the close-out meeting.

The close-out session is an opportunity to discuss possible remediation actions. The written response is required to be submitted within 15 business days. The company must treat the violations with the same weight as a 483 form because failure to address them adequately can lead to a warning letter or even an import alert (Figure 2) (3–7). The company gets a copy of the final report after the FDA assesses the response to the RIE observations.

TABLE II: Considerations for document sharing and discussion with SMEs at spectroscopy laboratory control

Points to Consider	What to Do	What Not to Do
• Analytical batch records e.g. Sample preparation records • Analytical worksheet • Instrument log books e.g. balance, pH meter, spectrometer • Preventative maintenance records • Calibration and reference standards • Availability of SOP and analytical procedures in electronic format • OOS Results: Number, invalidated and review (17)	• Keep the microphone on mute when there is no communication from your side • During break time, put yourself on mute but keep the camera on • Provide the outline when presenting the prerecorded video • Requesting feedback when the playback should be paused • Screen sharing of computerized system (e.g. review of audit trails, print screen and searchable PDF of spectra and reports where technology allows)	• Don't interrupt investigators during the desktop review • Don't use virtual background • Don't remove timestamps from prerecorded video • Don't switch off the camera without getting permission from the lead investigator

TABLE III: Comparison of Drug Inspection versus Remote Interactive Evaluation

Item	Drug Inspection	Remote Interactive Evaluation
Pre-notification	Not required	Phone call/email
Planning meeting & agenda	Opening meeting	Virtual meeting
Notice Form	FDA Form 482	None
Recording	Taking photographs	Not stated in RIE guidance[1]
Observations	FDA Form 483	List of observations
Classification of observations	NAI /VAI /OAI[2]	Not stated in RIE guidance
Company response timeframe	15 Business days	
FDA review response	Within 90 days of inspection	Not stated in RIE guidance
FDA report	Establishment Inspection Report (EIR)	RIE Report

[1] The RRA draft guidance states that there will be no recording.

[2] NAI – No Action Indicated, VAI – Voluntary Action Indicated, OAI – Official Action Indicated

Follow-Up Activities

These are marked in blue in Figure 2. The nature of the observations *and* how the company responds to them determines how the FDA will react. For example, the RIE finds that there are conflicts of interest or shared user identities on a single standalone spectrometer. There are two options. The first is that the laboratory takes a systematic approach and checks all computerized systems and resolves any similar systems. This may be acceptable to the agency. In contrast, just fixing the system where the problem was identified is an unacceptable approach because there may be other systems where the problem exists.

On the positive side, an outcome of a RIE could be that an on-site inspection is avoided or that a submission is approved. On the negative side, a meeting with the FDA, a warning letter, or an import alert for companies outside of the United States could be received. Instead of an Establishment Inspection Report after an on-site inspection, the organization will receive the RIE report.

What's Missing from the Draft Guidance?

The draft guidance does not mention the following points:

- Can the FDA or the company record the RIE sessions? This subject is not mentioned in the RIE guidance. However, in the RRA draft, guidance footnote 26 states that *the FDA does not intend to record RRAs conducted via livestream, video, or screen sharing; however, FDA may request records* (e.g. documents) *we review during those sessions (8)*. As noted earlier, in an inspection, the company uses a person to document what was seen and handle inspector requests.
- There is no mention of the duration of a RIE. However, the ICMRA states that the duration of the remote inspection is longer than an onsite inspection (14).
- Although it is not mentioned in the guidance, laboratories should ensure that the agenda contains a daily wrap up session if the RIE has a duration longer than one day.
- Even though RIE is voluntary, the timeframe for submitting the written consent should be specified.
- A 483 form is formally signed by the inspectors, but for RIE observations, there is nothing stated in the draft guidance.
- 483 observations are classified, as shown in Table III, which can lead to the issuance of a warning letter and/or import alert. However, the draft guidance does not mention how RIE observations will be rated. As RRA has resulted in the issuance of warning letters as shown earlier, can we assume the same approach for RIE?
- The timeline for arranging the briefing meeting, as well as the required time for report distribution and response review, should be defined.

When Is An Inspection Not An Inspection?

When it is Remote Interactive Evaluation! Table III shows the comparison between the Drug Inspection and RIE and highlights the differences between the two. Although a form 483 is not issued at the end of a RIE, both have a list of observations that must be addressed by the laboratory management. RIE is equivalent to an inspection as outcomes could be the same: a warning letter and an import alert for foreign companies.

The view of ICMRA on remote inspections is:

- *Remote inspections are an enabling tool to maintain at least a minimal regulatory oversight during the pandemic. It is not the view that remote inspections would fully replace an on-site inspection programme* (14). This is echoed by the EMA guidance (12).
- *Conducting effective interviews under remote inspection approaches is not as effective as on-site, as inspectors are not able to assess body language fully and identify evasive and nervous behaviors. Due to the potential lack of spontaneous response when working remotely, this also creates some challenges in knowing how well inspectees know their own procedures and follow them* (14).

Similar views about RIE and RRA were voiced at a U.S. Congressional hearing in February 2024, that described *alternative inspection methods, such as virtual inspections, record reviews, and reliance on home-country regulators, inadequate to oversee foreign drug operations. "These tools are no substitute for in-person inspections, given the risk of coverup and fraud (16)."* A possible way to mitigate some of this concern could be the use of the FDA's risk-based site selection tool (15).

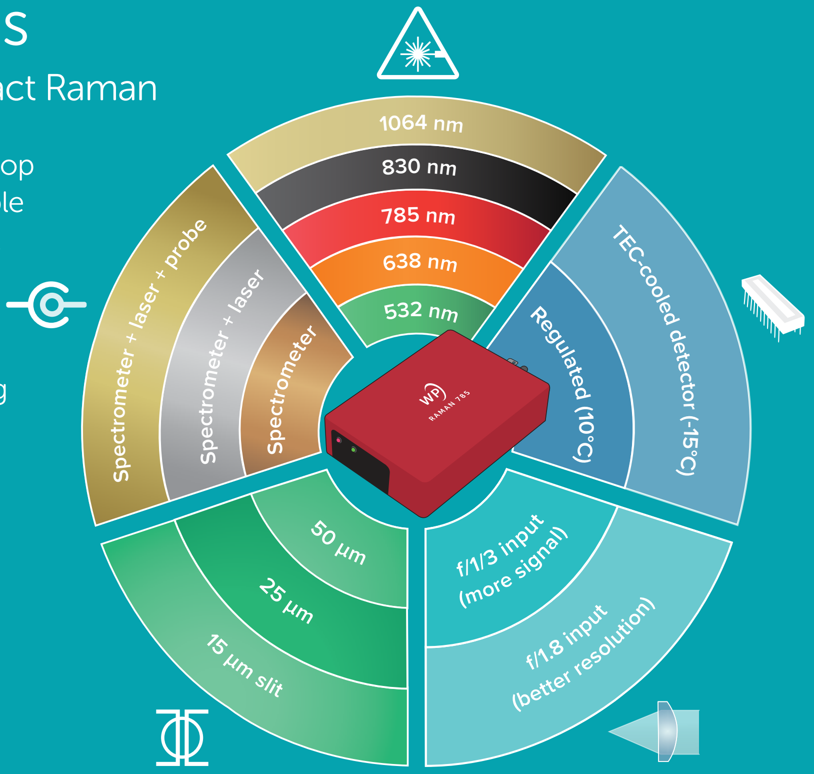
FDA Strategy to Develop Integrated Remote Tools

RIE is not going away, as a post on the FDA website last year makes clear (20). The FDA is developing Artificial Intelligence (AI) tools/models in four areas: video transcription of voice, translation to English, document and evidence management, and co-working space. If successful, the translation element could overcome the GAO criticism about the FDA relying on translators paid by the inspected company (16). The coworking space portion appears to be a joint project with the University of Maryland to build a system to manage different documents and evidence and share with Agency co-workers. The system consists of three sub-systems: (a) document classifier; (b) video/audio classifier; and (c) an interactive middleware that connects the trained model at the backend and the input at the frontend (20). Let's see what happens!

Use of a Mixed Reality Device for Inspections

Recently, Baker and others (21) have published their work of a pilot study through using a mixed-reality (hybrid) device to

(Continued on Page 24)



Infrared Spectral Interpretation, In The Beginning I: The Meaning of Peak Positions, Heights, and Widths

Brian C. Smith

I have been writing this column for almost 10 years, and we have reached a watershed moment. We have covered what I call the beginning and intermediate topics. However, before we venture off into advanced topics, a review is in order. I will spend the next four columns summarizing what we have learned so far so that the advanced topics will make more sense.

The emphasis in these reviews will be on foundational theory, the interpretation process, and interpretation aids. For a detailed discussion of what functional groups have peaks where, please look back at some of my previous columns. I originally introduced the material in this column way back in January of 2015 (1). In this retelling, I will take more time than I did then, and hopefully I will do a better job of explaining things now that I am older and wiser.

The Information Contained in an Infrared Spectrum

Infrared (IR) spectra contain three pieces of information: peak positions; peak heights; and peak widths. All these pieces of information tell us about the structure, concentration, and condition of molecules in a sample. An important part of learning the art and science of IR spectral interpretation is integrating the peak position, height, and width information together so that molecules can be identified and functional groups can be distinguished from each other. This is why tables listing only peak position ranges for different functional groups are useful, but do not tell the whole story. For instance, both O-H and N-H stretches appear in spectra around 3350 cm^{-1} (note that going forward all peak positions will be in cm^{-1} units even if not so stated). Based on peak position alone, you may not be able to distinguish between them. However, O-H stretching peaks are significantly broader than N-H stretching peaks, as seen in Figure 1.

Note that in both spectra, the peaks fall around 3350. However, the N-H stretches to the left are approximately 200 cm^{-1} wide, while the O-H stretch to the right is approximately 1000 cm^{-1} wide. This makes distinguishing O-H and N-H stretching peaks relatively easy based on width. The cause of the width differences has to do with the strength of hydrogen bonding in amines versus alcohols, something we have discussed in the past (2).

Peak Positions

As you have hopefully learned from these columns, when molecules absorb IR light, their chemical bonds stretch and bend; furthermore, the main reason that IR spectroscopy is useful is that the wavenumbers of absorbed light correlate with molecular structure (3). Absorbance of light by molecular portions called functional groups are responsible for most of the peaks we see in IR spectra. Thus, we speak of, for example, O-H stretching, C=O stretching, and CH_3 bending peaks.

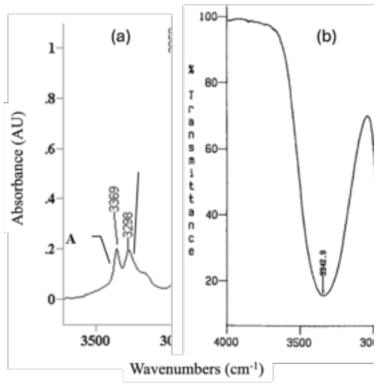


FIGURE 1: (a) The N-H stretching peaks of propylamine plotted in absorbance (the peaks point up). (b) The O-H stretching peak of ethyl alcohol plotted in % Transmittance (the peak points down). Note that although all these peaks fall around 3350 cm^{-1}, their widths are significantly different, making them easy to distinguish from each other.

Our goal here will be to derive an equation that relates peak positions in cm^{-1} to molecular structure. To do this, it is helpful to simplify our picture of molecules and their vibrations by considering the diatomic molecule seen in Figure 2. In the figure, atoms are represented as balls and the chemical bond between them is represented as a spring. This "ball and spring" model of molecules and their vibrations, though oversimplified, is useful for our purposes here. The atoms in our molecule have masses M_1 and M_2 respectively, and their relative sizes in the figure indicate that $M_1 >> M_2$. A real-world example of a molecule like this would be hydrogen chloride, H-Cl, where the hydrogen has a mass of 1 and the mass of the chlorine is 35.

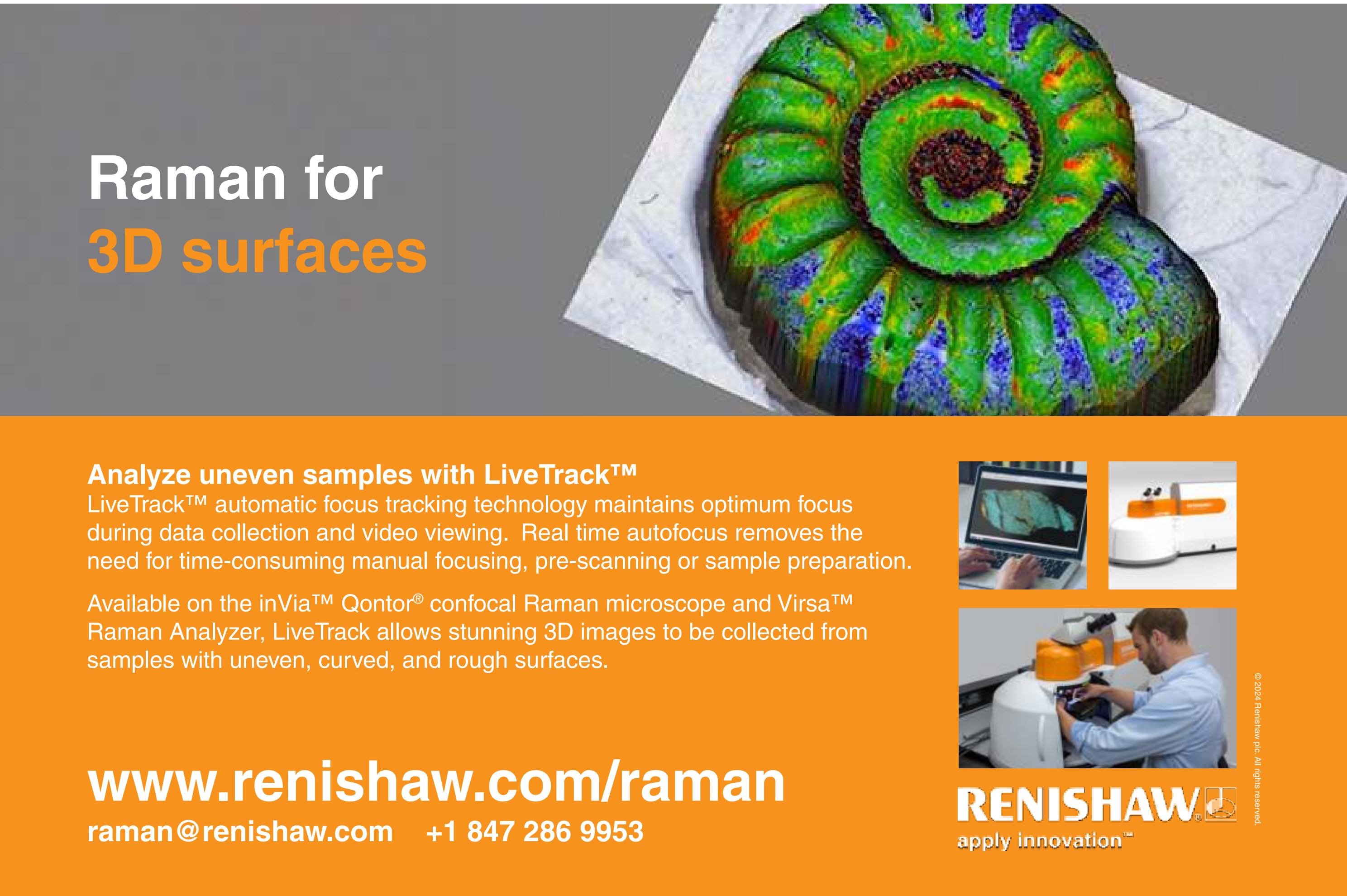
The number of vibrations for a linear molecule such as H-Cl is 3N-5, where N is the number of atoms in the molecule (3). Thus, for a diatomic molecule the number of vibrations is (3*2)-5, or 1. For non-linear molecules, the formula to calculate the number of vibrations is 3N-6 (3). Our goal then is to derive an equation that would allow us to calculate the peak position for the one vibration for the molecule seen in Figure 2.

It is useful in physics, when describing a two-mass system, to calculate what is called the reduced mass, which is given by equation 1:

$$M_R = (M_1M_2)/(M_1+M_2) \qquad [1]$$

where M_R = reduced mass; M_1 = mass of atom 1; and M_2 = mass of atom 2.

Equation 1 allows us to use one number, M_R, to represent the mass of a two-mass system.



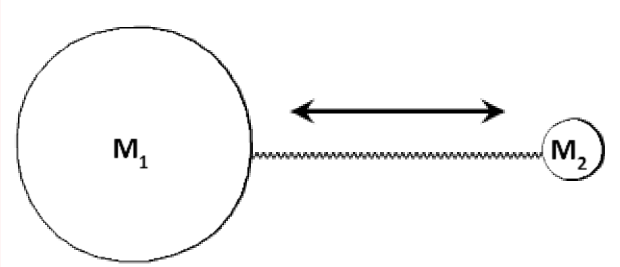


FIGURE 2: The ball and stick model for a generic diatomic molecule containing atoms of masses M_1 and M_2. The arrow indicates that the molecule has a stretching vibration along the bond axis.

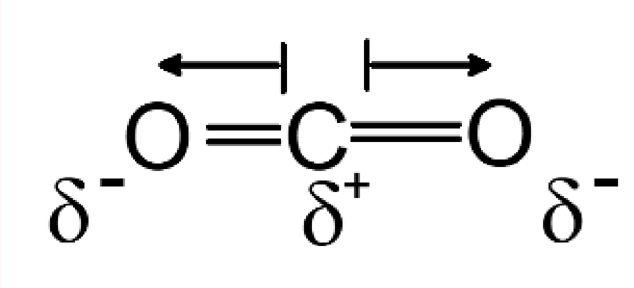


FIGURE 3: The dipole moments of the CO_2 molecule. Partial positive and negative charges are represented by lower-case deltas, δ+ and δ-, respectively. Dipole moment vectors are represented by arrows. Note that the dipole moment vectors point from the positive charge to the negative charge.

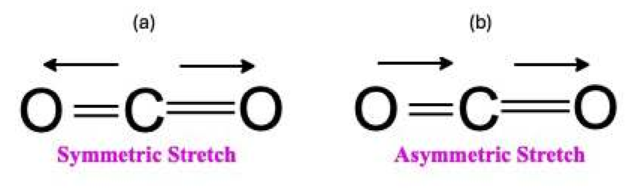


FIGURE 4: (a) The symmetric stretch of the CO_2 molecule; (b) the asymmetric stretch of the CO_2 molecule.

Imagine the one vibration of our molecule is a stretch along the bond axis, as indicated by the arrow in Figure 2. Our representation of the chemical bond here as a spring is quite appropriate because the stretching and bending of chemical bonds is very much the stretching and bending of springs.

An equation called Hooke's Law describes the properties of springs, as seen in equation 2:

$$F = -kx \qquad [2]$$

where F = restoring force of spring; k = force constant of the spring; and x = distance.

Anyone who has ever stretched a rubber band, a type of spring, has an intuitive grasp of Hooke's Law. F is the amount of force needed to stretch and maintain the rubber band at a given length. The negative sign to the right in equation 2 is because we are calculating the amount of force, the rubber band is putting pressure on the person trying to stretch it, otherwise known as the restoring force. Experience shows it takes more force to stretch a rubber band a long distance than a short distance, which is why the variable x appears in Hooke's Law. Experience also shows that it takes more force to stretch a stiff spring than a weak one, which is why the force constant appears in Hooke's Law. The force constant is a measure of the stiffness of a spring, rubber band, and chemical bonds. In fact, k is related to chemical bond strength (3).

We now have all the pieces we need to derive the equation we desire, Figure 2 and equations 1 and 2. The complete derivation of an equation relating peak position to molecular structure involves solving a partial differential equation and other fun stuff, which is beyond the scope of this column; this derivation can be found elsewhere (3). Once we crank through all the math, we obtain equation 3:

$$W = (1/2\pi c)(k/M_R)^{1/2} \qquad [3]$$

where W = peak wavenumber position in cm^{-1}; c = the speed of light; k = force constant; and M_R = reduced mass.

Equation 3 is what we seek. It predicts that the peak position in the spectrum of a diatomic molecule, like the one seen in Figure 2, depends upon the variables k, the force constant, and M_R, the reduced mass, both of which are molecular properties. Note that k is in the numerator, which means that as molecular bond strength goes up, peak position goes up. Also note that M_R is the denominator, so as the mass of the atoms in a vibrating diatomic molecule goes up, the peak position goes down.

Equation 3 is perhaps the most important equation in IR spectroscopy because it is the cause of the correlation between peak position, an experimentally measured property, and molecular structure. Equation 3 is why IR spectra are such useful molecular fingerprints. If two molecules have different chemical structures, they will have different values of k and M_R and, hence, different peak positions. In other words, an IR spectrum is unique to a given molecular structure and can identify a given molecule, like a fingerprint or DNA can identify a person.

Now, equation 3 and our entire discussion here are simplifications. We derived equation 3 assuming the stretching vibration of our diatomic molecule was harmonic; that is, the two atoms moved along the bond axis in phase with each other. Hence, equation 3 is sometimes called the harmonic oscillator model of molecular vibrations (3). We assume harmonic motion because it is simple and easy to characterize motion. Macroscopic examples of a harmonic oscillator include a swinging pendulum and wheels going around on a car. Another problem with equation 3 is that real molecules and functional groups typically have

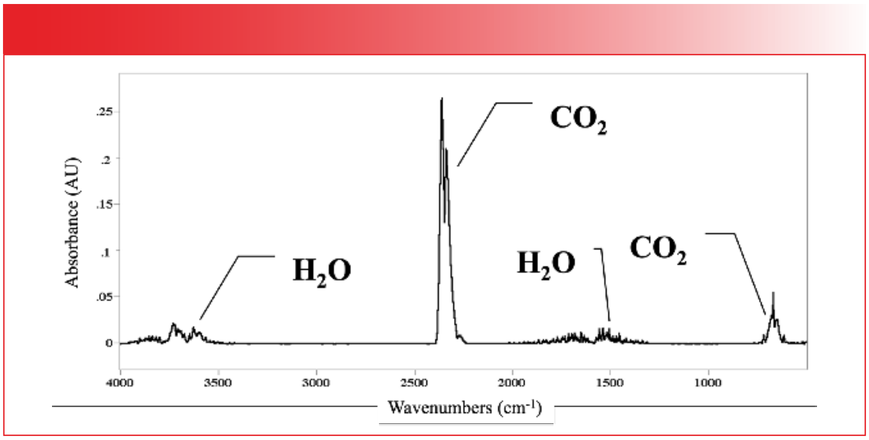


FIGURE 5: The mid-infrared (mid-IR) spectrum of the earth's atmosphere. The CO_2 peaks at about 2350 and 667 are labeled.

multiple vibrations, and their motion is not always along the bond axis. A mathematical treatment of these is beyond our scope here, but suffice it to say that they all start with equation 3. At the end of the day, it is still k and M_R that are the largest determiners of IR peak positions in molecules.

Peak Heights

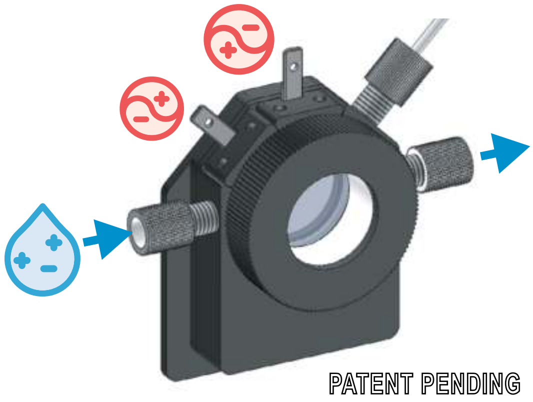
When plotted in absorbance, the peak heights in an IR spectrum are proportional to concentration, allowing infrared spectra to be used to determine the concentration of chemical species in samples (4). The relationship between absorbance and concentration is summarized by Beer's Law (4):

$$A = \varepsilon lc \qquad [4]$$

where A = absorbance; ε = absorptivity; l = pathlength; and c = concentration.

Concentration can be in units of moles/liters or any other traditionally used concentration units. The pathlength is the thickness of sample seen by the infrared beam. Nominally, absorptivity is the proportionality constant between absorbance and concentration. The absorptivity is also a physical constant for a given pure molecule at a given wavenumber under conditions of standard temperature and pressure. If we control l and c, then $A = \varepsilon$, and we can see that the absorptivity is a measure of the amount of light a pure substance absorbs at a given wavenumber under standard conditions.

Given the absorptivity is defined for a fixed set of conditions, this means it can change with those conditions. Thus, for a given molecule, ε changes with temperature, pressure, wavenumber, and of course chemical structure. Thus, ε for acetone at 1700 cm^{-1} is different than 1600



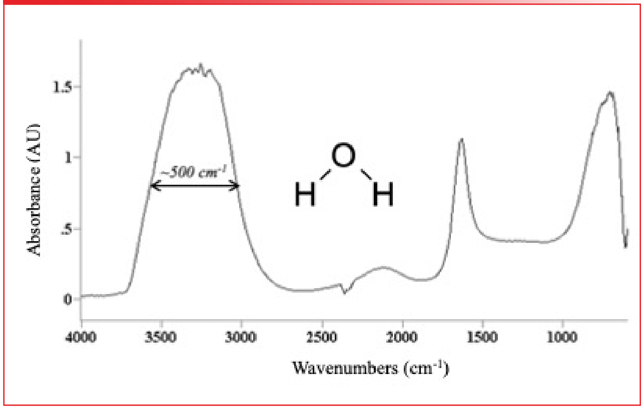



FIGURE 6: The IR spectrum of liquid water. The O-H stretching peak centered near 3300 cm^{-1} has a full width half maximum (fwhm) of approximately 500 cm^{-1}.

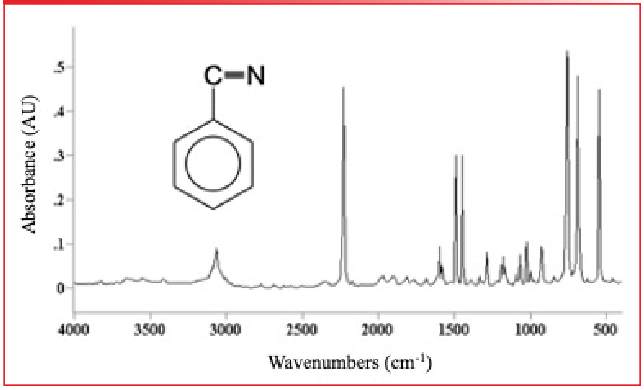


FIGURE 7: The IR spectrum of benzonitrile. Note the narrowness of the peaks.

cm^{-1}, ε is different at 100 °C than 25 °C for acetone, and of course, ε for acetone at 1700 cm^{-1} is different than that for water at the same wavenumber. I will define the temperature (*T*), pressure (*P*), concentration (*C*), and composition of a sample as its chemical environment. Imagine you are a molecule, then your chemical environment would be everything that is around you, including the number and identity of the nearest neighbor molecules and the state of the sample, including *T* and *P*. Another name for the chemical environment of a sample is its matrix. A dirty little secret of infrared spectroscopy is that the absorptivity is matrix sensitive; that is, it changes with *T, P, C,* and composition. This means that in IR spectroscopy, peak heights and sometimes even peak positions change with the sample matrix.

The absorptivity also has a quantum mechanical definition that relates it to the nature of the chemical bond. To understand this connection, we must first understand the concept of dipole moments, which are illustrated by looking at the charge distribution in the bonds of carbon dioxide illustrated in Figure 4.

In CO_2, the electronegativity difference between the carbon and the oxygen atoms causes the electrons to be shared unevenly, leading to a partial positive charge on the carbon (δ+) and a partial negative charge (δ-) on the oxygens. A dipole moment is simply two charges separated by a distance, so each of the bonds in CO_2 has a dipole moment called a bond dipole. The dipole moment is a vector quantity; that is, it has a magnitude and a direction as represented by the arrows in Figure 3. The length of the arrows denote the magnitude of each bond dipole, whereas the arrow tips represent their direction. Note that the dipole moment vectors in Figure 3 point from the positive charge towards the negative charge.

A bond dipole's magnitude is equal to the size of the charges in a bond times the distance they are held apart, as seen in equation 5:

$$\mu = qr \qquad [5]$$

where μ = dipole moment; q = charge; and r = distance.

As the size of the charges increases, the dipole moment increases, and similarly, as the distance between the two charges goes up, the dipole moment goes up. All chemical bonds have dipole moments, and yes, $\mu = 0$ is possible. What the dipole moment truly represents is a measure of charge asymmetry. Polar bonds such as O-H and C=O have large charge asymmetry and hence large dipole moments. Covalent bonds such as C-C bonds have evenly shared electrons, and hence, small dipole moments. The net dipole moment for a molecule is the sum of the bond dipoles for that molecule. Note in Figure 3 that for the CO_2 molecule, the two bond dipoles are equal in magnitude and opposite in direction, so when these are summed, they cancel each and the net dipole for CO_2 is zero.

Imagine the CO_2 molecule stretching symmetrically; that is, the two oxygens move back and forth along the bond axis in phase with each other as seen to the left in Figure 4.

At all times during this vibration, the two bond dipoles are equal in magnitude and point in opposite directions. Thus, the net dipole throughout the vibration is zero. As a result, we say the change in dipole moment, $d\mu$, with respect to bond length, dx, during the symmetric stretch of CO_2 is zero. In other words:

$$d\mu/dx = 0 \qquad [6]$$

A close examination of the IR spectrum of carbon dioxide shows that the intensity for this peak is zero (that is, there is no peak in the spectrum of CO_2 assignable to the symmetric stretch).

Now imagine the CO_2 molecule executing an asymmetric stretch where the two oxygens move along the bond axis in opposite directions, as illustrated to the right in Figure 4. During this vibration, the bond dipoles no longer cancel at all points because the oxygens are different distances from the carbon at most points during the vibration. In other words, there is a change in dipole moment with respect to bond length during this vibration, as summarized in equation 7.

$$d\mu/dx \neq 0 \qquad [7]$$

In fact, $d\mu/dx$ for the asymmetric stretch of CO_2 is quite large. The corresponding peak in the molecule's infrared spectrum falls around 2350 cm^{-1} and is quite intense, as seen in the IR spectrum of the earth's atmosphere seen in Figure 5.

To summarize then, when $d\mu/dx = 0$, peak intensity is zero, and when $d\mu/dx$ is large, peak intensity is large. But how does this new discovery of ours fit in with Beer's Law? I will skip the derivation here, but quantum mechanics tells us that (4,5):

$$\varepsilon = (d\mu/dx)^2 \qquad [8]$$

Thus, equation 8 tells us that the absorptivity depends upon the square of du/dx. Figure 3 illustrates what is called the electronic structure of CO_2. That is, it shows us where the positive and negative charges lie. Thus, according to equation 8, the absorptivity depends upon dipole moments which are determined by electronic structure of a molecule and how it changes during a vibration. Polar functional groups such as O-H and C=O bonds will have large dipole moments, will frequently have vibrations for which $d\mu/dx$ is large, and will have intense peaks. Non-polar functional groups such as C-C bonds will have small dipole moments, will frequently have vibrations for which $d\mu/dx$ is small, and will have IR features that are weak or even non-existent. This means that IR spectroscopy is better at detecting some functional groups than others, and that polar functional groups are generally the easiest to detect. Equation 8 is why different functional groups have different peak intensities.

To summarize then, in IR spectroscopy, peak heights are determined by concentration, pathlength, and absorptivity. As we have seen, ε is a fundamental physical constant of a molecule, but it depends upon its chemical environment, which affects electronic structure, which affects dipole moments.

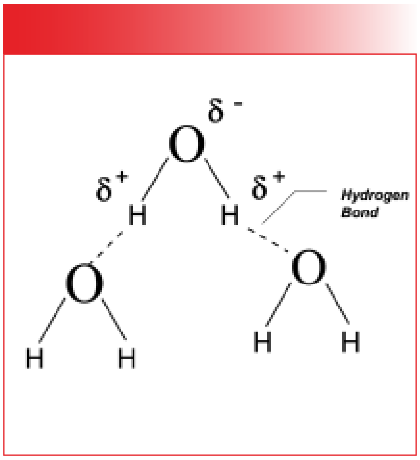


FIGURE 8: An illustration of the hydrogen bonding that takes place in liquid water.

Peak Widths

IR peak widths vary greatly across the spectrum of known molecules. Figure 6 shows the infrared spectrum of liquid water.

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The full width half maximum (fwhm) is a measure of peak width that is calculated as the width at the half height of a peak. The fwhm for the O-H stretching peak of water near 3300 in Figure 6 is about 500 cm^{-1}. This is an unusually broad peak for an IR spectrum.

Figure 7 shows the IR spectrum of the organic molecule benzonitrile.

In this figure, the peaks are generally narrow and the fwhms are less than 50 cm^{-1}. There is an order of magnitude difference then in peak width between water and benzonitrile, but why? The answer is in the strength of the intermolecular interactions for the two compounds. Water engages in hydrogen bonding, as seen in Figure 8, which is a strong type of intermolecular interaction.

Hydrogen bonding occurs because the partial positive charge on the hydrogen atoms coordinates with the partial negative charge on a neighboring oxygen.

In general, functional groups that have strong intermolecular interactions will have broad peaks. For example, most molecules containing the O-H functional group engage in hydrogen bonding and have broad peaks. Functional groups that have weak intermolecular interactions will generally have narrow peaks, such as the peaks from the vibrations of the benzene ring in benzonitrile. It is the varying strength of intermolecular interactions that cause different functional groups to have different peak widths.

Conclusion

IR spectroscopy is used to detect functional groups in samples. Infrared spectra contain peak position, height, and width information. Peak positions are determined the force constants and reduced masses of a vibrating functional group. Peak heights are determined by Beer's Law, including the absorptivity, pathlength, and concentration. The absorptivity depends upon $(d\mu/dx)^2$ for a given vibration of a given functional group. Peak widths are determined by the strength of intermolecular interactions in a sample. All of these pieces of information need to be understood and integrated properly to successfully distinguish the spectra of different functional groups from each other.

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facilitate remote inspections. As preparation, both sides ensured the availability of SMEs and technology platforms and performed practice runs. Two of the authors, who are ex-FDA investigators with a representative from Northeastern University, conducted a one-day mock inspection of a manufacturing facility covering QC, production, and warehouse. Areas captured by the device during a remote facility tour could be pinned and held for future evaluation during the inspection. Accessing the Internet via wireless hotspots was unsatisfactory, especially in production, resulting in poor image quality. Participants from several National Regulatory Authorities, as well as WHO representatives, observed and performed a pilot remote inspection using their own procedures and feedback to the main inspectors. *Overall, use of a platform for mixed reality remote inspection is feasible to perform GMP inspections and further testing of improved technology will provide a more seamless experience* (21).

Summary

We have discussed Remote Interactive Evaluation, where spectroscopists may find the FDA so close yet so far away! RIE is not a substitute for an on-site inspection, but it is an alternative for laboratories with a good compliance history.

Our column highlights the challenges and advantages for laboratories. The fundamental challenge is around spectroscopic standalone system design and ability to share records and data easily with the investigators. Has the spectroscopist who gets the short straw to be interviewed been trained to handle remote evaluation including investigator's questions?

RIE should be an opportunity to support timely regulatory decisions and laboratories selected should take advantage of this approach.

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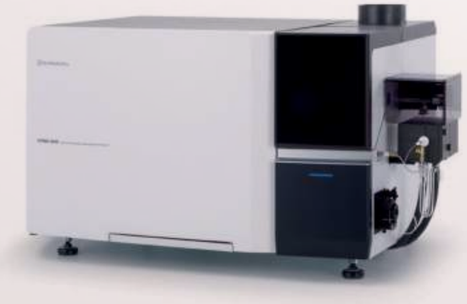


William F. Meggers: The Dean of American Spectroscopists

Jerome Workman, Jr.

William Frederick Meggers, honored as the Dean of American Spectroscopists by the US National Bureau of Standards (NBS), dedicated over five decades of his career to NBS, which later became the US National Institute of Standards and Technology (NIST) in 1988 under the United States Department of Commerce. Throughout his extensive tenure, spanning over half a century, Meggers made significant contributions to the fields of spectroscopy, atomic physics, and photographic techniques. Retiring officially at the age of 70 in 1958 as Chief of the Spectroscopy Section of the NBS organization, his impact endured. He was notably recognized as the first recipient of the Society for Applied Spectroscopy Gold Medal and remains immortalized through the Meggers Award, an annual accolade bestowed for the most outstanding paper published in the journal *Applied Spectroscopy.*

William Frederick Meggers, born on July 13, 1888, in Clintonville, Wisconsin, a small town with a population of approximately 1450 at the time, spent his formative years immersed in academic pursuits amidst the rural backdrop. Raised on a farm near Clintonville, young Bill balanced his chores with schoolwork and various activities, demonstrating both diligence and academic promise. Graduating as valedictorian from Clintonville High School in 1906, Meggers harbored aspirations for a robust college education. He pursued this dream at Ripon College, where he earned an academic scholarship and further supplemented his income by organizing a dance band, showcasing his musical talents on the slide trombone, violin, and trumpet—a youthful period he fondly reminisced about later in life (3–5).

At Ripon College, Meggers distinguished himself in the field of physics under the tutelage of Professor William H. Barber, a figure well-regarded for his pedagogical expertise. Achieving his Bachelor of Arts in physics in 1910, Meggers proceeded to a role as a graduate assistant within the Physics Department, a period during which he refined his technical competencies and established the groundwork for his later significant contributions to spectroscopy and atomic physics. Professor Barber's influence extended beyond conventional teaching; he was instrumental in guiding Meggers and many others toward advanced studies in physics, thereby reinforcing his impact on the scientific community documented in Ripon College's historical records (6,7). The mentorship between Barber and Meggers, characterized by a profound academic collaboration, was crucial in motivating and directing Meggers' path to becoming a leading authority in the spectroscopy and atomic physics domains.

Early Portrait of William F. Meggers (1)

With this excellent foundational beginning in physics, Meggers joined the University of Wisconsin, Madison, only 77 miles from Ripon College, and served as a laboratory assistant and graduate student during the academic year 1911–1912 under the supervision of several prominent academicians of his time: Charles Max Mason, a mathematical physicist who became the President of the University of Chicago in 1925; Charles Elwood Mendenhall, an extremely diverse and active physicist; and Leonard Rose Ingersoll, who is memorialized at the University of Wisconsin by the L. R. Ingersoll Physics Museum formed in his honor. In 1914, Meggers' interest in spectroscopy was secured and accelerated while reading Niels Bohr's influential series of papers on the "Constitution of Atoms and Molecules" (8).

Joining NBS and Completing His Formal Education

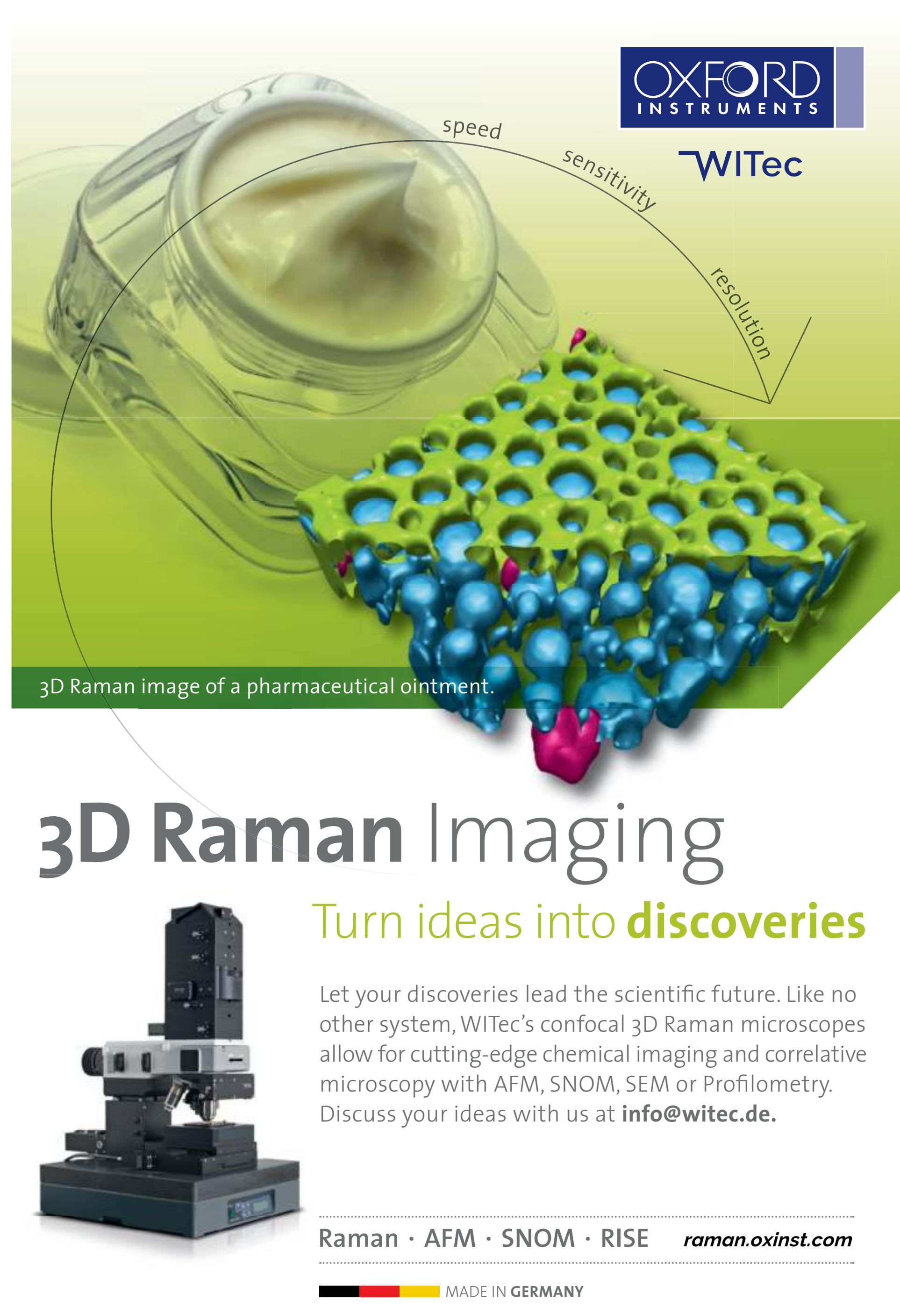
In September 1912, at the age of 24, Meggers embarked on a new phase of his career by joining the Carnegie Institute of Technology in Pittsburgh as a physics instructor. Despite this role, Meggers was deeply captivated by the pioneering work of Niels Bohr in spectroscopy. This fascination spurred him to pivot his career towards spectroscopy research exclusively. Convinced that the US National Bureau of Standards (NBS) would provide an unparalleled environment for dedicated research in this field, backed by substantial government funding, Meggers determinedly pursued an opportunity there. His commitment led him to successfully pass a rigorous two-day Civil Service examination held at the Pittsburgh Post Office, culminating in his appointment as a laboratory assistant at the NBS on June 12, 1914 (4).

Meggers worked diligently in measuring accurate wavelengths for standard materials using interferometers, as well as in developing photographic techniques to detect beyond the visible red spectral region, and also measured accurate refractive indexes of the atmosphere, which are essential for many optical calculations involving spectroscopy, physics and optics. This work was completed and published while he finished his PhD in physics from The Johns Hopkins University in 1917 (9). In all, he worked for over five decades at NBS, with many significant contributions to the fields of spectroscopy, photography, and atomic physics. Despite officially retiring at age 70 in 1958 as Chief of the Spectroscopy Section at NBS, he continued his research work until just before his death in 1966.

Five Decades at NBS

Throughout his career, Meggers made numerous significant contributions across various aspects of spectroscopy. His lifework can be summarized under four main headings (4,5,13–22):

- **Precision Measurement of Standard Wavelengths:** Meggers set world records for contributions to the precision measurement of standard wavelengths for over five decades. He initiated a program of interferometric measurement of absorption lines in the solar spectrum in 1925, laying the foundation for modern spectroscopic standards in astrophysics. His iron emission lines from 2100 to 10,216 angstroms (210 to 1021.6 nm) became unique standards



under the supervision of the International Astronomical Union, to which Meggers was a chief contributor.

- **Detailed Descriptions of Photographed Spectra:** Meggers pioneered the use of photosensitizing dyes to record spectra in the long-wave visible and the near-infrared regions. He extended records of laboratory arc spectra and the sun's spectrum, utilizing dicyanin-stained photographic plates and later infrared-sensitized emulsions, thereby significantly advancing spectral observations. By 1934, using new infrared-sensitized emulsions prepared by the Eastman Kodak Company, he succeeded in observing laboratory spectra beyond 13,000 Å (1300 nm).

- **Quantum Interpretation of Spectra:** Meggers unraveled the spectra of numerous heavy elements and ions over several decades, contributing to the quantum theory interpretation of complicated spectra. He discovered multiplets in 1922 and proposed the vector model of the atom in 1924-1925 to explain multiplet structure and the anomalous Zeeman effect. Over his career, he disentangled the spectra of some eighty heavy elements and ions, determining their various quantized energy states and the binding forces on their electrons.

- **Practical Applications of Spectroscopy:** Meggers demonstrated the practical utility of spectrochemical analysis, advocating for its adoption in laboratories as early as 1914. He provided crucial spectral-line intensity data for over 70 metallic elements, essential for both qualitative and quantitative analysis. In 1961, after twenty-eight years of intermittent investigation, Meggers published Tables of Spectral-Line Intensities containing relative energies of 39,000 spectral lines in the range 900 to 9000 Å (90 to 900 nm) characteristic of 70 metallic elements observed under standardized conditions. Nearly every scientist is familiar with the Welch charts of the periodic table of the elements that hang on the walls of most college and high school laboratories. These were first pictorially developed by Henry D. Hubbard and after his death were continually revised and extended by Meggers together with a descriptive booklet or explanatory key summarizing the physical properties of the elements.

Scientific Accolades

Meggers' impact transcended his achievements in spectroscopy; he also held crucial positions in various scientific organizations. Leading as the president of the Optical Society of America (OSA) from 1949 to 1951, he guided the society through significant changes. Moreover, Meggers served as the OSA's representative on the governing board of the American Institute of Physics (AIP) from 1952 to 1958, influencing the broader scientific community's governance and trajectory.

Recognizing his invaluable contributions, Meggers was bestowed with honorary membership in the Optical Society of America, a testament to his enduring impact on the field. His exceptional achievements were acknowledged through multiple key awards, including the Frederick Ives Medal in 1947 and the C. E. K. Mees Medal in 1964. He received the Department of Commerce Gold Medal in 1949, the inaugural Gold Medal of the Society for Applied Spectroscopy (SAS) in 1952, the Cresson Medal of the Franklin Institute in 1953, and the Pittsburgh Spectroscopy Award in 1963, highlighting his many contributions to the broader scientific and spectroscopic communities (4,5).

Meggers in 1935 at 47 years old (2)

Meggers' eminent stature in the scientific community was further underscored by his election to the National Academy of Sciences in 1954, a recognition of his gravitas and scholarly prowess. Throughout his career, he assumed various leadership roles, including chairing the National Research Council (NRC) Committee on Line Spectra and presiding over the International Joint Committee for Spectroscopy. Moreover, he served as the president of the Wavelength Commission of the International Astronomical Union (IAU), demonstrating his global impact and leadership in shaping the direction of astronomical scientific research.

Notably, Meggers' commitment to academic excellence extended beyond his research and leadership roles. He was a member of Phi Beta Kappa and Sigma Xi, actively participating in numerous technical societies and organizations, contributing to their advancement and fostering collaboration among scholars and researchers. Meggers' comprehensive engagement in scientific leadership, research, and academic endeavors solidified his legacy as a leading influencer in the field of spectroscopy and a valued figure in the scientific community (4,5).

Film Archives

Meggers was an avid musician in his younger years (4,5) and also an enthusiastic "home" movie maker for over 32 years. Throughout his lifetime he filmed many movies, including thirty-

SCAN THE CODE
To read the full version of this article, with all tables and references.

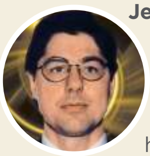
nine reels of 16 mm film consisting of both black and white and color film currently housed at the AIP (10). Themes of his movies include family milestones, first steps, birthdays, graduations, family reunions, as well as coverage of his local and international travels, for pleasure, as well as for important professional meetings.

The movie archive list from William Meggers chronicles a series of significant scientific meetings and visits across Europe and the United States from 1927 to 1954, highlighting the vibrant international collaboration and exchange in the physics and astronomy communities during this period. Meggers documented interactions with notable scientific figures such as Pieter Zeeman, Heinrich Kayser, James Franck, and Arthur Eddington in locations ranging from Amsterdam to Berlin, and from Göttingen to Cambridge, Massachusetts. His movie archive encompasses pivotal moments such as meetings at the International Bureau of Weights and Measures, the International Astronomical Union gatherings, and an expedition to observe a solar eclipse in Sweden, illustrating the breadth of scientific inquiry and discovery he pursued, including advancements in physics, the calibration of international standards, and pioneering astronomical observations (10).

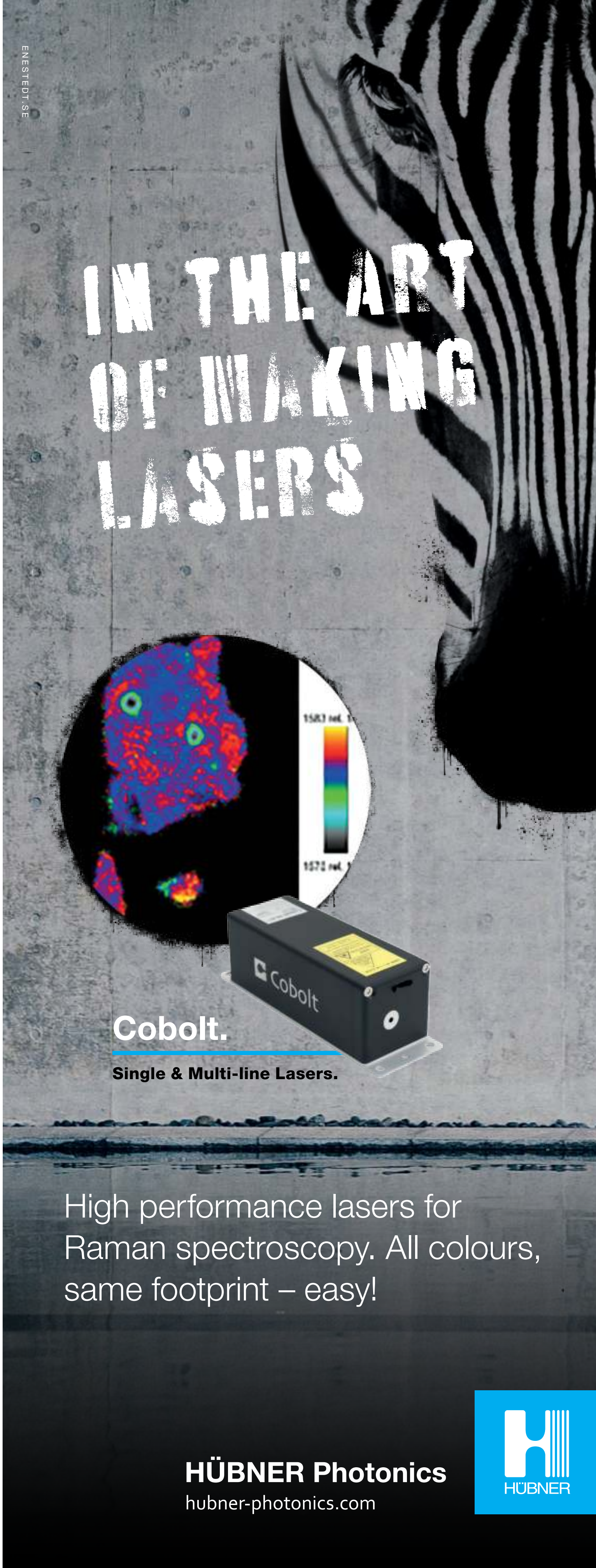
Legacy

William Frederick Meggers died November 19, 1966, after a brief illness, at the age of seventy-eight, leaving behind a legacy of innovative and significant research and a profound impact on the field of spectroscopy. At that time he was survived by his wife, Edith Marie Raddant, a daughter, Betty Jane Evans, a son, William Frederick Meggers, Jr., a physicist and electronic engineer; and three grandchildren. A second son, John Charles Meggers, an engineer, preceded him in death by only a few weeks. Meggers enduring contributions continue to inspire and shape the field of spectroscopy to this day. In 1970 the International Astronomical Union (IAU) designated a far side lunar crater after him (11). In sum total, William Frederick Meggers is indeed a Dean of American Spectroscopists (12).

ABOUT THE AUTHOR



Jerome Workman, Jr. serves on the Editorial Advisory Board of Spectroscopy and is the Senior Technical Editor for LCGC and Spectroscopy. He is the co-host of the Analytically Speaking podcast and has published multiple reference text volumes, including the three-volume Academic Press Handbook of Organic Compounds, the five-volume The Concise Handbook of Analytical Spectroscopy, the 2nd edition of Practical Guide and Spectral Atlas for Interpretive Near-Infrared Spectroscopy, the 2nd edition of Chemometrics in Spectroscopy, and the 4th edition of The Handbook of Near-Infrared Analysis. ●



Getting accurate IR spectra on monolayer of molecules

Precise process control of surface modification and functionalization.

Creating uniform and repeatable monolayers is incredibly important for both scientific pursuits as well as the manufacturing of products in semiconductor, biotechnology, and other industries. However, measuring monolayers and functionalized surfaces directly is difficult, and many rely on a variety of characterization techniques that when used together can provide some degree of confidence. Even so, inconsistent results from well controlled processes hint that there is more to learn. Infrared Photo-induced force microscopy (IR PiFM) is becoming a genuinely unique tool in the analysis of ultrathin films of organic and inorganic materials based on their IR spectra. By combining non-contact atomic force microscopy (AFM) and IR spectroscopy, IR PiFM provides sensitive and accurate analysis of sub-monolayer of molecules without the concern of tip-sample cross contamination. Spectroscopy spoke with Dr. Sung Park, CEO, Molecular Vista, to provide insights on how IR PiFM can acquire an IR signature of monolayer films due to its unique implementation.

Sung Park, Ph.D., Applied Physics
CEO
Molecular Vista

Sponsored by

MOLECULAR VISTA

SPECTROSCOPY: It sounds like one of the main benefits of this PiFM technique that your company has developed is that it can characterize monolayers directly. Can you share more about how that is used?
DR. SUNG PARK: Let us look at aminosilane glass substrates that are used with DNA capture and sold by a few companies. When one looks at these substrates with a Scanning Electron Microscope (SEM) or AFM, it commonly will show 1 ~ 10 nm sized granules that are sparsely and homogeneously distributed across the surface. The assumption is that between these granules is a monolayer of self-assembled aminosilane. This is a reasonable assumption since people will use techniques such as water contact angle, Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS), and/or Fourier-transform infrared spectroscopy (FTIR) measurements to infer or verify the presence of aminosilane.

However, when we look at these samples, that is not what we see. Instead, in many cases, only the granules show the amine peaks, and the rest of the substrate shows glass peaks along with some contaminant peaks. So, when researchers are using samples like this, they are then susceptible to getting unexpected results. See the aminosilane glass data by visiting the QR code in the sidebar.

Scan the QR code to see the aminosilane glass data.

SPECTROSCOPY: Is this an isolated example or more commonly observed?
DR. PARK: Actually, this example sheds light on why so many experiments and processes that depend on surface modification seem to be random in their success rate and why the yields on devices that employ these steps are poor. We are currently helping a biotech company that has a yield problem. Their product employs several surface functionalization steps, and even though they follow a very strict process control, some final products pass but some fail the actual loading test, seemingly randomly. This leads to lost revenue and wasted time. With our technique, they are successfully improving the manufacturing process because now they can directly observe the surface chemistry on these devices at different points in the process.

As another example, we partnered with researchers at Lawrence Berkely Lab on a webinar. That talk did a great job of showing how much of a difference it makes when you are able to properly characterize your work. Our guest speaker shared how our technique helped her to develop a reliable process to grow monolayer of peptoid molecules. I encourage readers to view the webinar since it describes how water contact angle and ellipsometry measurements can mislead the outcome of surface modification. Like the aminosilane example, it can sometimes be quite shocking to see the results of a direct measurement when so much is done by making inferences.

SPECTROSCOPY: What allows IR PiFM to be sensitive enough to analyze sub-monolayer of molecules?

DR. PARK: We are not the only company offering an AFM-IR type of instrument. However, there are subtle differences that give PiFM a real advantage. In ultra-high vacuum (UHV) environments, AFM can be operated via a non-contact mode by measuring attractive forces to achieve true atomic resolution. What we have done at Molecular Vista is take that idea and expand on it with the IR component. PiFM measures attractive forces between the tip and the sample that are induced by the absorption of the enhanced IR illumination. While we don't operate in UHV, the measurement of the attractive force in a non-contact manner allows us to offer our customers the ability to directly measure surface chemistry in a way that is otherwise very difficult.

SPECTROSCOPY: It is interesting to hear that you operate in a non-contact manner. Are there other benefits to doing that?

DR. PARK: Other AFM-IR techniques tend to employ either contact or hard tapping AFM modes to measure the repulsive forces that an expanding sample imposes on the AFM tip upon absorbing the IR light. If the technique is sensitive, whether one operates in non-contact mode or in tapping mode makes an important practical difference. When the AFM tip touches, even briefly as in tapping mode, the tip can easily pick up a molecule, especially if the sample is soft. From the moment of contamination, the instrument will measure the IR signature of the molecule that is on the tip in addition to that of the sample underneath the tip, complicating the results. With regards to hard samples, the fragile metal coating that generates the tip-enhanced field will be easily damaged upon contact with the sample, necessitating a tip change.

WEBINAR

Precise Testing of Surface Modification and Functionalization

Listen to guest speaker Dr. Beihang Yu discuss how modern nano chemical analysis techniques, PiFM and PiF-IR, helped her solve process issues for grafting ultra-thin peptoid monolayers, analyze DNA origami, and investigate substrate contaminant materials.

~~May 23, 2023 10 – 11 AM PDT~~ Recording available

Scan the QR code to view Molecular Vista's webinar with researchers at Lawrence Berkeley Lab.

SPECTROSCOPY: Do you have any parting thoughts for our audience?

DR. PARK: While I could delve into the specific engineering innovations in our tool, at the end of the day, details like that don't really matter to customers. Most of our customers need results that help them accomplish their goals. Like that biotech company I mentioned, they have been a loyal client because having this monolayer sensitivity greatly helps them identify and solve problems in their processes, saving them both time and money. If you can't directly measure the surface of these ultra-thin materials, then it is extremely difficult to make progress when things start going wrong. Your readers can utilize our technique to monitor their processes without having to purchase our tool if they utilize our contract service offering.

Molecular Vista advances nano chemical characterization with PiFM and AFM-IR. To learn more about Molecular Vista, visit https://molecularvista.com.

2024 Review of Spectroscopic Instrumentation

Ellen Miseo

TABLE I: Index of companies and the categories where their products appear

Company	Categories
908 Devices	Raman
Agilent	Accessories
Analytik Jena	Accessories, Atomic
Anton Paar	Mid-IR
Armadillo SIA	Components
art photonics	Accessories
DialAct Corporation	Raman
Horiba Instruments	Raman, Software
Hübner Photonics	Raman
HySpex	Imaging
Metrohm	Software
Molecular Vista	Mid-IR
Nikalyte	Accessories
Oxford Instruments WITec	Raman
PerkinElmer	Atomic
PhaseTech Spectroscopy	Accessories
Rigaku Analytical Devices	Raman
Shimadzu	Atomic, Mid-IR
Spectrolight Inc.	Fluorescence, Imaging
S.T. Japan-Europe GmbH	Software
Thermo Fisher Scientific	Far-IR
Wasatch Photonics	Raman

Pittcon, the traditional venue for the introduction of new analytical instrumentation, was held in San Diego, California in February, the first time the conference was on the West Coast. When Pittcon began, analytical chemistry was important to the chemicals and polymers industries; the Midwest and Northeast were major locations for those industries. Now, biotechnology and pharmaceuticals are the important industries in the analytical sciences and San Diego is a major hub as is Philadelphia, where Pittcon 2023 was held, and Boston, the venue for Pittcon 2025.

This changing dynamic also means product introductions may not always be tied to conferences and if they are, the conferences may be more targeted to the product being introduced. For example, last fall at SciX 2023, we saw a few new products by small companies focused on spectroscopy.

This review covers products introduced in the spectroscopy space between May 2023 and April 2024, to give complete coverage, and it will be broken into four sections: instrumentation, accessories, software, and components. The difference between an accessory and a component is that an accessory is designed to be used with a complete instrument, while a component can be used to construct the instrument.

Table I lists companies that submitted new products, the product categories, and links to company home pages. As in 2023, we also have tables with information on the products, and in these tables, we have provided links to the pages associated with each product. We will not describe every entry in detail, but refer the reader to further information.

Instrumentation

The first category is major instrumentation. Design of a new analytical system, regardless of the technology used, requires inputs from a number of technical areas, so most projects are multi-year ventures for the instrument company. As I mentioned in last year's review, it appeared that there may have been many projects held up by the pandemic that were then introduced in 2023, so that may have reduced the number of full instruments this year. Considering this, it should be no surprise there are fewer full instrument systems introduced this year compared to last year.

Atomic

Both Shimadzu and PerkinElmer introduced inductively coupled plasma–mass spectrometry (ICP-MS) systems this year, as shown in Table II (all tables are accessible through the QR code at the end of the article). According to product descriptions supplied to the author, both instruments use modern designs to minimize the environmental footprint, improve efficiency, and simplify operations. These are features that many instrument designers aim to achieve in a modern instrument.

Analytik Jena introduced a total organic carbon/total nitrogen (TOC/TN) analyzer to simplify this critical analysis. Though it might seem simple in the modern instrument era, TOC and TN analyses are critical for environmental monitoring and quality control in the pharmaceutical industry.

Molecular

Unlike 2023, when there were instruments in both ultraviolet-visible (UV-vis) and fluorescence categories as well as infrared (IR) and Raman, this year for the molecular spectroscopy category, all entries were vibrational spectroscopy instruments, both IR and Raman.

Mid-IR

Table III illustrates entries in the mid-infrared (mid-IR) category. Anton Paar has entered the Fourier transform infrared (FT-IR) market with a benchtop instrument designed for routine analysis. Technical specifications, listed on the Anton Paar website, show an instrument with components and specifications on the level with traditionally recognized FT-IR vendors.

Thermo Fisher Scientific has added another FT-IR instrument, the Nicolet Apex FT-IR, described as for both research and quality control applications. It can be equipped to cover the near- and mid-IR as well as to use a thermoelectrically (TE) cooled mercury cadmium telluride (MCT) detector.

Shimadzu has introduced the IRSpirit-X FT-IR, described on its website as small and light. The author will admit that the image on the website does not do it justice. It wasn't until I scrolled further that I realized exactly how small and light the instrument is.

Last in the mid-IR category, Molecular Vista has introduced the Vista 200, a photoinduced force microscope, another entry in the field of combined chemical imaging with atomic force microscopy (AFM) topography measurements. This instrument seems to be aimed directly at the semiconductor market.

Raman

Raman applications and instruments have been growing rapidly, with devices for the laboratory, field, and process. Table IV has entries in all categories. Horiba Instrument has introduced a version of the LabRaman confocal Raman microscope specifically for the semiconductor market. It is optimized for photoluminescence and Raman mapping, and it works from deep UV to near-IR.

Oxford Instruments WITec has also introduced a Raman microscope system aimed at the semiconductor market. The alpha300 is designed for 300 mm (12-inch wafers) and can be used on conventional semiconductor materials as well as novel two-dimensional (2D) materials such as graphene.

At the other end of the size spectrum, Rigaku Analytical Devices has introduced a 1064-nm handheld called the Narc-ID for presumptive identification of narcotics and precursors.

The team at 908 Devices appears to have gone back to the roots of their founders, all from Ahura Instruments, by introducing the Maverick, a purpose-built Raman process analytical technology (PAT) instrument that can simplify conventional model building inherent in other process instruments.

Wasatch Photonics has added another spectrometer to the family of compact devices for which it is known. The X series Raman has an integrated single wavelength laser module with an excitation wavelength from 532 nm to 1064 nm. This allows users to do proof of concepts and migrate to large volume original equipment manufacturer (OEM) applications.

Finally in the Raman category, we would like to note that DialAct Corporation has entered into a partnership with Elodiz, from the UK, to distribute Elodiz Raman spectrometers.

Imaging Instruments

Imaging instruments can cover a variety of technologies and applications from laboratory-based to remote imaging. The two products discussed in Table V, though from the same company, illustrate the breadth of applications. The first, Mjolnir, is an imager from HySpex designed for unmanned aerial vehicle (UAV) applications. This small form factor imager, when used in a UAV, is appropriate for agriculture, geology, mining, and other applications.

The Core Scanner, also from HySpex, is at the other end of the application spectrum. It is designed to profile minerals from drilling cores, and to scan and classify the composition of the cores.

Accessories

An instrument is designed to do a particular analysis, but accessories are designed to make that instrument more flexible and efficient. Considering that when looking at Table VI, which covers accessories, we see applications are as broad as instruments discussed elsewhere.

The first accessory, clinPAL from Analytik Jena, is designed to automate sample handling for ICP-MS analysis of clinical samples. It is equipped with a vortex mixer to ensure sample homogeneity and integrated bar coding for sample recognition.

Agilent has introduced an auto-dilution system to be used with their ICP-OES and ICP-MS instruments. This accessory

automates the tedious tasks such as preparing standards and accurately diluting over-range sample.

A series of fiber optic probes useful for remote spectroscopy are available from art photonics. The FlexiSpec Multispectral Combi Probe is designed to integrate into a number of optical spectroscopy applications including UV-vis, near-IR, or fluorescence. A second fiber optic accessory from art photonics is the FlexiSpec Raman probe. This has two variations, one for excitation in the 630 to 785 nm region or one for single wavelength excitation. The third accessory probe is the FlexiSpec Transmission Fiber optic probe, for use with spectrometers from UV to near-IR.

Surface-enhanced Raman spectroscopy (SERS) substrates are becoming more and more important, and Nikalyte has introduced a silver nanoparticle SERS substrate to complement existing gold SERS substrates.

Finally, PhaseTech Spectroscopy has introduced a transmission electrochemical sample cell called the VOLT IR. This is a transmission design and the electrode surfaces are transparent in the infrared, enabling a transmission experiment in situations in which other sampling geometries would not work.

Software

In all analytical instruments, software is a major part of the overall package, and in many cases the only component that the customer actually interfaces with. Some software packages are part of the instrument while others are add-on components, and then there are third-party packages designed to make using the instrument and interpreting the data easier. The software that is part of the instrument is not covered here but the other two categories, efficiency packages and data interpretation software, are included in Table VII.

Horiba has introduced a Good Manufacturing Practice (GMP) compliance package for the Aqualog A-TEEM Industrial QC–QA (quality control and quality assurance) Analyzer, providing tools to enable the A-TEEM to implement methods for a GMP environment.

Spectral libraries are an important software component for data interpretation, and Metrohm has introduced a 20,000-compound Raman library covering a wide range of application areas.

S.T. Japan-Europe GmbH, which supplies software and libraries to the vibrational spectroscopy community, has introduced the Spectra Genius, a software package for display, search and mixture analysis.

Components

As mentioned above, components are used in constructing an instrument whether built in your laboratory or by an instrument vendor. These are as varied as the instruments themselves and as Table VIII shows, we have optical fibers, light sources, and lasers in the category this year.

Armadillo SIA has introduced a line of multimode step-index optical fibers designed to transmit from 180 nm to 18 microns providing coverage in all the optical spectroscopy regions. These have uses in areas such as forensics, semiconductor manufacturing, and laser delivery applications.

Light sources are another component area where new products have been introduced. Spectrolight, Inc. has introduced three sources. The first is a tunable light-emitting diode (LED) light source covering the range of 430 to 700 nm. The second is a picosecond tunable supercontinuum laser source with a wavelength coverage range of 400 to 1700 nm. And the third source is another picosecond tunable supercontinuum laser source that covers the range of 225 to 1700 nm.

Complementing these sources, Spectrolight, Inc. also introduced two tunable bandpass filters to work with any collimated light source and have similar spectra ranges as the tunable supercontinuum laser sources mentioned above.

Finally, Hübner Photonics has introduced a single frequency 785 nm laser, the Cobolt Disco 785, appropriate for Raman spectroscopy.

Trends and Conclusions

New product introductions continue to trend smaller and lighter, with more features and more straightforward use. Service typically becomes simpler and more cost effective, since it may be possible to swap major assemblies in the field or better yet, swap the entire instrument.

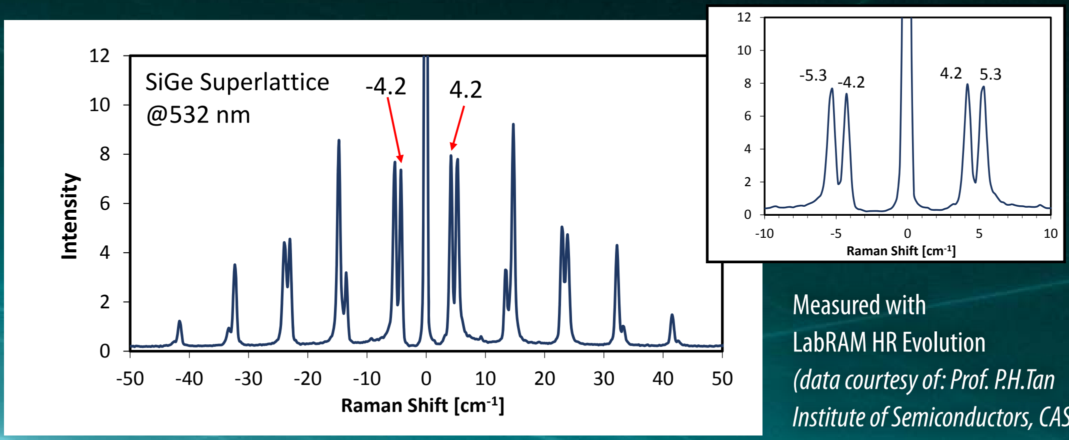
With these ease-of-use features comes a different set of problems. The expertise to recognize if the experiment and the data are valid may not be available to the user. The author recently saw a preprint on a preprint server where all the spectra presented had a significant experimental issue, and it was obvious the authors did not recognize there was a problem. Making the instrument user-friendly may mean a data file is delivered, but means nothing. This becomes more of an issue when the final output to the user is significantly processed before reporting, as in an FT-IR instrument.

So how do we as a community of analytical chemists and spectroscopists cope with this problem? Through education. The educational resources offered by Pittcon, SciX, and EAS can help fill these gaps. Both in-person and online offerings are available. And as I mentioned in this review last year, the professional societies are on hand to help. They have education programs that can fill the gaps. Working together as a community between instrument companies, professional societies, and publishers, we can provide the resources to make a measurement easily, interpret it appropriately, and report it accurately.

If your organization plans to introduce a new product after this article appears, please submit the 2025 Spectroscopy New Product form that can be found at **www.spectroscopyonline.com/view/spectroscopy-new-product-review.** *We will be accepting submissions as the products are introduced and include the appropriate products in the 2025 review.*

Ultra-Low Frequency Raman Spectroscopy

"Extend your Raman system into THz frequency range (5-200 cm^{-1})"



Measured with
LabRAM HR Evolution
(data courtesy of: Prof. P.H.Tan
Institute of Semiconductors, CAS)

BragGrate™ Bandpass and Notch Filters

Spectral and spatial laser line cleaning filters and ultra-narrow line notch filters for low frequency Raman Spectroscopy

Wavelengths in Production (nm)
405, 442, 458, 473, 488, 491, 514, 532, 552, 561, 568, 588, 594, 632, 660, 785, 830, 980, 1064, 1550

- **Frequencies below 10 cm^{-1} with single stage spectrometer**
- **Angle tunable for precise wavelength adjustment**
- **Stokes and anti-Stokes Raman bands**
- **Unlimited optical life-time**
- **Custom wavelengths in range 400–2000 nm**

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