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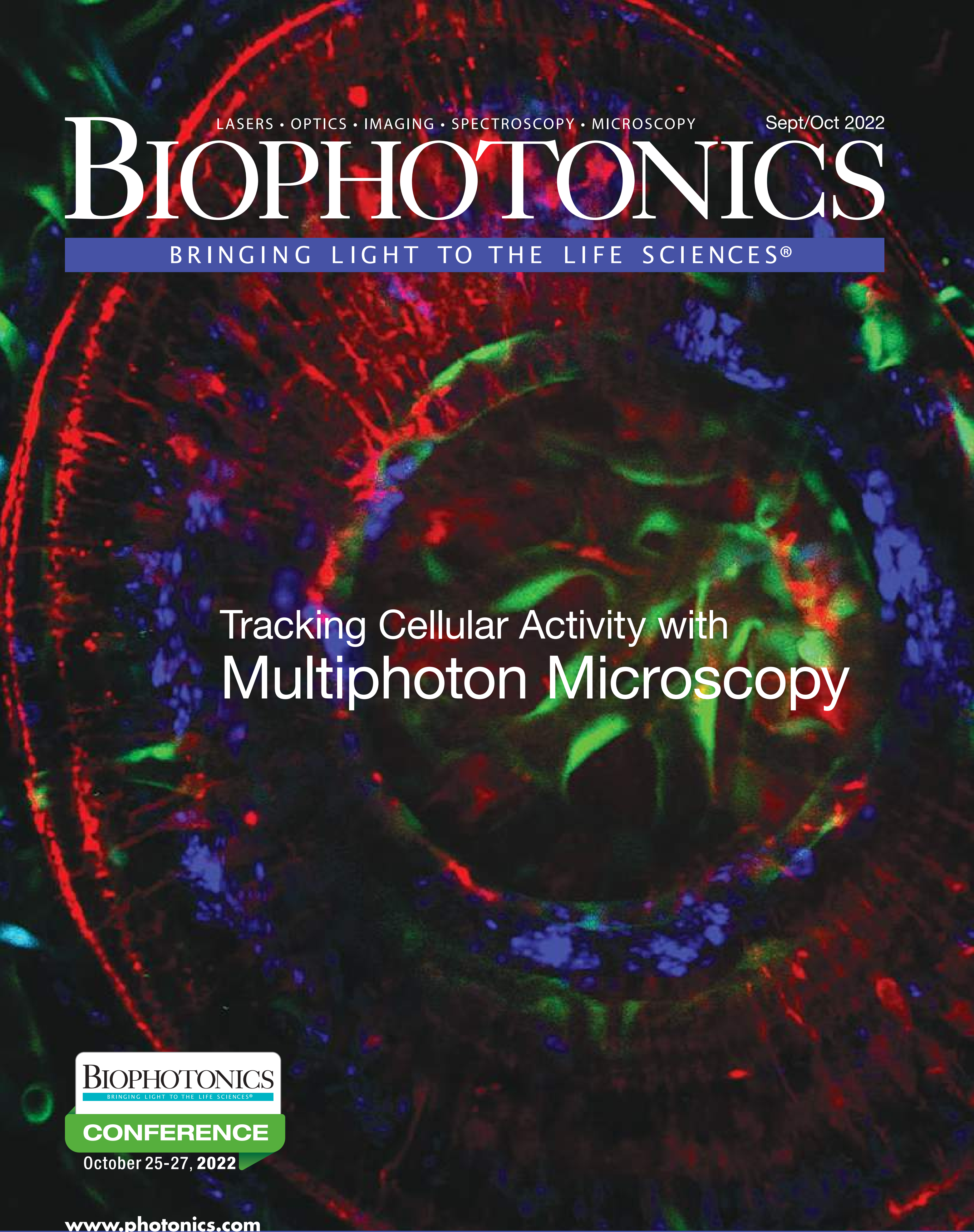

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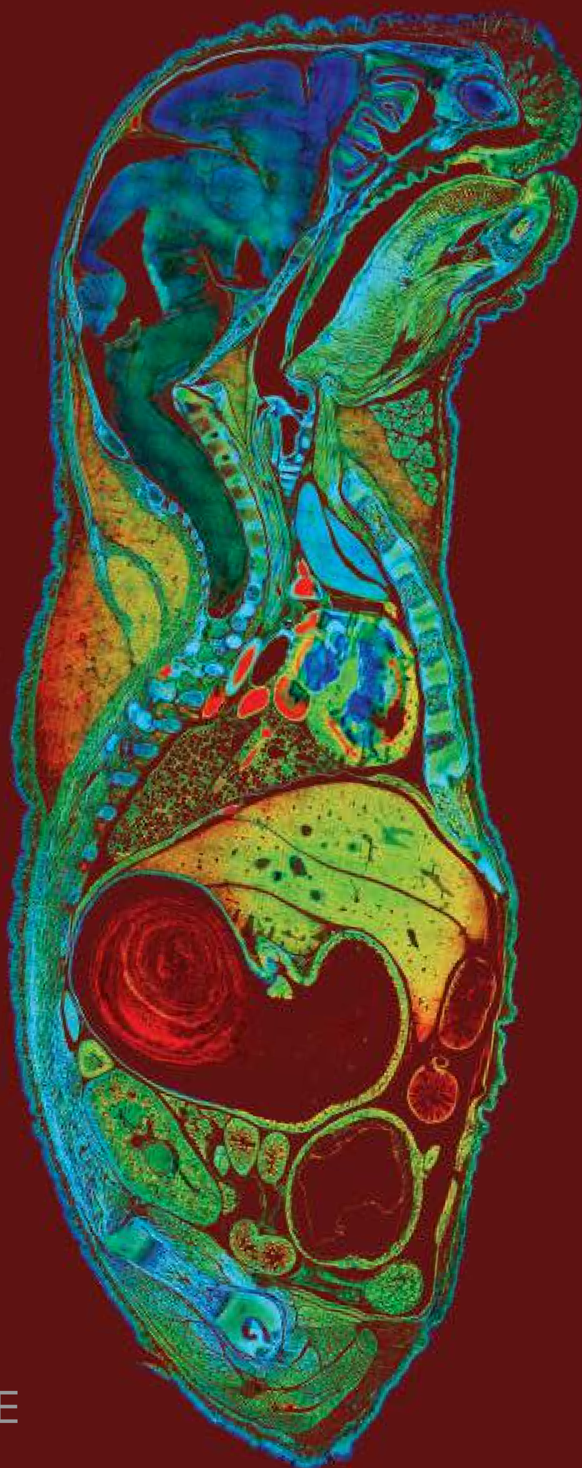
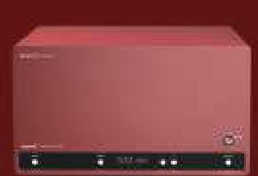


Confocal microscope image of a mice. Credits: Leica Microsystems



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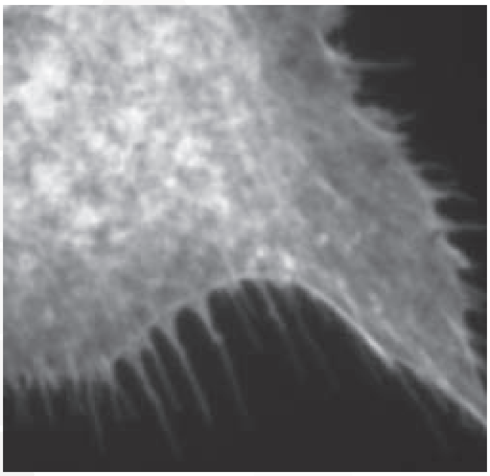

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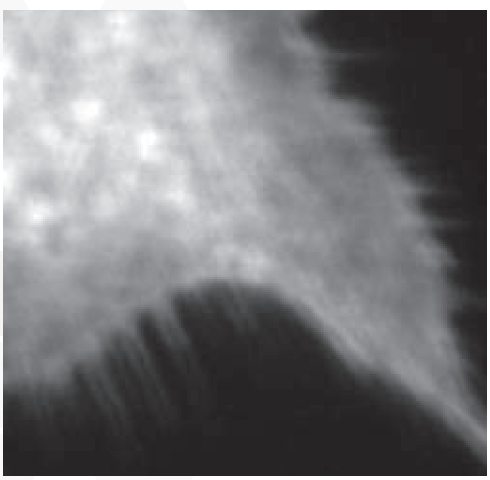

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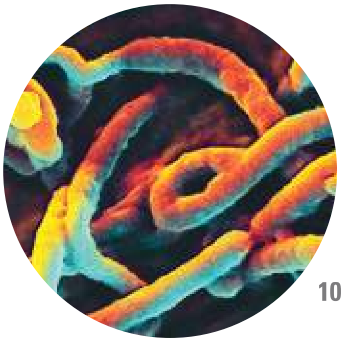

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BioPhotonics editors curate the most significant headlines for photonics in the life sciences — and take you deeper inside the news. Featured stories include:

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- Micro-ring resonator enables fast, accurate detection of Ebola virus
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The mobile design featuring built-in laser scanning provides key insights into animal tissue samples and offers a window into human systems to help guide treatment.

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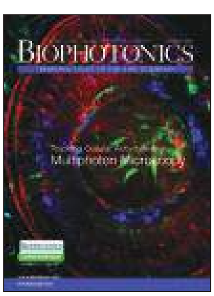
Robust physical properties and enabling capabilities make optical fiber-based sensors attractive for biomedical applications ranging from light delivery and imaging to robotic procedures.



THE COVER

Multiphoton microscopy captures a 3D z-stack image of the eye of a living zebrafish larva. See page 20. Image courtesy of Prospective Instruments. Cover design by Art Director Suzanne L. Schmidt.

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PHOTONICS

The technology of generating and harnessing light and other forms of radiant energy whose quantum unit is the photon. The range of applications of photonics extends from energy generation to detection to communications and information processing.

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Multiphoton techniques go deeper into detail

As scientists seek to image deeper in tissue with high enough resolution to track cellular processes, they are increasingly turning to multiphoton techniques. In multiphoton microscopy, longer-wavelength photons, which have lower energy and penetrate further than their shorter-wavelength counterparts, cause less tissue damage while imaging at greater depths. But, historically, these systems have required sophisticated and complex instrumentation that has put them out of reach for many clinical and laboratory settings.

This situation is changing. In our January/February issue, we published a story by Mihaela Balu, who wrote about a compact imaging head that could house a femotesecond fiber laser along with associated optics and mechanics and a rack-mounted power supply. She said it could remove the inefficiencies created by steering mechanisms, and she described how these developments could enhance the resolution of features when imaging the skin.

In this edition of *BioPhotonics*, authors Michael E. Holmes, Nkechi Holmes, Stefanie Kiderlen, and Lukas Krainer explain that using light in the NIR range leads to lower scattering in tissue, with less photobleaching — for example, capturing fluorescent tags in animal brains that indicate specific neuronal activity. The authors also cover the importance of the scan head design, which needs to include galvo-resonant mirrors, photo multiplier tubes, objectives, a wide-field camera, illumination, and lasers. As they illustrate on page 20, when these elements are combined into one form factor, the design of the scan head is adaptable to virtually any experiment.

The desire for compactness is also addressed by McKenzie Peterson, who writes that a number of companies and universities have set to work to configure an effective and portable OCT device. The light source, reference arm, and sample arms have been moved to the scanner, with only the spectrometer and computer located in the device itself. 3D printing has helped produce the unique parts that these devices require, in far shorter time than traditional machining. Learn more on page 28.

Elsewhere in this edition, Alexis Méndez writes about how thin, flexible, dielectric optical fibers have been used in endoscopes for many years and are being used in minimally invasive and robotic surgery. Read about these exciting developments on page 36.

Amanda Dobbins, Stephanie Herzog, and Mathias Strackharn write about a laser scanning method that is already used in additive manufacturing and that takes full advantage of a galvanometer motor, reduces errors, and can scan various shapes and structures. The technology could be the foundation of the next generation of ophthalmic procedures. Discover on page 32 what the future may hold.

Finally, in "Biopinion," Jenna Mueller discusses the impediments to accessing safe and effective surgeries in low- and middle-income countries, where state-of-the-art operating suites are often unavailable, and portability and versatility are vital when using imaging technology. Her research team has been developing a laparoscope that is designed for surgeons in these settings. She argues that engineers of biomedical optics need to develop systems that require fewer consumables, such as syringes and oxygen, and limited maintenance to bring the benefits of safer operations to those who need them most. Regulatory processes must also be streamlined to produce real change in developing parts of the world. Read what she has to say on page 7.

Enjoy the issue!
Douglas J. Farmer

doug.farmer@photonics.com

Portable photonics technologies increase access to needed surgeries

BY JENNA MUELLER, UNIVERSITY OF MARYLAND

In health care systems located in low- and middle-income countries, addressing the growing burden of cancer diagnosis and surgery may require a new vision — one that leverages affordable, portable, electricity-independent, and accessible biomedical technologies. Technologies that leverage biomedical optics are poised to meet this need because they can capture relevant morphological and physiological information that guides cancer diagnoses and excisions. These technologies can also be developed to enable procedures that are fast, low-cost, noninvasive, and nondestructive to tissue, making such devices potentially well suited for areas where surgical space is limited.

According to the World Health Organization, 4.8 billion people worldwide lack access to safe, timely, and affordable surgical care and anesthesia. The vast majority of these people reside in low- and middle-income countries, where over 70% of the global cancer-related deaths now occur.

These more accessible medical devices could ultimately reduce the burden of disease experienced by the most marginalized populations.

To develop technologies enabled by biomedical optics, engineers are turning to human-centered design during product development, an approach that involves the perspective of the end user — the surgeon and surgical staff that work in the operating room — throughout the design process. Through an iterative process of designing devices together with the perspective of end users in lower-income areas, researchers from the University of Maryland and other institutions recently learned about key design considerations involving adaptability in the field that were not initially apparent to system designers.

The initial cost for purchasing devices can be an obstacle, but ongoing costs are also an impediment to the implementation of new technology. For example, it costs more than $130,000 to purchase laparoscopic equipment to outfit a single operating room for laparoscopic surgery. To maintain equipment in higher-income countries, medical device companies sell expensive service contracts to hospitals and typically keep representatives on call who can perform repairs in between or during surgical procedures.

Our collaborators in East Africa, who would like to perform a majority of their surgeries laparoscopically — due to the significant and well-documented benefits to patients compared to traditional open surgery — applied for a grant and coordinated with their Ministry of Health to secure state-of-the-art laparoscopic equipment. However, their laparoscope remains largely unused due to the need for ongoing maintenance that is not affordable or locally accessible.

Another key design consideration for lower-income areas is that consumables are often inaccessible, including anything from medical consumables (catheters, needles, syringes, gloves, drapes, oxygen, and carbon dioxide) to infrastructure consumables (electricity and running water). Biomedical technologies for these lower-income areas should ideally be designed to avoid the constant need for consumables. This would cut down on ongoing expenses because many procedures require hundreds of dollars in consumables for each patient. Our group is exploring whether gasless laparoscopy, which does not require carbon dioxide, is possible by mechanically lifting the abdomen, for example.

When devices are properly designed for low- and middle-income countries, the designers must also navigate the complex world of regulatory bodies. Due to a lack of established regulatory bodies in these countries, many medical device companies choose to pursue the expensive and time-consuming process of going through the U.S. FDA or the European Medicines Agency. Our group and others have called for a streamlined regulatory process that would facilitate bringing medical devices to African markets.

As engineers with expertise in optics, we have an opportunity to increase global access to health care by developing biomedical technologies designed with these key considerations in mind. These more accessible medical devices could ultimately reduce the burden of disease experienced by the most marginalized populations. Additionally, these redesigned devices could facilitate more equitable access to health care in rural areas in higher-income countries, where patients often face similar obstacles to accessing health care services.

Meet the author

Jenna Mueller, Ph.D., is an assistant professor in the Fischell Department of Bioengineering at the University of Maryland and in the Department of OB-GYN and Reproductive Science at the university's School of Medicine. She is also a member of the Program in Oncology at the university's Marlene and Stewart Greenebaum Comprehensive Cancer Center. She received her bachelor's degree in bioengineering, with a minor in global health technologies, from Rice University, and received both a master's degree and a doctorate in biomedical engineering at Duke University for her work developing optical systems and automated algorithms to improve the accuracy of cancer excision during surgery. She completed her postdoctoral training at Duke University, during which she worked with a multidisciplinary team to develop the Pocket colposcope, an optical device to diagnose cervical pre-cancer in women in low- and middle-income countries; email: mueller7@umd.edu.

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Stephanie Herzog is European sales team leader in medical technology at SCANLAB. Since 2005, she has proved her application know-how and technical competence in various technical sales roles. **Page 32**.

Michael E. Holmes, Ph.D., is founder of two-level systems, a distributer of novel scientific laser and microscopy solutions and the exclusive U.S. partner of Prospective Instruments. He received his doctorate in physics, with a research focus on ultracold atoms and molecules, from the University of Rochester. He has held various executive roles within the scientific laser and cryogenic industries. **Page 20**.

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Lukas Krainer, Ph.D., founder and CEO of Prospective Instruments, provides the creative inspiration and intellect for the new philosophy of turnkey and portable multiphoton imaging. **Page 20**.

Alexis Méndez, Ph.D., is president of MCH Engineering LLC. He received a doctorate in electrical engineering from Brown University and has 30 years of experience in optical fiber technology, sensors, and photonics. **Page 36**.

Jenna Mueller, Ph.D., is an assistant professor in the Fischell Department of Bioengineering at the University of Maryland and in the Department of OB-GYN and Reproductive Science at the university's School of Medicine. She is also a member of the Program in Oncology at the university's Marlene and Stewart Greenebaum Comprehensive Cancer Center. She received her bachelor's degree in bioengineering, with a minor in global health technologies, from Rice University, and received both a master's degree and a doctorate in biomedical engineering at Duke University. At Duke, she worked with a multidisciplinary team to develop the Pocket colposcope, an optical device to diagnose cervical pre-cancer in women in low- and middle-income countries. **Page 7**.

McKenzie Peterson is sales and marketing associate at Lumedica Vision Inc. She is a writer by training, with a degree from the University of Georgia. She has a special interest in health care and topics concerning medical devices and their usability. **Page 28**.

Mathias Strackharn, Ph.D., has a doctorate in physics. He is a product manager at SCANLAB, with strategic responsibility for scan systems made for medical applications. **Page 32**.

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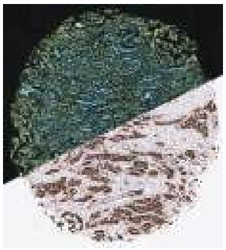
Virtual Biomarkers: An Emerging High-Throughput Research Tool

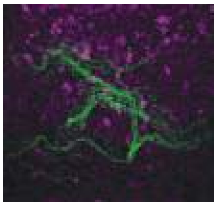


Pathology underlies every facet of health care, influencing more than 70% of all medical decisions. Yair Rivenson, Ph.D., of Pictor Labs demonstrates how it is possible to alter the centuries-old practice of histopathology using a digitized process in a nondestructive fashion. The process is enabled by a machine learning-based virtual staining technology that allows fully digital and virtual multiplex tissue platforms to substantively improve the quality and quantity of pathology samples. Rivenson also discusses the additional benefits of the technology.
To view, visit **www.photonics.com/w636**.

Intraoperative OCT in Veterinary Surgery for Cancer

Surgery is a common cancer treatment for dogs and cats, but the process of assessing the tumor takes several days and only evaluates a small portion of the tissues. Optical coherence tomography (OCT) is a noninvasive optical imaging technique that provides a solution for real-time intraoperative surgical margin assessment and allows rapid visualization of the tissue microstructure at the surgical margins. Laura Selmic of Ohio State University and her team have found high sensitivity and specificity for the detection of incomplete margins after surgical excision of skin tumors — including soft tissue sarcomas and mast cell tumors — in dog and feline injection-site sarcoma. The results she shares reveal OCT's potential for showing the demarcation between tumor and normal tissues, including muscle, fat, and skin.
To view, visit **www.photonics.com/w641**.

Sub-Cellular Biology at Tissue Scales with Cleared Tissue Axially Swept Light-Sheet Microscopy



Large-scale interdisciplinary efforts have worked to comprehensively catalog cellular architectures in health and disease. Kevin Dean, Ph.D., of the University of Texas discusses cleared-tissue axially swept light-sheet microscopy (CT-ASLM), a scalable imaging platform that leverages high-speed, aberration-free, remote focusing to achieve an isotropic resolution of 300-nm-scale subcellular imaging with an unparalleled optical sectioning capacity and large field of view. The platform provides global tissue architectures and also quantitatively detailed morphological and biochemical descriptions of the individual cells that compose healthy and diseased tissues. Sponsored by Power Technology Inc., Intelligent Imaging Innovations Inc. (3i), and Applied Scientific Instrumentation Inc.
To view, visit **www.photonics.com/w642**.

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A closer look at the most significant biophotonics research and industry headlines

Signal sorting method suppresses noise in STED microscopy

BELLINGHAM, Wash. — Researchers from Zhejiang University proposed a novel technique that selectively and effectively suppresses background noise in stimulated emission depletion (STED) microscopy. The approach bypasses drawbacks of current methods used to suppress noise in STED imaging.

STED microscopy was developed in 1994, demonstrated in 1999, and earned its developer, Stefan Hell, the Nobel Prize in chemistry, along with two other scientists, in 2014. STED microscopy is a superresolution technique for nanoscopy, which refers to the ability to see beyond the generally accepted optical limit of 200 to 300 nm, a feature that is particularly useful in cell experiments. When put into practice, however, STED microscopy generates undesirable background noise that affects spatial resolution and image quality. In general, this noise comes from two signal sources: fluorescence generated by reexcitation caused by ultrahigh light doses from the depletion beam, and residual fluorescence due to insufficient depletion of the inhibition beam.

Though powerful methods to remove the background noise have been developed, impediments to their implementation include image distortion, prolonged acquisition times, or the introduction of shot noise. These methods can be divided into three categories: time-domain, space-domain, and phasor-domain. The more selective and effective method proposed by the Zhejiang researchers is called dual-modulation difference STED (dmdSTED) microscopy. It works by sorting space-domain signals into the frequency domain so that the nondepleted fluorescence and STED-induced background are conveniently separated from the desired fluorescent signals.

The excitation and the depletion beams are loaded, respectively, with different time-domain modulations. Since it avoids the reexcitation caused by the depletion beam, a depletion laser with a wavelength closer to the peak of the fluorescence emission spectrum of the sample can be selected, which reduces the required depletion intensity.

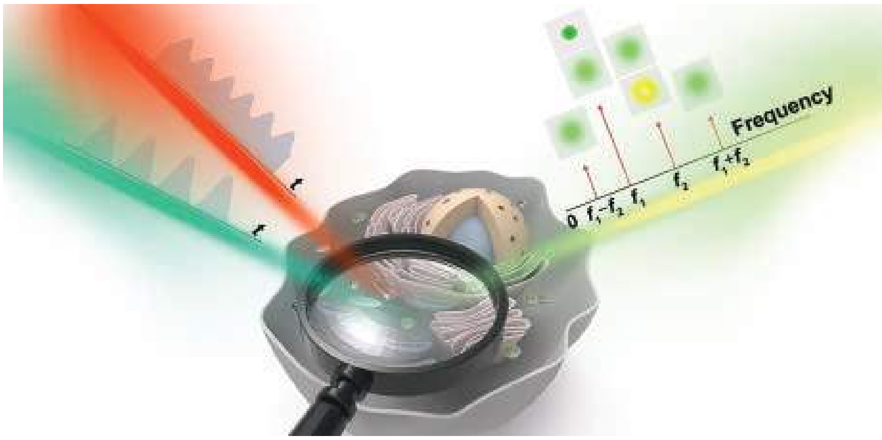
The current version of dmdSTED performs with spatial resolution of $\lambda/8$, higher than that of the phasor-domain methods, which are prone to shot noise. Theoretically, potential signal loss by time-domain approaches, such as time-gating, can be avoided by using the researchers' approach, they said.

Their method is also compatible with either pulsed or continuous-wave scenarios, and hardware for time-correlated single-photon counting is not required. Compared with space-domain methods, the time resolution of dmdSTED is not confined. As a result, the researchers' method is advantageous in acquisition of comprehensively fine microscopy images, accounting for spatial resolution, signal-to-noise ratio, and time resolution.

According to senior author Xu Liu, director of the State Key Laboratory of Modern Optical Instrumentation, the frequency domain method has the potential to be integrated into other dual-beam point-scanning techniques. These include excited-state saturation microscopy, charge-state depletion microscopy, and ground-state depletion microscopy.

In addition, Liu said, the method can accept more types of samples with spectral characteristics that differ from the fluorescent dyes commonly used in STED imaging, such as some quantum dots that may demonstrate wider excitation spectra.

The research was published in *Advanced Photonics* (www.doi.org/10.1117/1.ap.4.4.046001).



An illustration of the frequency-domain method developed by researchers at Zhejiang University that selectively suppresses backgrounds in stimulated emission depletion (STED) microscopy. The method improves upon existing noise-suppression techniques that impede imaging performance. Courtesy of Longgang Mulin Graphics.

Micro-ring resonator enables fast, accurate detection of Ebola virus

ST. LOUIS — A diagnostic technique for the Ebola virus uses a micro-ring resonator to detect a biomarker of the infection and quickly identify the virus in blood samples during the crucial early days of the infection. Researchers at Washington University School of Medicine in St. Louis developed the technique in collaboration with colleagues at the University of Michigan and biotech company Integrated Biotherapeutics.

In tests, the team's micro-ring resonator sensor detected the biomarker for the virus — soluble glycoprotein (sGP) — in less than 40 min and at low nanogram-per-milliliter concentrations.

Micro-ring resonators operate on the principle of whispering-gallery mode sensing. Light at a specific resonant wavelength is trapped in small micro-ring cavities, and, as light circulates within the micro-ring, it interacts with biomolecules deposited on the surface of the ring. This results in a shift in the ring's resonant wavelength that is proportional to the amount of the surface-adsorbed material.

The researchers used their method to trap light in the resonators and then used resonance to boost the signal they obtained. By monitoring where the resonance wavelength occurred, they could tell how much of the molecule was present.

The researchers developed a highly sensitive antibody to detect the sGP molecule at low levels and integrated the antibody into the sensor. On tests of the device, using blood from infected animals, they detected the biomarker as early as or earlier than the most sensitive test for viral genetic material currently available. They also quantified the amount of sGP in the blood. The higher the level, the more serious the disease.

"Looking at these data, we can say, 'If you're above these levels, your chance of survival is low; if you're below it, your chance of survival is high,'" researcher Abraham Qavi said.

With 128 active sensors per chip, the micro-ring resonator platform showed high multiplexing potential. These capabilities will enable the current sensor design to be adapted for use with a broader range of pathogens and will make it possible to incorporate other biomarkers relevant to infection detection, the researchers said.

In addition to multiplexing, whispering-gallery mode devices offer high analytical sensitivity, quick time to result, and ease of integration with microfluidics. Another advantage of the platform is the addition of unfunctionalized thermal control micro-rings, which negate any environmental fluxes that could influence measurements.

Current diagnostic tests for Ebola are not reliable until the virus has multiplied to high levels in the body — a process that can take days. A rapid, early diagnostic could help public health workers track the virus's spread and implement strategies to limit outbreaks.

A colorized scanning electron microscopic image depicts Ebola virus particles budding from the surface of a cell. A study from researchers at Washington University School of Medicine in St. Louis, along with colleagues at other institutions, details a tool that can quickly identify the presence of the virus in blood samples. The researchers said the technology has the potential to be developed into a rapid diagnostic test. Courtesy of the National Institute of Allergy and Infectious Diseases.

"Using a biomarker of Ebola infection, we've shown that we can detect Ebola infection in the crucial early days after infection," Qavi said. "A few days makes a big difference in terms of getting people the medical care they need and breaking the cycle of transmission."

The team still needs to validate its research in infected individuals, Qavi said. If the approach works, doctors could use the information to tailor treatment plans for individual patients and allocate scarce medications to the patients most likely to benefit.

The research was published in *Cell Reports Methods* (www.doi.org/10.1016/j.crmeth.2022.100234).

Hamamatsu to acquire NKT Photonics

HAMAMATSU, Japan — Hamamatsu Photonics announced that it will acquire Danish fiber laser manufacturer NKT Photonics. The companies expect to close the deal next year, through Hamamatsu's wholly owned subsidiary Photonics Management Europe SRL, located in Belgium.

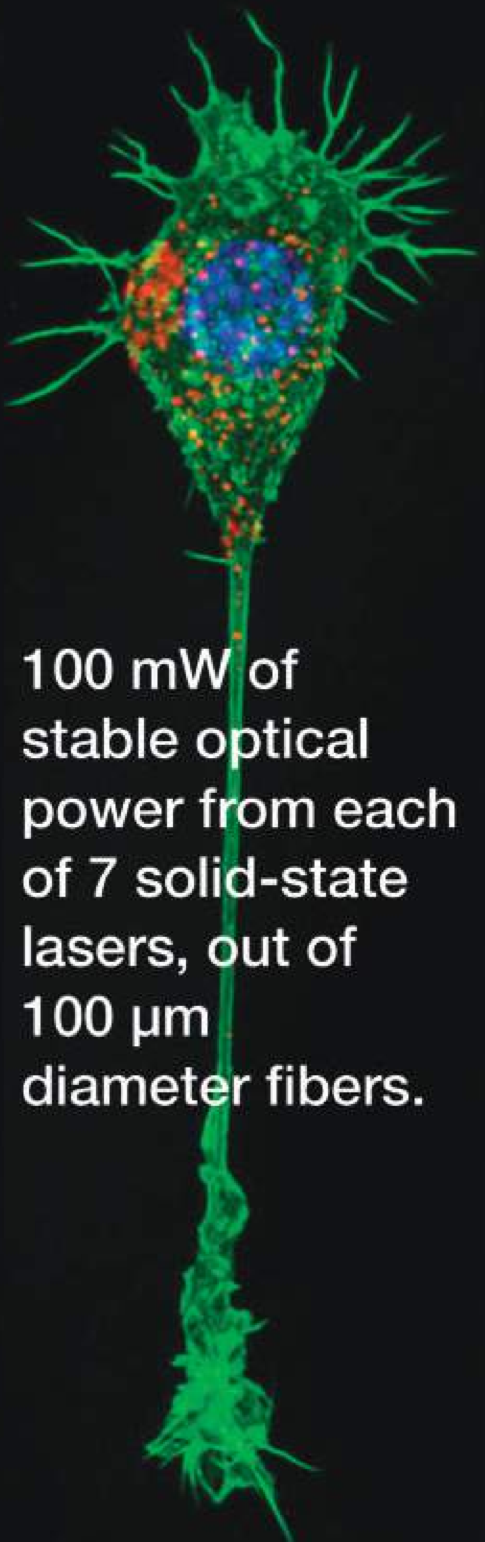
NKT Photonics will become a Hamamatsu subsidiary. The deal carries an enterprise value of ~€205 million ($210 million).

NKT A/S said the full divestment of its photonics business — together with the photonics business' previous divestment of its subsidiary LIOS to Luna Innovations in March — carries an enterprise value of ~€225 million.

NKT Photonics' primary focuses include the medical, life sciences, and nanotechnology markets. In 2021, the company employed 400 people and reported total revenues of €68 million.

The complementary relationship between the companies will support Hamamatsu as it expands its laser application business, the company said. NKT Photonics specializes in fiber lasers and uses its photonic crystal fiber production to enable ultrashort-pulse amplification and fiber transmission. Its fiber laser portfolio supports applications in microscopy, ophthalmology, and other fields.

NKT Photonics' mainstay products include a supercontinuum white-light laser, a single-frequency fiber laser, and an ultrafast fiber laser. Supercontinuum white-light lasers are used in microscopy and as light sources for inspecting semiconductor devices. Ultrafast lasers are used as surgical lasers in the ophthalmology field.



In memoriam: Laura Madden

Long-time Photonics Media employee Laura Madden died on July 31, at age 67, after a sudden illness. Madden began her career with the company in 1987 as an administrative assistant, and her hard work and reliability led to increasing responsibilities at the company. Her roles included managing advertising production for *Photonics Spectra*, *BioPhotonics*, and *EuroPhotonics* magazines, as well as helping to produce the *Photonics Buyers' Guide* as a member of the digital media department. In the last two years, Madden also supported advertising needs for the company's virtual conferences.

"It is with great sadness that we share the news of Laura's passing," said Tom Laurin, CEO and president of Photonics Media. "She spent over 35 years with us, contributing greatly to the company's success in several different roles. On behalf of the Photonics Media family, we extend our condolences to Laura's children — Theresa, Rebecca, and Daniel — and to her grandchildren and many friends."

More about Madden's life can be found online at www.photonics.com/a68253.

High-throughput imaging links microbial metabolism with cell identity

BOSTON — Researchers at Boston University, the University of Vienna, and Aalborg University collaborated to develop an imaging platform for investigating microbiomes in medical and environmental samples. The platform performs high-throughput metabolism and cellular identity analyses with single-cell resolution using a technique called stimulated Raman scattering two-photon fluorescence in situ hybridization (SRS-FISH).

The technique offers an imaging speed of 10 to 100 ms per cell, enabling the researchers to detect the metabolic responses of more than 30,000 individual cells to various mucosal sugars in the human gut microbiome.

To detect low concentrations of metabolites inside small cells with diameters of ~1 µm, the researchers developed a protocol that maximizes the isotope label content in cells and exploits the intense SRS signal from the Raman band used for isotope detection. They created a system that implements highly sensitive SRS metabolic imaging with two-photon FISH using the same laser source. These efforts collectively led to the SRS-FISH technique, which the researchers classified as an integrative, high-throughput platform that combines the advantages of SRS for single-cell stable isotope probing with two-photon FISH for identifying cells quickly and with a high level of sensitivity.

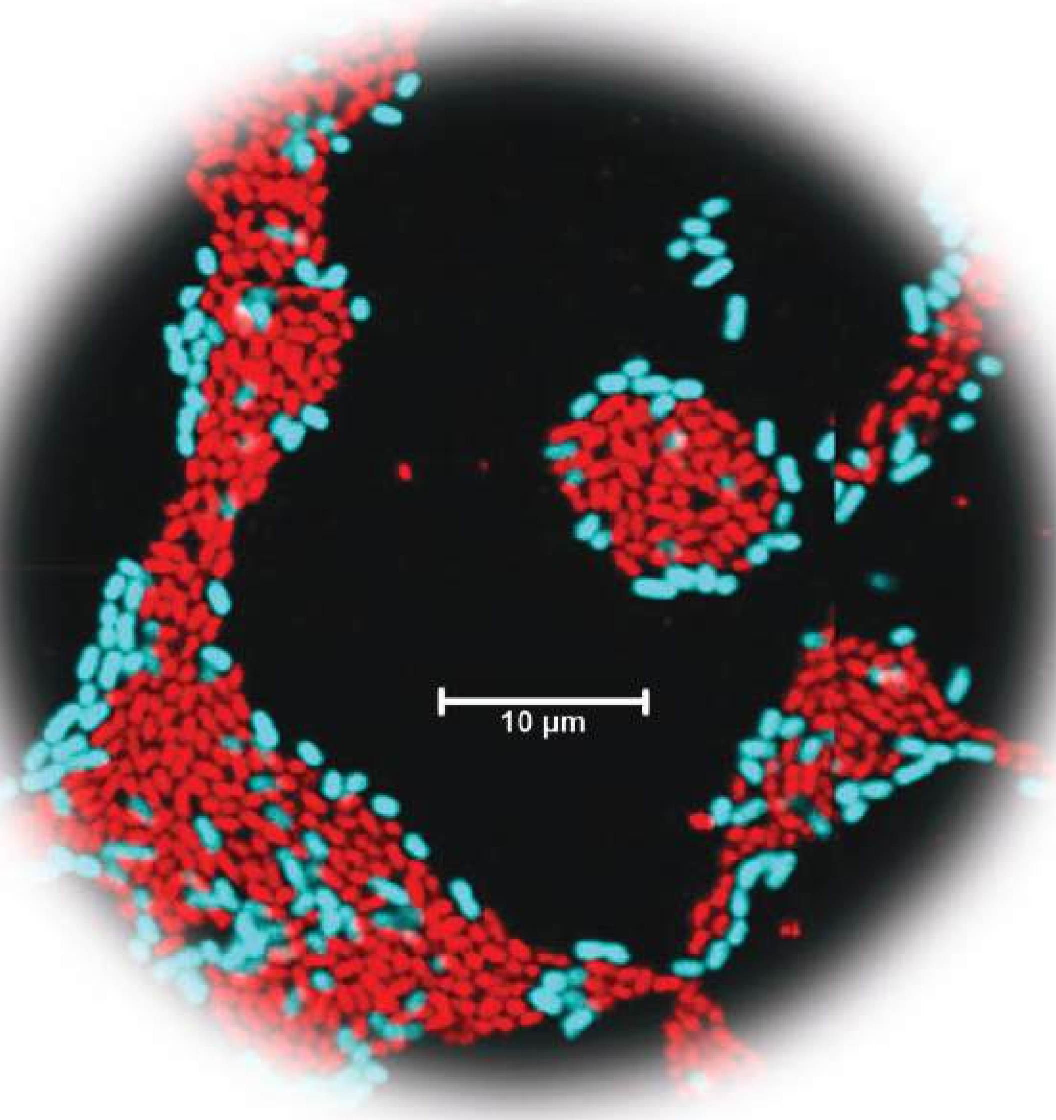
Due to its exceptionally high imaging speed, SRS-FISH could fill a gap in the tools available for linking microbiome metabolism to cell identity in complex microbial communities.

"SRS-FISH enables correlative imaging of cell identity and metabolism at a speed of 10 to 100 ms per cell. In comparison, it takes about 20 s to record a Raman spectrum from a single cell in a conventional spontaneous Raman FISH experiment," said Ji-Xin Cheng, the Theodore Moustakas Chair Professor in Photonics and Optoelectronics at Boston University.

Professor Michael Wagner of the University of Vienna said, "Until now, microbiologists have only been able to study the function of the most abundant microbes at the single-cell level. This enormous increase in speed means that less abundant representatives of microbiomes are now also accessible for single-cell isotope measurements."

To demonstrate the capability of SRS-FISH to link phylogenetic identity (genotype) with metabolic activity (phenotype), the researchers incubated live-cell samples in heavy water — deuterium oxide (D_2O) — enabling D_2O's incorporation into metabolically active cells. This step can be combined with Raman-based approaches to track metabolic activity at the single-cell level in response to a variety of compounds.

SRS-FISH was shown to enable fast and sensitive determination of the D_2O content of individual cells while simul-



An international team of researchers introduced an integrative, high-throughput platform that combines the advantages of Raman scattering microscopy for single-cell stable isotope probing with two-photon fluorescence in situ hybridization to identify cells quickly and with a high level of sensitivity. Courtesy of Xiaowei Ge et al./*PNAS*.

taneously revealing their phylogenetic identity.

The researchers applied the approach to complex microbial communities and locally tracked the metabolic responses of two phylogenetic groups of microbes in the human gut: *Bacteroidales* and *Clostridia*. Metabolism and identity analyses revealed that *Clostridia* may contribute more to mucosal sugar degradation than previously thought.

The results demonstrated the potential of SRS-FISH to identify the metabolism of specific microbes in microbiomes. At the same time, the application of the technique revealed findings related to mucosal sugar foraging in the human gut. Insights into the function of the human microbiome are essential to better understand its role in human health and to develop more targeted probiotics, Wagner said.

The sensitivity and resolution of the SRS-FISH platform could be improved in the future by implementing visible SRS. Further, the researchers said the SRS-selective scanning of FISH-targeted cells could improve the technique's throughput, especially when the taxa of interest is low. Upgrading the wavelength tuning speed of the laser equipment could also potentially increase throughput.

The SRS-FISH technique can be applied to a broad range of environmental samples, ranging from marine sediments to soil. Because SRS is resilient to sample autofluorescence, it can also be used with samples in which an autofluorescence background is present. Additionally, the technique is applicable to eukaryotes.

"Conventional approaches to imaging individual microbes in their environment, such as single-cell isotope probing, allow only a few cells or samples to be analyzed at one time," Cheng said. "SRS-FISH allows multiple samples to be scanned with high speed and sensitivity, revealing details that existing low-throughput methods might miss and providing a more complete understanding of the function of microbes in their natural environment."

The research was published in the *Proceedings of the National Academy of Sciences* (www.doi.org/10.1073/pnas.2203519119).

BIOSCAN BRIEFS

Spectroscopic systems developer and manufacturer **Ocean Insight** announced that it will expand its Monroe County operations in Rochester, N.Y., and create up to 100 new jobs over the next five years. The company plans to invest almost $1.8 million to expand the facilities at its Village Gate location and purchase new machinery and equipment. The company said the expansion should be completed by October. Empire State Development is providing up to $1 million to Ocean Insight through the Excelsior Tax Credit Jobs program in exchange for performance-based job creation commitments.

II-VI finalized its acquisition of laser developer and manufacturer **Coherent**. The combined company will be named **Coherent**, trade under the ticker symbol COHR on the Nasdaq stock market, and be organized into three business segments: Materials, Networking, and Lasers. Mark Sobey, former COO and executive vice president of Coherent, will be the president of the Laser segment. A timeline of the acquisition history prior to the finalization is available at Photonics.com.

Microscopy and imaging company **Carl Zeiss Meditec** and **Precise Bio**, a regenerative medicine company focused on advancing the use of bioprinted tissues and organs, announced a partnership to develop and commercialize fabricated corneal tissue for transplants in patients who require endothelial keratoplasty and natural lenticule transplants to treat keratoconus and for vision correction. Carl Zeiss Meditec will invest in Precise Bio to fund further development of Precise Bio's two cornea transplant products.

Precise Bio's biofabricated cornea. Courtesy of Precise Bio.

SCHOTT AG subsidiary **SCHOTT MINIFAB** announced it will open a manufacturing facility in Phoenix to provide design and manufacturing services for diagnostic and life sciences companies. SCHOTT MINIFAB — formerly Applied Microarrays Inc., which SCHOTT acquired in October 2021 — produces glass and polymer substrates and integrated cartridges.

Medical technology company **PreciPoint Group** closed a €10 million ($10.3 million) series A financing round to expand international commercialization of its in vitro diagnostic platform, gain market entry into the U.S., and develop the technology further. The company is expected to launch the iO:M8 ROSE product this year. Designed to digitize intraoperative assessments during cancer surgeries, the solution is an alternative to examinations that are traditionally bound to location and time with classic microscopy.

Hamamatsu Photonics completed construction of a building at its Joko factory site. The project will accommodate the company's intention to boost production capacity to 1.7× its current level. The building provides an expanded space in which to integrate production functions such as assembly and adjustment of digital cameras for scientific measurement and digital slide scanners for pathology. Operations at the facility started in August.

Biosensor R&D startup **Delta Diagnostics** received a seed investment from The Netherlands Organization for Applied Scientific Research and PhotonDelta, an ecosystem of photonic chip technology organizations. The investment primes the startup to further develop and validate its biosensor systems in preparation for a series A investment round. Delta Diagnostics' biosensor technology uses photonic chips to detect up to 16 biomolecules simultaneously.

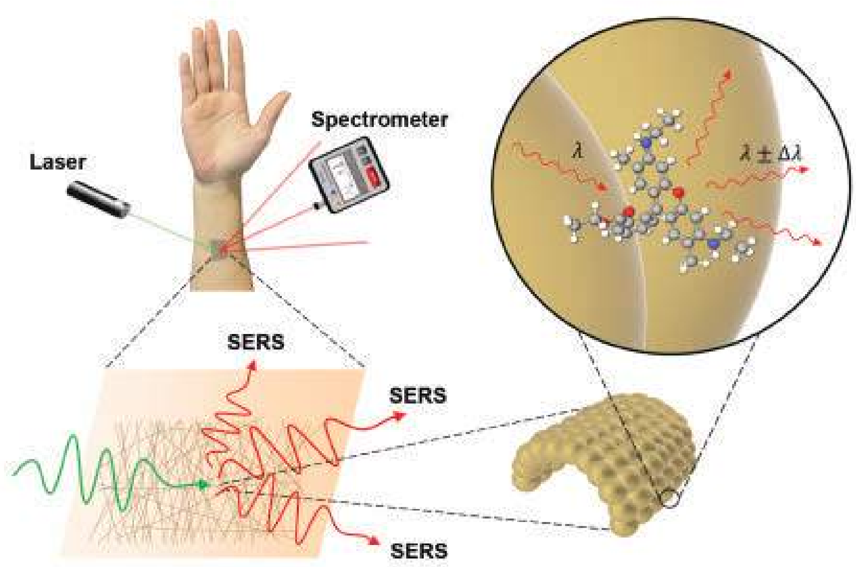
Wearable sensor uses Raman spectroscopy for chemical analysis

TOKYO — Researchers at the University of Tokyo developed an ultrathin sensor, spun from gold, that is designed to attach directly to the skin without causing irritation or discomfort. The sensor is enabled by surface-enhanced Raman spectroscopy and can measure various biomarkers and substances to perform on-body chemical analysis. It can be finely tuned to be extremely sensitive, and it is robust enough for practical use.

Current wearable health monitors are often bulky and costly, and they are typically limited to performing functions such as monitoring heart rate. The capability for wearables to measure chemical signatures for medical diagnosis has remained elusive. Prompted by these shortfalls, researchers from the Department of Chemistry at the University of Tokyo sought to develop a cost-effective wearable that could sense a person's health conditions and environment.

The team's sensor design built upon

Surface-enhanced Raman spectroscopy (SERS) can be used to indirectly detect the presence of a chemical via laser light and a specialized sensor. Gold mesh provides an ideal surface for the sensor because gold is unreactive. When it comes into contact with a substance that is to be measured, gold does not chemically alter the substance. Courtesy of Goda et al.

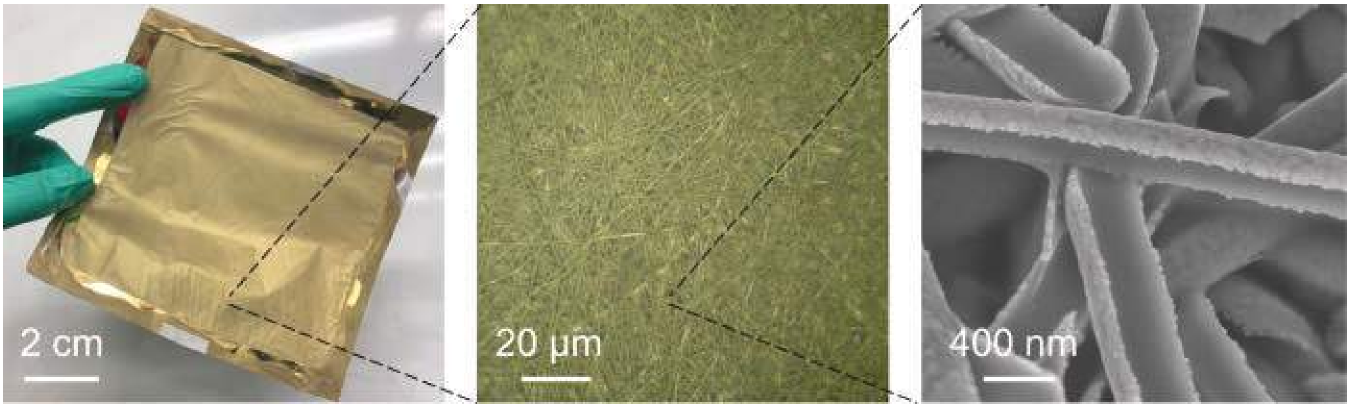


another University of Tokyo research group's method for producing stretchable electronic components. The first group had developed devices that it spun from ultrafine gold-coated threads. This design took advantage of the fact that gold can be attached to the skin safely because it does not react with or irritate the skin in any way.

"As sensors, [these devices] were limited to detecting motion, however, and we were looking for something that could sense chemical signatures, biomarkers, and drugs," said Limei Liu, a lecturer at Yangzhou University in China and a visiting scholar who worked with the group on the recent study.

The group chose fine gold mesh as the main component of the new sensor. Because gold is unreactive, when it comes into contact with a substance that is to be measured, it does not chemically alter the substance. And because gold mesh is so fine, it provides a surprisingly large surface for the biomarker to bind to, the researchers said.

The other components included a low-power laser. When it is pointed at the gold mesh, some of the laser light is absorbed and some is reflected. Of the



The gold nanomesh component of the wearable sensor at various magnifications. The individual fibers are ~1/500th the thickness of a human hair. Courtesy of Goda et al.

light reflected, most has the same energy as the incoming laser light. However, some incoming light loses energy to the biomarker or other measurable substance, and the discrepancy in energy between reflected and incident light is unique to the substance in question. A spectrometer then uses this unique energy fingerprint to identify the substance.

According to assistant professor Tinghui Xiao, the sensors must be finely tuned to detect specific substances. The team plans to increase the sensor's sensitivity and specificity even further to potentially enable applications such as glucose monitoring and virus detection, he said.

"There is also potential for the sensor to work with other methods of chemical analysis besides Raman spectroscopy, such as electrochemical analysis, but all these ideas require a lot more investigation," Xiao said.

The research was published in *Advanced Optical Materials* (www.doi.org/10.1002/adom.202200054).

Neuroscience conference returns to San Diego as live event

SAN DIEGO — The Society for Neuroscience will return to the San Diego Convention Center Nov. 12-16 for Neuroscience 2022, the society's annual conference. The largest neuro-specific conference in the world for physicians and scientists who are devoted to understanding the central nervous system will be held in person for the first time since 2019, with portions of the event available virtually.

The conference attracts more than 30,000 researchers, scientists, students, and physicians from around the world to hear about the latest advancements in neuroscience. Though the conference is not exclusively a photonics-focused event, light-based technologies are becoming increasingly important in neuroscientific research. Optogenetics, optofluidics, superresolution microscopy, and optical coherence tomography are just a few of the optical technologies driving the advancements that will be discussed in sessions at Neuroscience 2022.

The conference will feature a variety of lectures from leading scientists, including "Organization of Neuronal Activity Across the Brain," presented by Matteo Carandini of University College London; "Mapping and Rewiring Neural Circuits Underlying Emotions," presented by Kafui Dzirasa of Duke University School of Medicine; and "Cerebellar Interactions with the Basal Ganglia: Does This Thing Come with an Instruction Manual?" presented by Kamran Khodakhah of the Albert Einstein College of Medicine.

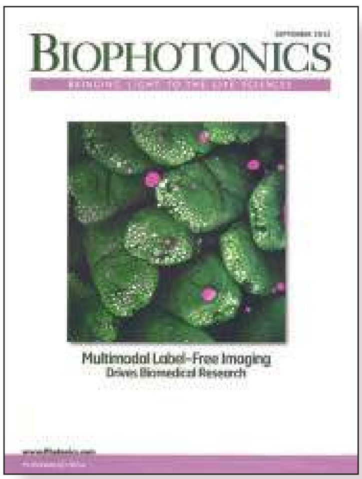
The event will also offer a variety of symposia and minisymposia, with topics covering the gamut of neuroscientific en-

The Society for Neuroscience will hold its Neuroscience 2022 conference at the San Diego Convention Center Nov. 12-16. Courtesy of San Diego Convention Center.

deavors. Among the selected presentations are “Recent Advances at the Interface of Neuroscience and Artificial Neural Networks,” “Synapse and Circuit Function in the Retina,” “Super-resolution Imaging *In Vivo* Opens New Doors to the Nanoworld,” and “Interfacing Glial Cells with Materials, Devices and Optogenetics: An Emerging Path to the ‘Other Brain.’”

Up to 24 lectures will be streamed live, and the recordings will be made available on demand. The virtual component of the five-day show will also include a sampling of livestreamed symposia and minisymposia to illustrate the breadth of the field. Virtual attendees will be able to participate in the live Q&A for all livestreamed events. All on-demand recordings will be available from their date of broadcast until Dec. 16.

For more information and to register, visit www.sfn.org.



Ten years ago, *BioPhotonics* reported on a new optical microscope developed at UCLA. The high-throughput flow-through microscope detected rare cells with a sensitivity of one part per million in real time. The instrument was equipped with photonic time-stretch camera technology developed by the research team three years earlier.

2012

‘To catch these elusive cells, the camera must be able to capture and digitally process millions of images continuously at a very high frame rate,’ said Bahram Jalali, who in 2012 held the Northrop Grumman Endowed Optoelectronic Chair in Electrical Engineering at the UCLA Henry Samueli School of Engineering and Applied Science.

BioPhotonics BioScan, September 2012

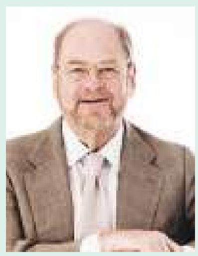
PEOPLE IN THE NEWS

Carl Zeiss AG expanded its executive board, adding **Susan-Stefanie Breitkopf** as chief transformation officer. **Matthias Metz**, member of the company's executive board and responsible for the ZEISS Consumer Markets segment, will switch to BSH Hausgeräte GmbH, where he will take over as CEO beginning Oct. 1. Additionally, **Georg von Erffa** was appointed head of corporate human resources of the ZEISS Group, succeeding Breitkopf. **Arlett Hesse** has been named Zeiss Group's head of corporate human resources Germany.

Susan-Stefanie Breitkopf. Courtesy of Carl Zeiss AG.

Dental laser company BIOLASE named **Jennifer Bright** CFO and **Steven Sandor** COO. Bright served as the company's vice president of finance beginning in April 2021. Sandor joined the company in 2019 and served as senior director of commercial operations and service.

Biophotonics company Atonarp appointed Nobel laureate **James Rothman** to serve on its board as an independent director. Rothman is the Sterling Professor and Chair of the Department of Cell Biology at Yale University School of Medicine. He has also served as chief scientist of GE Healthcare and its predecessor, Amersham. Rothman is a recipient of the 2013 Nobel Prize in physiology or medicine and the 2002 Albert Lasker Basic Medical Research Award.



James Rothman. Courtesy of Alena Soboleva.

Biophotonics company DYSIS Medical appointed **Chris Arnold** chief commercial officer. Arnold has more than 20 years of medical device experience, most recently serving as vice president of sales at Z-Medica. DYSIS' solution combines computer-aided cervical mapping technology with advanced colposcope design to aid in detecting cervical lesions.

Rockley Photonics CFO **Mahesh Karanth** resigned from his role to pursue other interests. **Chad Becker**, vice president of financial planning and analysis, is serving as interim CFO. **Ciaran Rooney**, vice president of strategic relationships, was promoted to senior vice president of corporate development. Rockley has begun a formal search for a permanent CFO.

Tom Nunn. Courtesy of Tibidabo.

Tibidabo Scientific Industries named **Tom Nunn** vice president of sales North America for Tibidabo Scientific USA. Nunn has more than 25 years of experience in sales and management positions in the optics and photonics industry, most recently as global OEM sales manager at Andor Technology.

Fluorescence-guided imaging technology company Lumicell appointed **Brent Palmisano** chief commercial officer and **Lauren Cohen** vice president of marketing and communications. Palmisano previously served as senior vice president of global commercial operations for DYSIS Medical. He also spent 15 years at Boston Scientific in a variety of sales and marketing leadership roles. Cohen spent over 17 years at Boston Scientific, most recently as director of global digital marketing. She has held marketing positions at Endius, Odin Medical Technologies, and ESC/Sharplan Lasers.

Lauren Cohen. Courtesy of Lumicell.

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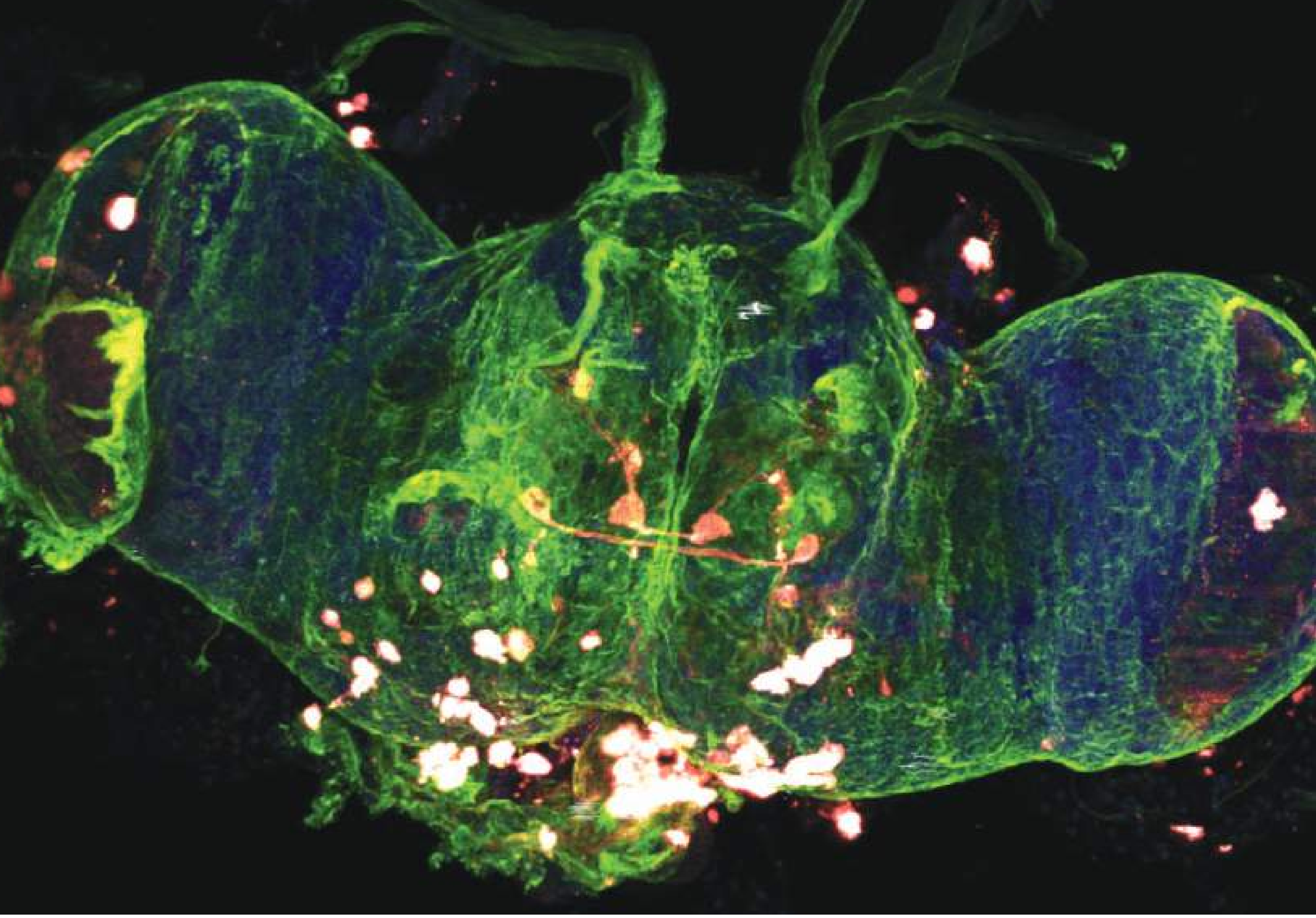

A multiphoton 3D z-stack image of a whole *Drosophila* (fruit fly) brain.

A **Multiphoton Microscope** Enables Portable 3D Biological Imaging

The mobile design featuring built-in laser scanning provides key insights into animal tissue samples and offers a window into human systems to help guide treatment.

BY MICHAEL E. HOLMES AND NKECHI HOLMES, TWO-LEVEL SYSTEMS, AND STEFANIE KIDERLEN AND LUKAS KRAINER, PROSPECTIVE INSTRUMENTS

For decades, optical microscopy has provided the mechanism with which to image cells and tissue for the purposes of cancer research, digital pathology, and the study of the brain. Samples are typically studied in frozen sections. Most of these systems use confocal microscopy and single-photon excitation, typically from a continuous-wave light source, to probe the sample. Multiphoton microscopy is used when deep-tissue and cellular-level resolution are desired to preserve the image of the tissue in its native environment. In laser scanning multiphoton microscopes, light from an ultrafast laser is tightly focused and scanned across the sample using fast mirrors. An image is created by detecting the fluorescence signal intensity at each point and mapping spatially with the aid of computer software.

The excitation source and signal detection implementation are critical for biological imaging, ease of use, and the uptime of the instrument. Multiphoton microscopy uses a highly focused laser beam in the near-infrared (NIR) range, typically between 780 and 1300 nm, to produce nonlinear optical effects based on the interaction of multiple photons arriving simultaneously at a molecule. Therefore, the intensity of the generated signal does not increase linearly with the num-

 Images courtesy of Prospective Instruments.

ber of irradiated photons but rather by the square power (for two-photon effects) or the third power (for three-photon effects). The phenomenon is confined to a very tight volume concentrated in the plane of focus, significantly reducing the absorption cross section from surrounding material. Moreover, using wavelengths in the NIR range leads to lower scattering in tissue and yields higher penetration depth compared to conventional linear confocal techniques. This allows 3D sectioning with less of the photobleaching and phototoxicity that plague single-photon techniques.

Real-time and extended-period measurements are possible — for example, in experiments studying live animals and drug target engagement. One prominent example of using laser scanning multiphoton microscopy is imaging deep in the living brain of animals (Figure 1d) by using standard markers such as GCaMP. GCaMP is a fluorophore-tagged and genetically modified calcium indicator that responds to the efflux of calcium ions (Ca^{2+}), indicating neuronal activity. Higher penetration depth combined with lower photodamage are major advantages to using laser scanning multiphoton microscopy for living or fixed native 3D samples such as brain, embryos, live organs, or animals, or for in vitro applications such as spheroids or organoids.

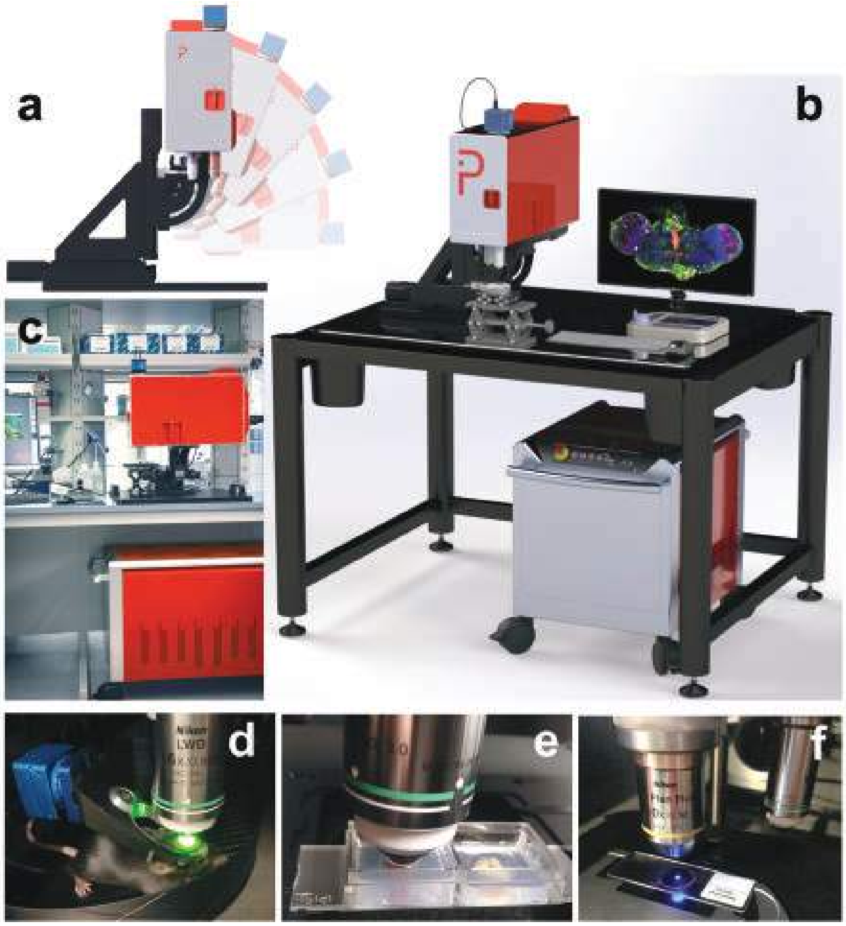

Figure 1. An ultrafast air-cooled fiber laser engine is integrated into the free-moving scan head of the MPX-1040 microscope **(a)**. The microscope consists of two parts **(b, c)** that are connected through a flexible umbilical cord. Example uses include live-mouse multiphoton imaging **(d)**, whole organ multiphoton imaging of a mouse kidney **(e, left)** and colon **(e, right)**, and imaging of standard 2D samples mounted on an objective slide **(f)**.

Finding versatile solutions

As the applications for multiphoton microscopy grow, so does the demand for an easy-to-use, transportable, and multimodal tool to adapt to any indoor working space. An ideal system should produce high-quality results and process high-volume data quickly while providing a powerful time-saving workflow. Also, the capability to perform multimodal analysis on the same region of interest without the inconvenience of moving the sample to another system maximizes content and provides more powerful complementary insights.

Rugged and industry-ready devices that can be used for clinical research and are capable of operating in any indoor environment are likely the future of laser scanning multiphoton microscopy. Commercially available systems lack the agility and mobility to be used outside of the laboratory. The scan head (including beam-steering optics) and ultrafast laser source design are critical to the overall functionality and usability of the microscope. Most systems separate the two components, and they are typically manufactured by separate suppliers.

The industry standard for the femtosecond laser system has been titanium:sapphire (Ti:sapphire) laser technology for nearly 40 years. These systems are very complicated to operate, typically requiring a trained expert, and they pose a significant safety risk. They require a large optical table, a chilled water supply, and special infrastructure, and they are fragile. Their size and weight and the amount of power they consume make them inappropriate for most clinics, and they are impossible to transport. Clinical researchers need a portable and turnkey multimodal microscope that can be incorporated in any indoor environment to be usable by most staff.

Next-gen instrumentation

The design of an ultraflexible laser scanning multiphoton microscope for in vivo imaging is predicated on a highly flexible front end and laser design. The ability to easily maneuver the scan head is key to allowing adaptability to a broad variety of setups, from slides to even live mice. The design of the scan head is crucial to enabling the microscope to be adaptable to almost any experiment. It should include the galvo-resonant scanners, photomultiplier tubes, objectives, wide-field camera and illumination, complete scan-path optics, and lasers — all in one compact, ready-to-go, modular form factor (Figure 1)[1].

The power and size of the laser source are critical in the design of a truly portable and agile laser scanning multiphoton microscope. Fiber lasers are well

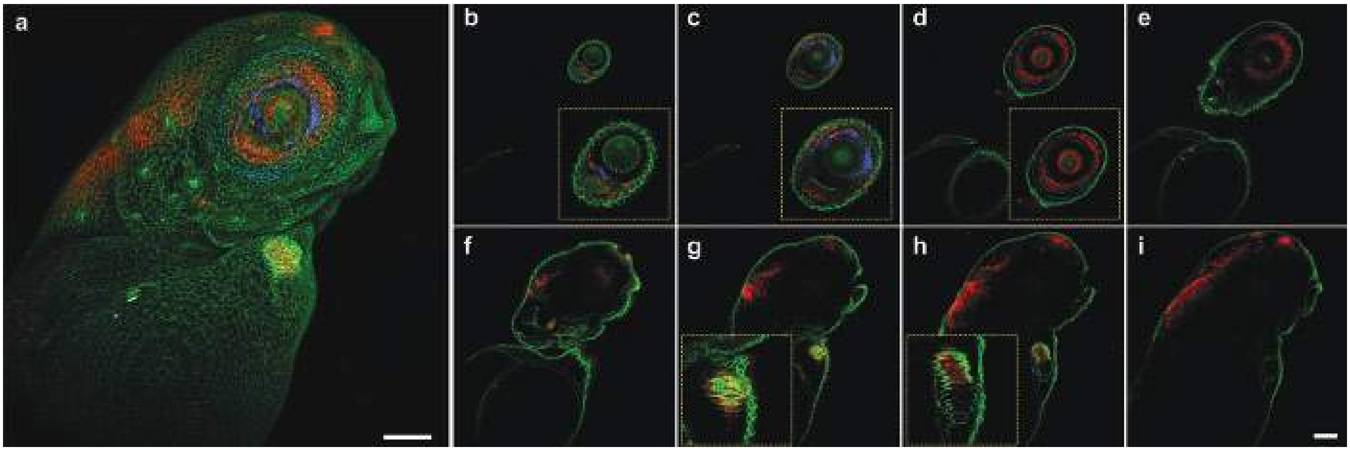

Figure 2. Multiphoton 3D z-stack imaging of a living zebrafish larva, expressing alpha-catenin-YFP (yellow fluorescent protein) **(green)** and tp1:mCherry-NLS (nuclear localization signals) **(red)**. Maximum intensity projection of a 510-μm z-stack with a step size of 10 μm — second-harmonic generation (SHG) **(blue)** and two-photon channels **(green and red) (a)**. Z-layers going from 20 μm **(b)** to 300 μm **(i)** in 40-μm steps. Close-ups depicting specific features such as the eye **(b-d)** or the beating heart of the zebrafish larva **(g, h)**. Scale bar: 100 μm.

suited for this purpose because they are compact, rugged, and energy-efficient for almost any indoor workspace. They are air-cooled and maintenance-free; therefore, there is no need for a chilled water supply or service. For example, the MPX-series microscope, recently developed by Prospective Instruments, is engineered with a dual-wavelength femtosecond fiber laser with a fixed output at 1040 nm (>500 mW) and a second widely tunable laser in the range of 750 to 960 nm and 1150 to 1300 nm (>200 mW). The pulse duration is <140 fs when operating at 80 MHz repetition rate. These parameters are all measured at the sample position and are sufficient for sectioning >1 mm.

High-resolution multiphoton imaging has been demonstrated on animals, including zebrafish and the fruit fly (*Drosophila*). Both provide invaluable information for understanding and advancing human pathophysiology. In recent experiments, both excitation (130 fs at 1040 nm) and detection signals were imaged through a 20× water objective (NA 1.0).

The fixed *Drosophila* samples were immunohistochemistry (IHC) stained with fluorophores (Hoechst and Alexa-Fluor 488), whereas the living zebrafish larvae expressed fluorophore-tagged proteins

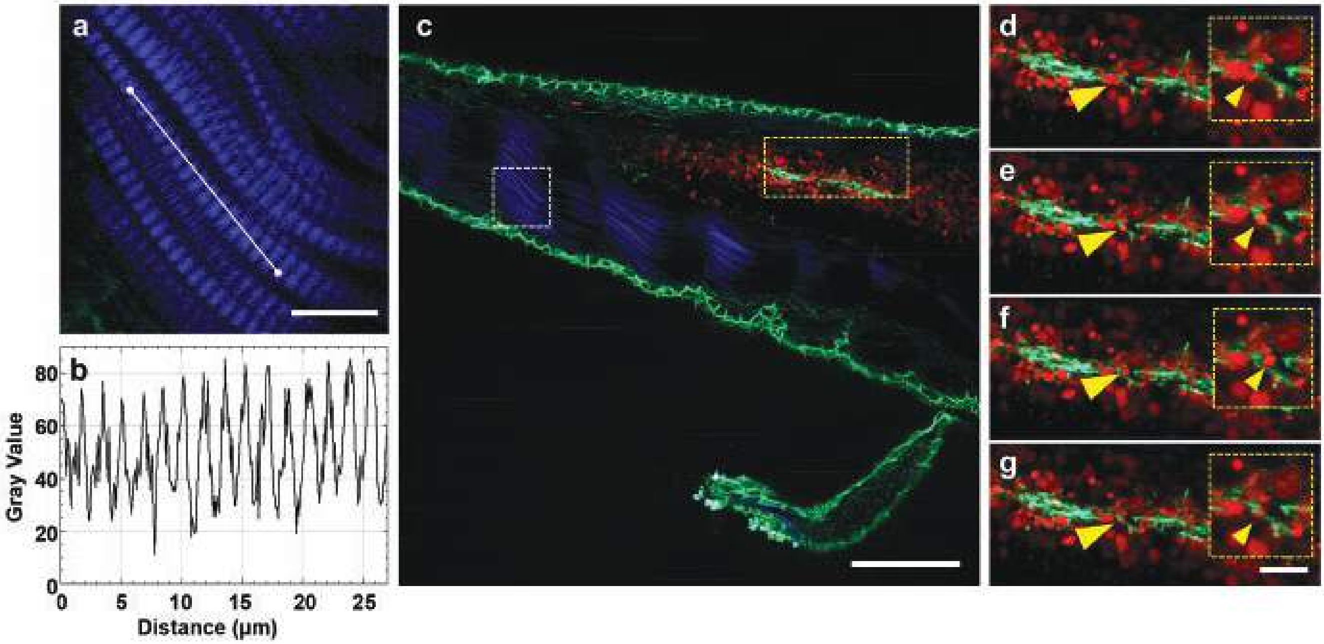

Figure 3. Multiphoton time-lapse imaging of a living zebrafish larva, expressing alpha-catenin:YFP **(green)** and tp1:mCherry-NLS **(red)**. A close-up of the SHG signal **(blue)** originating from the muscles **(a)** and the respective intensity plot to distinguish the z-bands **(b)**. An overlay of the SHG signal **(blue)** and the two-photon channels for YFP **(green)** and mCherry **(red)** expressed in the cell-cell contacts and the nuclei of cells in Notch-expressing tissues, respectively **(c)**. Close-ups of different timepoints, with 1-min steps in between. Migrating cells **(yellow arrows, d-g)**. Scale bars: 10 μm **(a)**, 100 μm **(c)**, and 20 μm **(d-g)**.

(green fluorescent protein, or GFP, and mCherry).

Structural and functional details were observed using complementary two-photon and second-harmonic generation (SHG) imaging (Figure 2) with z-stack and overlayed images of a living zebrafish showing differentiated features such as the beating heart. Another example, in Figure 3, shows features of the muscle (z-bands) and a migrating cell, with dual modality overlayed. SHG is a label-free method of differentiating collagen and muscles from the surrounding environment. Contrast from colors enhances the image specificity that is necessary for understanding the relationship between healthy, damaged, and diseased tissue, or between different cell types and extracellular matrix components.

Zebrafish imaging

The zebrafish has long served as an invaluable subject in the fields of metabolic pathology, developmental biology, and neuroscience. Its status as a vertebrate, as well as its ability to lay large numbers of collectible, transparent eggs, and its sustained transparency in the larval stage make it a highly practical and expedient live model for research. The genetic composition of zebrafish shows about 70% homology with human genes and a high sensitivity to pharmacological and genetic manipulations[2], allowing it to serve as a model for understanding various neurological disorders such as Parkinson's disease, Alzheimer's disease, and epilepsy, as well as psychiatric disorders, including attention deficit hyperactivity disorder and schizophrenia.

Imaging the zebrafish brain does not capture the full psychosocial complexity of the human brain, as the fish's neurological circuit system contains fewer neurons, and there is linear organization of brain regions. But its optimal translucency allows its full volume to be captured in one image with maximized clarity. As displayed in Figure 3, the use of multiphoton imaging enhances these features, as the reduced phototoxicity allows live imaging of the zebrafish from its neural network down to its subsynaptic components[3].

This is especially beneficial for retinal imaging. The zebrafish has a vertebrate-like retina with a complex and self-contained network of neuron populations. Overall, there are five different types of neurons in the retina: photoreceptors, bipolar cells, retinal ganglion cells, amacrine cells, and horizontal cells. The ganglion cells are the only ones that fire action potentials, while photoreceptors are the only neurons that respond directly to light. There are also two types of photoreceptors, called rods and cones. Rods are large and cylindrical and much more sensitive to light. Cones are shorter and are solely responsible for color vision. The cones have subtypes that contain photopigments that are sensitive to different wavelengths. Incorporating genetic techniques with the help of advanced multiphoton microscopes can enhance our understanding of retinal development, morphology, and diseases such as macular degeneration[4].

In the referenced zebrafish studies, the living larvae were treated with tricaine to immobilize the sample. Then they were mounted in 0.8% agarose in a 35-mm petri dish. When the agarose was polymerized, the larvae were covered with 0.5× E2 medium and imaged. Near-field 3D imaging (Figure 4) allows detailed visualization of neurons in the eye within the anterior region of the body. Utilizing the far-field magnification setting allows visualization of neurons running along the lateral line. It is also possible to use the near-field setting to create a high-resolution image of the retina and its neurons. Living zebrafish specimens, expressing fluorophore-tagged proteins, yield an intense and robust fluorescence signal, which therefore helps mitigate photobleaching. Time-lapsed migrating cells were imaged with filopodia over an extended time. Additionally, these changes in magnification permit stacking and animation of multiple images, providing additional visualization of the fish's musculature and vasculature that would not be produced using a traditional confocal microscope.

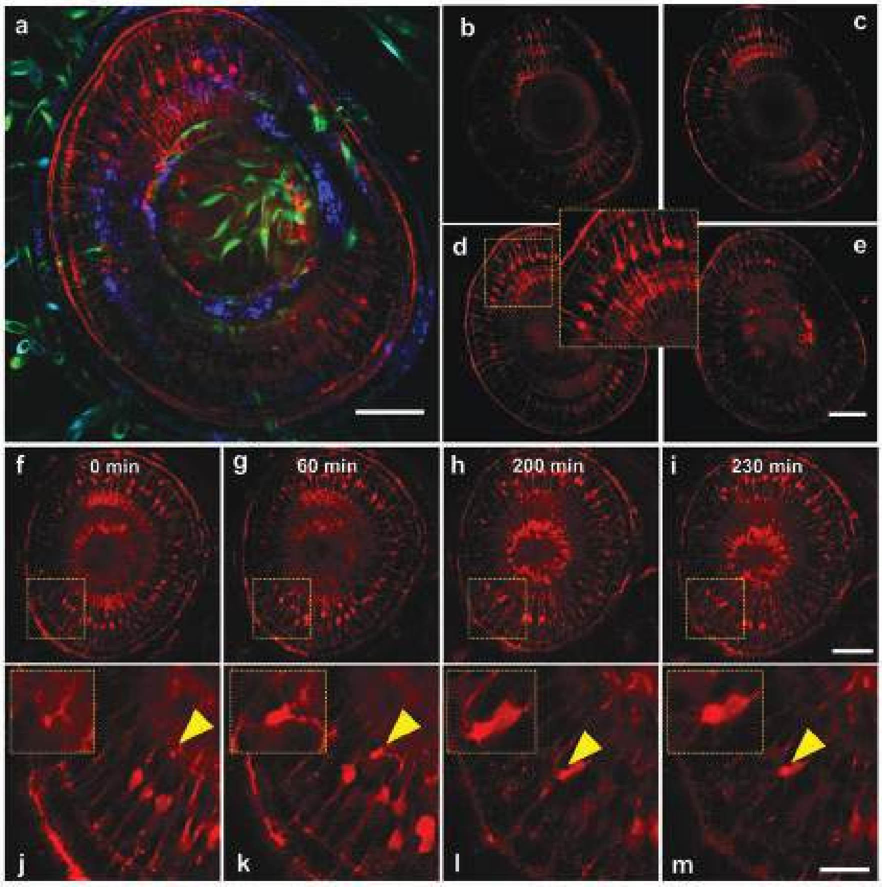

Figure 4. Multiphoton 3D z-stack imaging **(a-e)** and time-lapse imaging **(f-m)** of an eye of a living zebrafish larva, expressing tp1:LifeAct-mCherry **(red)** and Kdrl:GFP (green fluorescent protein) **(green)**. Maximum-intensity projection of a 200-µm z-stack with a step size of 20 µm — SHG **(blue)** and two-photon channels **(green, red) (a)**. Z-layers going from 20 µm **(b)** to 80 µm **(e)** in 20-µm steps. Timelapse of a zebrafish eye **(f-i)** with the respective close-ups showing a migrating retina cell **(j-m)**. Scale bars: 50 µm **(a-i)** and 20 µm **(j-m)**.

Imaging *Drosophila* brain

Drosophila melanogaster is another important organism whose neuroanatomy has been studied using multiphoton microscopy. The focused imaging of the common fruit fly has revealed several insights into the function of the olfactory system, neuroactivity, and neuronal tracing. This area of neuroscience focuses on the influence that different neuron populations have on each other and the functional connection between the anatomical regions of the brain. Additionally, the fruit fly has been used as a model in the study of neurodegenerative diseases, given that over half of the genes associated with neurodegeneration in *Drosophila* brain have counterparts in mouse or human brains[5]. The fruit fly also possesses several practical advantages, including its small size, rapid generation cycle, and ability to produce large numbers of genetically modifiable larvae[6].

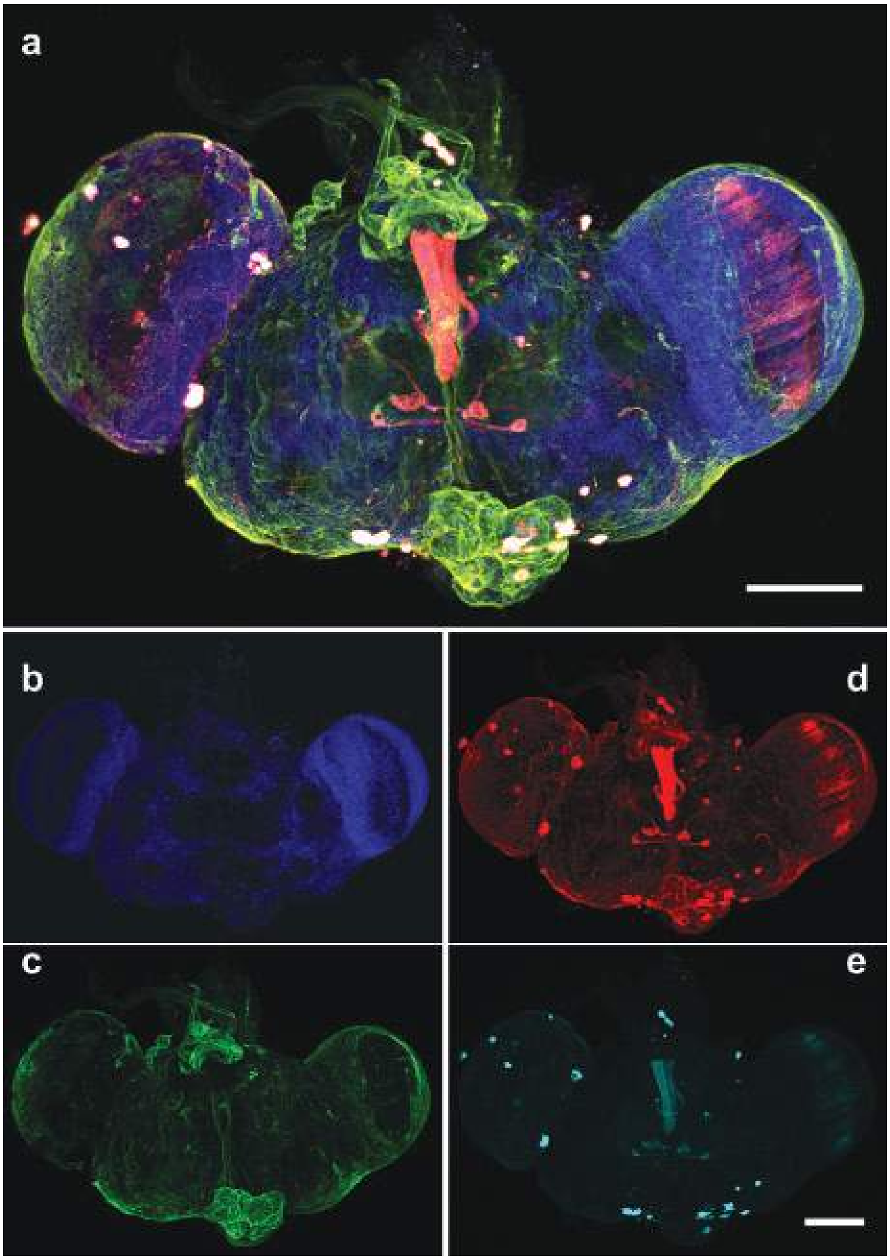

Figure 5. A multiphoton 3D z-stack of a whole *Drosophila* brain. An overlay of the cell nuclei (Hoechst) **(blue)**, different neuron populations — AF568 **(red)** and AF647 **(cyan)** — and the SHG signal **(green)**. An overlay of the maximum intensity projection of a 190-μm z-stack with a step size of 2 μm **(a)** and the respective single two-photon **(b, d, e)** and SHG **(c)** channels. An Olympus 20× water objective (NA 1.0) was used. Scale bars: 100 μm.

The olfactory system of *Drosophila melanogaster* allows it to recognize hundreds of distinguished odorants. Olfaction plays a critical role in allowing these insects to find shelter and food, and to mate. Olfactory receptor neurons detect and transmit chemical signals to the central nervous system. The process occurs within the fruit fly's primary olfactory sensory organs, the antennae, and the maxillary palps. On the surface of these organs reside sensory hairs called sensilla, which are connected to the dendrites of the olfactory receptor neurons and covered in sensillar lymph, a clear fluid containing several types of odorant-binding proteins[7].

The purpose of examining this network of neuron populations is to investigate the relationship between odor perception and behavior. In one study conducted by a research group at Stanford University, the antennae of the fruit fly were stained to visualize its neurons and compare the development of the olfactory neural circuit ex vivo with the in vivo conditions of the sample using time-lapsed images of the cells. One of the conclusions reached in the study was that the olfactory circuit in the explant culture develops similarly to the way it does in vivo but at a slower rate[8]. The use of two-photon microscopy has allowed researchers to differentiate between different populations of neurons in the entire brain and to simultaneously monitor their activity in 3D.

The whole *Drosophila* brain was resected, and the cell nuclei were stained with DAPI (4′,6-diamidino-2-phenylindole). The fruit fly was genetically modified to express different fluorophores, allowing easier differentiation between the neuron populations. An overlay of these stained cells is shown in Figure 5, while Figure 6 serves as its orthogonal counterpart, allowing complete 3D visualization of the brain along all planes. The nervous system is a complex network of various cells working in conjunction with each other. Imaging the different neuron cells all at once in their 3D environment can allow the ability to see how they interact with each other or their environment.

Neuroscientists see the importance of studying the entire brain and not just individual regions. It could be shown, however, that even in the resting state many brain areas are active simultaneously in *Drosophila*. For example, Maxwell H. Turner and his colleagues

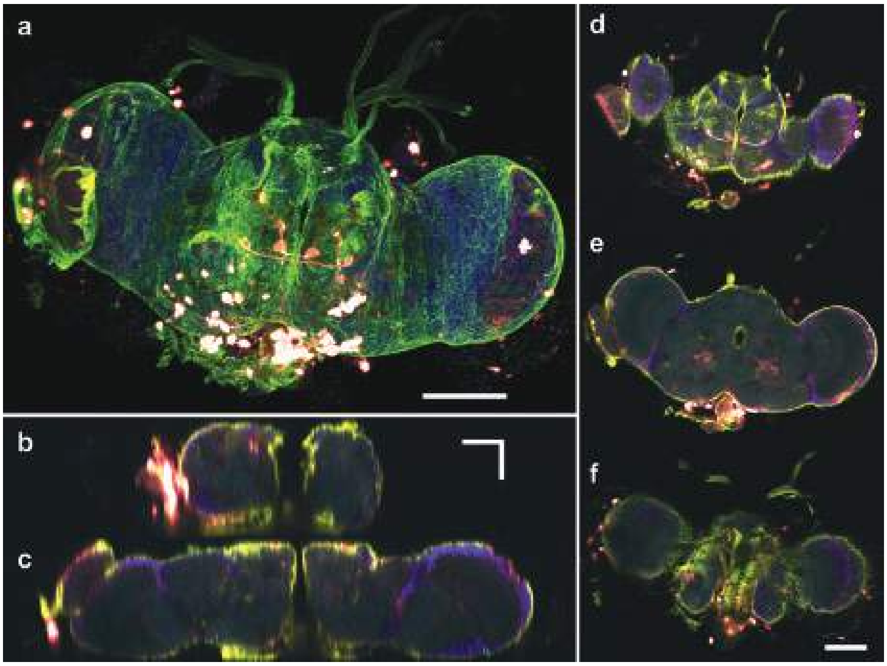

Figure 6. A multiphoton 3D z-stack of a whole *Drosophila* brain. An overlay of the cell nuclei (Hoechst) **(blue)**, different neuron populations — AF568 **(red)** and AF647 **(cyan)** — and the SHG signal **(green)**. A maximum-intensity projection of a 132-µm z-stack with a step size of 1 µm **(a)** and the respective orthogonal views in y,z **(b)** and x,z **(c)**. Top, middle, and bottom layers **(d-f)**, respectively. An Olympus 20× water objective (NA 1.0) was used. Scale bars: 100 µm **(a, d-f)** and 50 µm **(b, c)**.

have shown that several neurons in one region can have an impact on another region[9]. Overall, the fruit fly maintains good conservation of neural signaling pathways and overall cellular processes, which means there is a lot to be learned through studying this organism. This conservation has allowed biomedical researchers to not only image the fruit fly's anatomy, but also to assess the effects of certain treatments and drugs without the risks or ethical ramifications of testing on humans. For this type of assessment, it is essential to be able to image the whole brain in its full depth.

The use of laser scanning multiphoton microscopy is quickly growing throughout clinical and biological research for its superior benefits to traditional optical imaging. The instruments have helped deepen the understanding of various diseases, neuronal functionality, and structural relationships, as well as developmental processes. Until now, limitations on traditional instrumentation have slowed progress in mainstream research and industrial applications. However, the next generation of multiphoton microscopy systems will have the power to revolutionize biomedical research and overcome conventional barriers that are limiting access to deep-tissue imaging. Future developments and improvements to the platform include additional modalities such as three-photon and fluorescence lifetime imaging, improved optical performance using adaptive techniques, and a faster and more intelligent imaging workflow. And the systems could very well accomplish all of these improvements while maintaining the same physical form, efficiency, and agility.

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Above: Unlike its OCT predecessors, the OtoSight Middle Ear Scope generates a rolling A-scan in real time to provide a depth-over-time assessment. The device is housed on a freestanding rolling cart for easy access and mobility within the exam room. Courtesy of PhotonicCare.

Versatility in **OCT System** Design Opens the Door to New Clinical Applications

A more compact and portable design, achieved by separating the interferometer and light source from the spectrometer, may soon enable clinical uses beyond ophthalmology.

BY MCKENZIE PETERSON,
LUMEDICA VISION INC.

Optical coherence tomography (OCT), a noninvasive imaging technology, is a standard diagnostic tool used in the field of ophthalmology. With the advent of new compact form factors for the modality, as well as the assistance of artificial intelligence (AI) and other software innovations, OCT could be put to use in other clinical settings, such as optometry and family medicine. These and other specialties are taking notice of OCT's capacity to provide high-resolution cross-sectional images without the adverse effects of radiation or surgical incisions for the examination of tissue. Thanks to reconfigured and miniaturized components, as well as user-friendly interfaces, mobile clinics could reap the benefits of utilizing an accessible, easy-to-use OCT system.

The advent of OCT

The first recorded successful application of OCT was the imaging of an in vivo human retina by Eric A. Swanson and colleagues in 1993. The technology was ultimately commercialized in 2005 as a means for ophthalmologists to provide a noninvasive window into the delicate layers of the retina at the resolution required to monitor sight-threatening diseases. The technique has proved to be indispensable to retinal specialists and ophthalmologists, as well as for in vivo cardiovascular imaging. By the 2010s, however, access to OCT was still largely reserved for specialists and well-funded research. Recent innovation has enabled the development of novel point-of-care systems for generalists and practitioners of new medical specialties.

As an inspection tool, OCT has found a role in a variety of nonmedical fields such as food inspection and quality control. Essentially, any transparent or translucent sample with critical features on the micron scale is well suited for fast, nondestructive optical inspection. The human eye, as a natural system made to take in light, has historically been an ideal candidate for OCT inspection. Improvements to ophthalmic OCT systems have occurred in parallel with the development of new medical OCT devices for other parts of the human body. In health care diagnostics, the goal of OCT is to produce images to inform medical decision-making. Cost, however, plays a factor in which end users get access to OCT.

New design

Point-of-care imaging brings the technology to the patient at the moment of need or diagnosis. But bulky, expensive OCT systems, which often require their own room and are largely available only in specialists' offices, have been inaccessible to many patients worldwide. Many glaucoma cases remain undiagnosed for years and are diagnosed only when a patient visits a specialist who has an OCT system. Unfortunately, any damage done to the eye by glaucoma during this time is irreparable.

The pandemic has added to the backlog of eye diseases not getting diagnosed. As patients emerged from lockdown, health providers saw clinics flooded with overdue appointments and new patients. In many countries — including the U.S., China, and Japan — an aging population also contributes to the rising number of people needing eye care.

With clinic space and clinicians' time at a premium, providers need to consider the most efficient ways to spend their money. Having a compact OCT diagnostic device in every exam room at a clinic or doctor's office would decrease the time a patient spends waiting to be examined and would increase the number of patients a provider can see during a scheduled hour. To enable such availability, and to increase the ability for multiple personnel to use the devices, clinical OCT requires a low-cost, compact design with an emphasis on simple functionality.

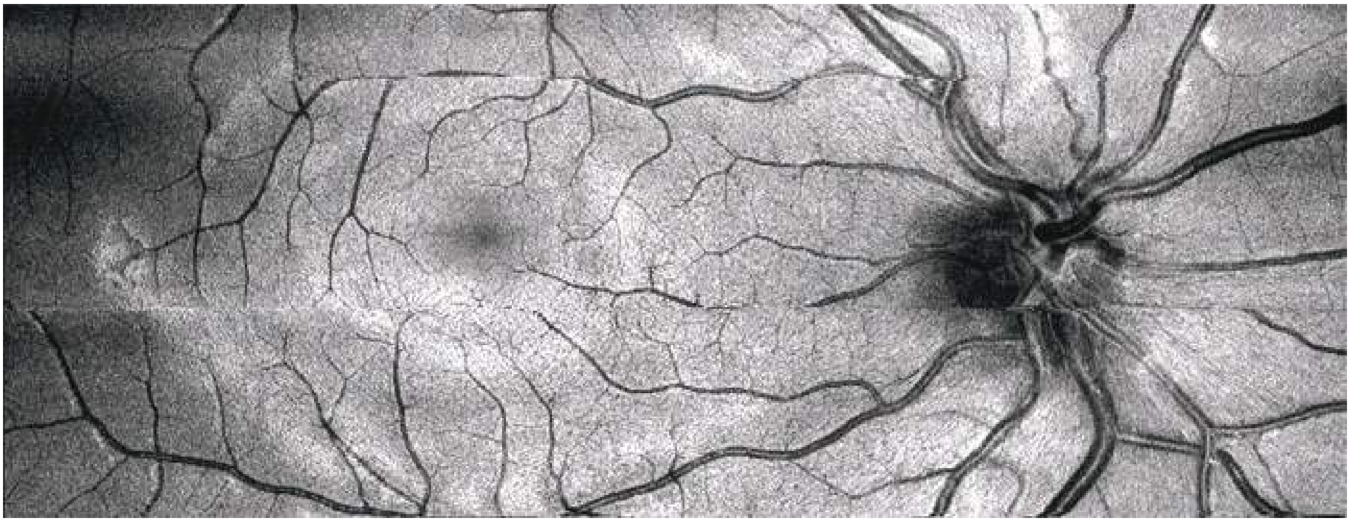
To achieve these requirements, optical engineers have considered various ways in which they could configure the basic components an OCT device. To make the design more compact, researchers rearranged the Michelson low-coherence interferometer, the basis of OCT, into smaller packages. In the first clinical application of this newly conceived low-cost OCT system, researchers moved the light source, reference arm, and sample arm to the scanner[1]. In this configuration, only the spectrometer and a computer were housed in the body of the device. 3D printing has been critical to prototyping a redesign because it has enabled the engineers to print overnight and iterate new designs in hours, a process that used to take weeks to accomplish on a shop floor.

This newly configured OCT design is almost ready for clinical application. Lumedica Vision Inc.'s OQ EyeScope 1.0 /X, a retinal spectral domain (SD)-OCT imaging system that features the compact and lightweight design, is in clinical-stage development, and FDA approval is pending. Excluding the chin rest, the system weighs just under 10 lbs. In the U.S., price is the most significant obstacle to using OCT in optometry, a field in which screening tools would have the most impact on eye disease diagnosis. Screening for glaucoma, age-related macular degeneration (AMD), and retinal disease in optometrists' offices using a low-cost tool such as the OQ EyeScope could prevent millions of undiagnosed cases of these conditions each year.

A goal of product designers is to make OCT more accessible to health care systems in developing nations, where the $50,000 to $100,000 price tag for traditional OCT machines is often too steep. Blindness attributed to glaucoma occurs more frequently in Africa than in other parts of the world. And in sub-Saharan Africa, most of the population lives in rural areas, while glaucoma specialists and eye care practitioners often practice in faraway cities. A mobile eye clinic equipped with low-cost screening tools could meet an urgent need in this area of the world and others.

OCT devices in the home

Diseases such as glaucoma and AMD progress slowly, so clinicians predict that daily monitoring would improve patient outcome by guiding early intervention and therapy. Because most health care clinics cannot provide this level of care, there is a significant incentive to move OCT into the patient's home for daily use. An at-home system presents challenges for OCT system designers: Since the device would be operated by the patient, both alignment and scanning would need to become automated tasks. And the system would need to be easy to use by people not familiar with operating medical devices. One 10-year study documenting the



VIS-OCT has the capability to capture a full fundus image. Courtesy of Hao Zhang.

The Aurora X2 is a clinical research system used at universities. Courtesy of Hao Zhang.

The OQ EyeScope 1.0 /X, a tabletop clinical OCT system, is currently awaiting FDA approval for clinical use. Courtesy of Lumedica Vision Inc.

utilization of a similar home-monitoring device (though not OCT-based) showed promising results[2].

Daily at-home monitoring, however, would produce an abundance of patient image data that would need to be translated appropriately between the patient and doctor. Research shows that AI algorithms may be more efficient than trained physicians at managing large amounts of image data. Even highly qualified retinal specialists do not have the time to set aside to look for irregularities in the images in the database created for each patient. Notal Vision, a digital health company, has set out to marry self-monitoring OCT technology with the wealth of data collected from this approach. The company provides a monitoring center from which physicians can access relevant data, curated by AI-based algorithms, to plan personalized patient care.

OCT for primary care

Research into low-cost OCT has contributed to the creation of hand-held OCT designs, which are ideal for examining hard-to-reach areas such as the human ear. The OtoSight Middle Ear Scope, which was developed by PhotoniCare Inc. and approved by the FDA in 2020, helps physicians to diagnose middle-ear infections and in some cases eliminates the need for exploratory surgery.

The current gold standard for diagnosing middle-ear infections, a pneumatic otoscopy exam, is correct only 50% of the time[3]. PhotoniCare advertises a 90.6% accuracy rate for detecting fluid buildup, the cause of middle-ear infections. When designers created the OtoSight, they determined that some capabilities were more important than others for its effective use. For example, to detect middle ear infection, primary care providers do not need to see the shape of the fluid buildup in the middle ear, but they do need to establish the existence of fluid and its turbidity. Therefore, instead of providing a complete B-scan, which is the depth profile of a sample over space, the OtoSight was designed to provide a rolling A-scan, or the depth profile over time, to supply the needed information. A simple point-and-shoot scanner enables the system to provide data on a single point as a series of images. This strategy reduces the size and cost of the design while making it easy for new users to interpret the system's images when making diagnoses. Researchers predict that the next area of expansion for OCT in otology will be the creation of an endoscopic device for use in the ear[4].

Even the use of near-infrared light, a fundamental element of traditional OCT, might be changed in future uses of the technology. This is because visible-light OCT (VIS-OCT) is showing promise as a retinal oximetry technique. The advantages of VIS-OCT include a higher axial resolution (<2 µm as compared to 6 to 7 µm in a typical OCT system) and higher image contrast. VIS-OCT systems are currently in early-phase clinical trials at leading ophthalmology clinics, including those affiliated with Hao F. Zhang at Northwestern University and others at New York University, Stanford University, the University of Virginia, and the University of Pennsylvania. Instead of the low-cost superluminescent diodes used in traditional OCT designs, however, most VIS-OCT designs depend on costly spatially coherent light sources, which is preventing the widespread adoption of VIS-OCT.

Open-source databases

Artificial intelligence is increasingly important in image analysis. Early data suggests computer vision will be able to identify retinal layer morphology and pathology. This work requires access to large databases of autonomous OCT retinal images. Several open-access OCT retinal image databases exist, including OCTID, published by Peyman Gholami and colleagues[5], and an annotated image database complied by researchers from the University Hospital Center of Zagreb[6]. Studies of deep learning models indicate that the identification of systemic retinal biomarkers could provide early warning for diseases found outside the eye, such as cardiovascular, kidney, and neurodegenerative diseases[7]. The increased availability of low-cost and hand-held OCT will lead to the expansion of image databases such as these.

As with any new medical device that is trying to improve upon a previous model, innovators must demonstrate that their solution is more effective than that of the predicate device. In most cases, OCT provides improved resolution and therefore improved clarity for diagnosis, but implementing the technology in new fields may require providing continuing education to interpret the data provided in images. The glaucoma study conducted in sub-Saharan Africa did not inquire about the potential for OCT use. In the U.S., most optometrists are familiar with OCT images; however, continuing education may be necessary enable complete glaucoma management. Workflows within OCT software should be optimized for use in all settings, including continuing education, research studies, and busy clinics.

Next-generation system design and software development will go hand in hand to build the OCT system for the clinical environment in which it is used. The emergence of compact, user-friendly, lower-cost OCT devices will help to establish the technology as a standard method for point-of-care imaging in many settings, inside the clinic and at home.

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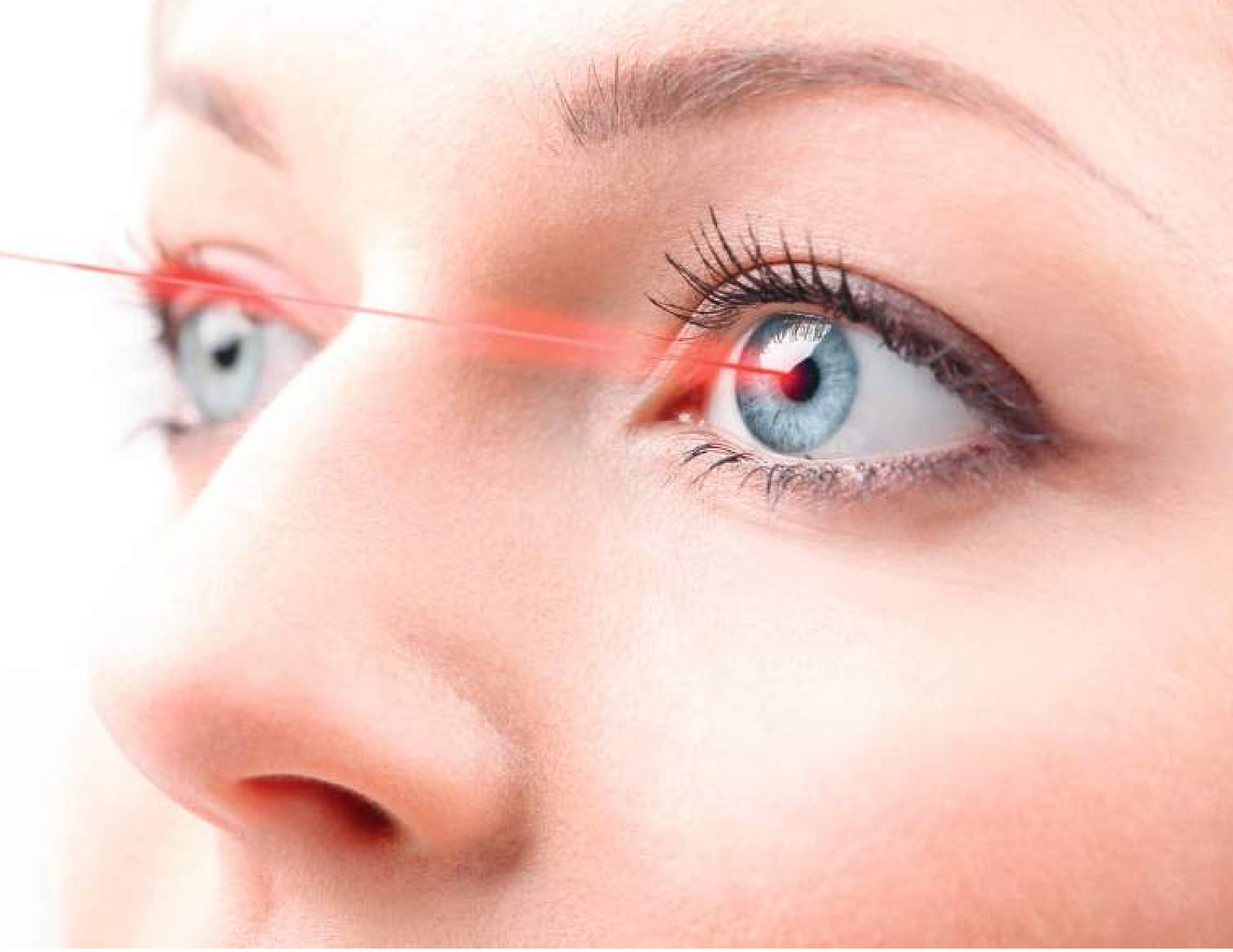

A medical laser treatment. Courtesy of SCANLAB/iStock.com/Szepy.

Advanced **Laser Scanning** Enables High-Precision Vision Corrections

Scan head control increases pattern fidelity, expanding the laser's use in multiple ophthalmic procedures.

BY AMANDA DOBBINS, STEPHANIE HERZOG, AND MATHIAS STRACKHARN, SCANLAB

Scan heads with innovative controls are already used in many industrial laser-based applications that require the highest precision and throughput. Now the benefits of scanning with zero tracking error are being positioned for ophthalmic applications related to vision correction, in which scan pattern fidelity is critical for a good patient care outcome. This smart control technology enables new and different strategies for diagnosis and treatment compared to the limitations of previous controls, which are affected by tracking error, especially when processing circles, spirals, and freeform structures. These advancements will allow completely new ophthalmic treatments, as well as successful and reproducible refractive surgeries. By using the full dynamic capabilities of the galvo motor in a laser scanning system, operation times can be significantly reduced.

General market studies show that the ophthalmic laser market includes several thousand installed surgical systems with typical life cycles of 10 to 15 years. Just as importantly, a fast-growing middle class in nations such as China, India, and Brazil is gaining access to ophthalmic surgeries, such as cataract removal and laser photocoagulation (treatment of retinal disease), thus creating additional market demand.

Nowadays, laser-based corneal refractive surgical interventions, such as lasik or lenticule extraction methods, are common. To modify the optical properties of the eye, it is necessary to move a micron-size laser spot with the highest precision as fast as possible over the surgery area to achieve a macroscopic change within short operational times. This is enabled by galvanometer scan systems (Figure 1),

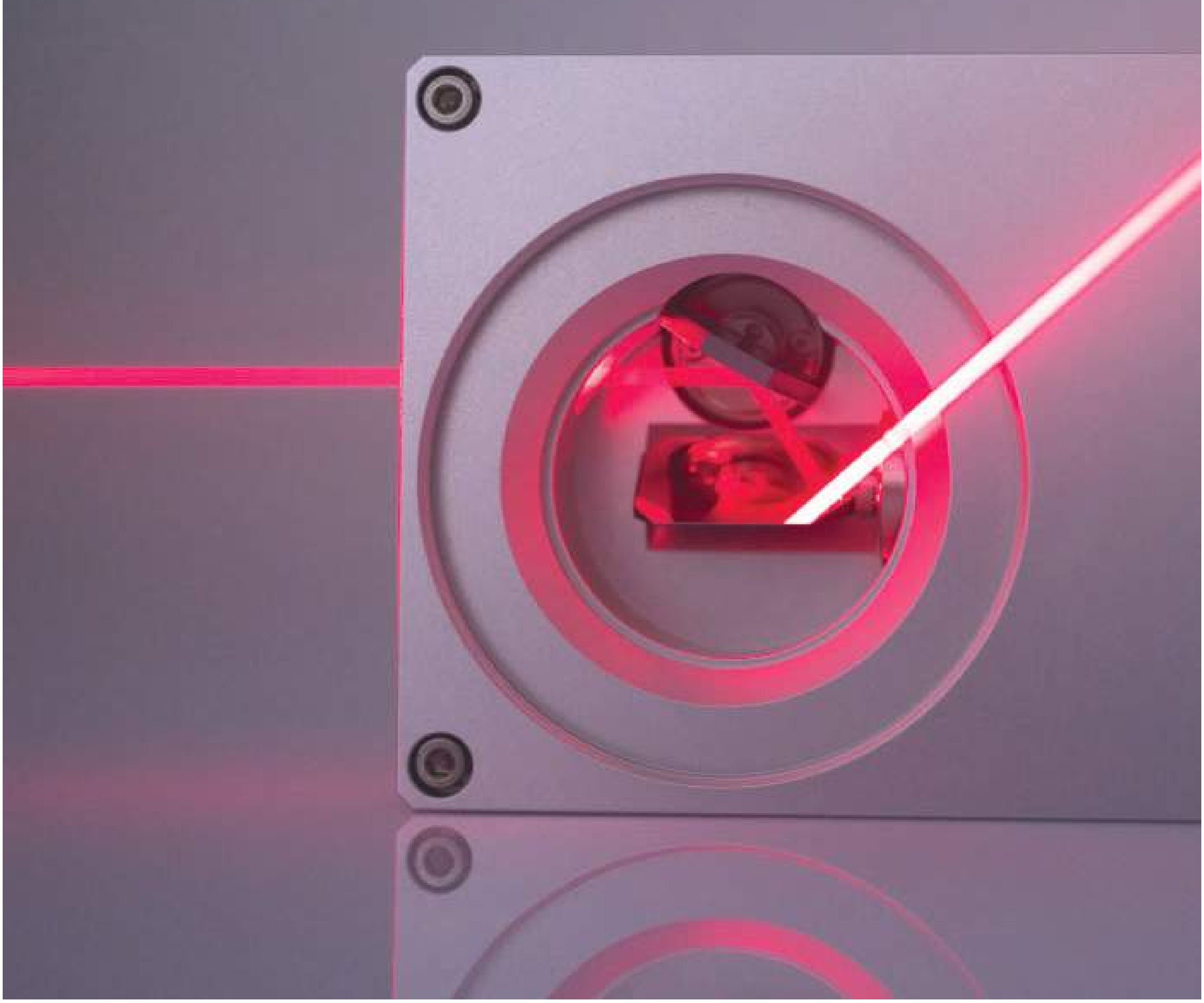

Figure 1. The principle of an xy scanning system positioning a laser beam. Courtesy of SCANLAB.

which are an approved and widespread technology.

Tracking errors limit applications

Current standard ophthalmic laser applications typically use scanners with conventional analog or digital controls. The control of these systems is constrained due to the tracking error, which is the difference between the command signal and the actual mirror position. The resulting position of the laser energy cannot be pre-calculated, and therefore the use of these scanning systems is limited in applications that include complex structures and elaborate process strategies. The tracking error is also independent from the set processing speed, meaning that the dynamic capabilities cannot be fully utilized, and throughput is therefore limited.

To avoid these tracking errors, SCANLAB developed a digital control technique, which has been deployed in many industrial laser-based applications — including micromaterials processing, laser marking, coding, scribing, and additive manufacturing. All require the highest precision and throughput.

The smart control technology enables new and different scanning strategies compared to conventional controls that are affected by tracking error, especially when scanning circular or spiral patterns and freeform structures. Furthermore, the full dynamic capabilities of the galvo motor are utilized. Thus, operation times can be significantly reduced.

Since many advantages of scan control have become obvious in industrial applications, engineers saw potential in using the technology for laser-based ophthalmological procedures, such as optical coherence tomography and laser ophthalmoscopy.

Pre-calculated scanning

The new scanning control is based on state-space control technology, which is governed by a set of equations describing how a system will evolve over time. The acceleration limiter, which is part of the processing chain of the controller, calculates an acceleration-limited motion profile in real time based on the velocity-limited motion profile received from the scan system's real-time control (RTC) board. This control board reads the algorithm parameters from the scan system and automatically plans the timing of the scan to obtain perfect corner sharpness, or rounding, if desired. The state-space controller can then follow the acceleration-limited profile without dynamic following errors or tracking delays in the laser scanning process.

The position detectors are located on one end of the rotor (Figure 2) to measure the scan angle. The scan mirror is mounted onto the opposite end of the rotor. In a first-order approximation, this can be described with a two-mass model, and as

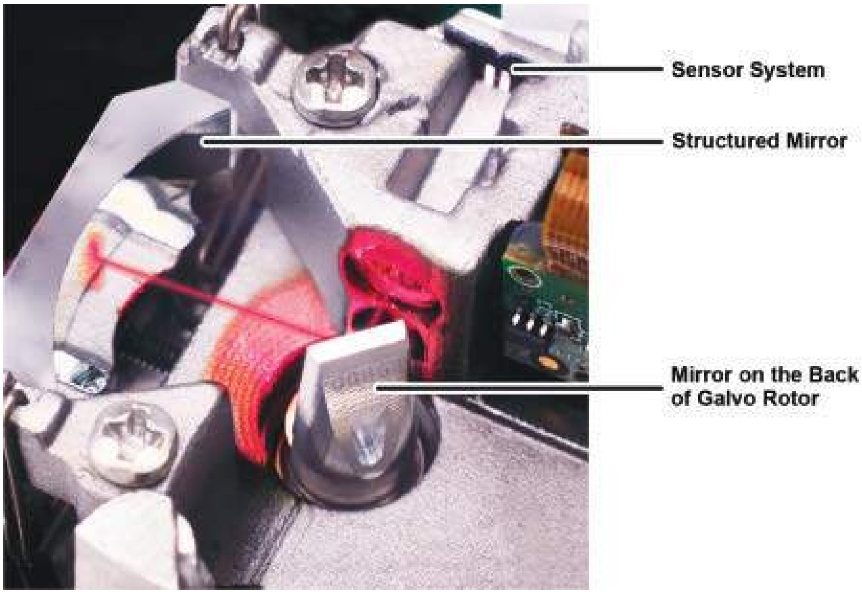

Figure 2. An internal view of a digital position detector inside a galvanometer scanner. Courtesy of SCANLAB.

a result torsional modes will occur. The new intelligent control algorithm includes a galvo mass model to compensate for potential vibration at high acceleration, so it calculates the actual mirror position instead of assuming that the raw position data from the encoder matches the mirror position. This minimizes position error further.

This scan control concept operates by always using the full acceleration potential of the galvanometer motor. A scanner that is controlled via this technology calculates a set trajectory during the preview time, which it follows with very high accuracy. This approach reduces the acceleration times to a minimum and at the same time allows a prediction of the motor's motion profile.

In comparison, conventional controls always have a constant acceleration time, they do not always make full use of the galvo motor's maximum possible acceleration, and they require notably longer times when the laser is off.

The system follows the trajectory with a constant tracking error. This ensures that the timing between the movement of the mirrors and the laser is fixed, independent of the set speed, but it also leads to unwanted effects such as distortion while doing fast circular or spiral movements (Figure 3).

Scan systems incorporating the new control concept will follow the given trajectory in real time. Due to this characteristic of the control and its predictability, users can even go as far as calculating motion profiles for the scanner. This allows full control over the scanner motion and adjusting dynamics.

In combination with an RTC board, laser delays and scanner delays do not need to be determined or programmed by the user. The system is capable of automatically synchronizing the scan head with the laser source.

The high dynamic behavior results in a more constant energy deposition along the trajectory, compared to scan heads with conventional controls, because less time is required to ramp up to constant velocity.

Ophthalmological requirements

Compared to industrial applications, scan systems for ophthalmological applications have very specific requirements. All components in the surgical system require the highest possible reliability. In addition, an extended set of operational status signals needs to be provided by the scan system to ensure patient safety. The highest accuracy, predictability, and repeatability are necessary to apply laser light precisely and achieve suitable energy distributions in the cornea.

The high dynamics of the system ensure that patient comfort is achieved by keeping treatment times as short as possible. And, of course, the final scanning solution needs to meet requirements of each individual medical application, with customer-specific mechanical and optical designs, as well as any required safety-related system status monitoring.

The well-known dynamic behavior of galvanometer scanners, together with the constant acceleration, make the trajectories very predictable. This especially enables highly complex scan patterns such as corners, spirals, polygons, or Bézier curves, therefore enabling new ophthalmic treatments, as well as successful and reproducible refractive surgeries. The problematic distortion of circular patterns is overcome by the innovative control technology.

In addition, these scan systems offer a wide range of status signals that can be implemented to ensure the highest possible safety during the operation. Within the machine controls, it is possible to read back the actual mirror position with 10-µs resolution and compare the target with the real position. Since the control concept includes algorithms to compensate for rotor distortion, the remaining errors are reduced to the range of just a few microradians. This improvement in the reliabi-

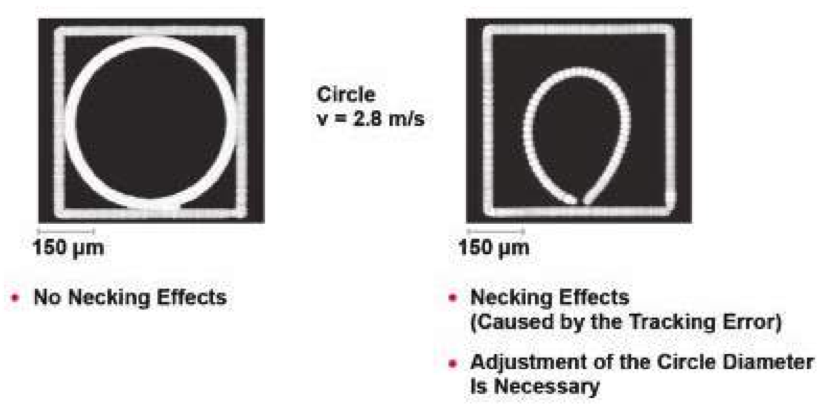

Figure 3. The processing benefits of *SCAN*ahead control **(left)** compared to conventional scan control **(right)** in circular movements and arcs. Courtesy of SCANLAB.

lity of the position data stream enables enhanced evaluation of the feedback signals and makes it possible to precisely identify critical errors in the scanner motion and trigger the appropriate fault protection.

Improved dynamic performance

Utilizing the full dynamic capabilities of scan systems with the innovative control concept significantly reduces the patient operation times. Depending upon the structure, a process time reduction of up to 25% can be realized. Due to the high dynamics of the scanner, the mechanical design of the scan heads should be optimized for thermal management and temperature stability.

For the realization of medical devices, a smooth interplay between several components must be achieved. Customization is key to making these complex systems successful. Precise position feedback signals are of utmost importance. However, other status signals may play important roles in the continuous monitoring of critical system properties. These signals can be chosen according to the overall system requirements.

The advanced control concept is usually combined with galvanometer scanners that are equipped with digital position detectors, but this is not a limitation.

In medical applications, analog signal pathways may be preferred for safety and regulatory reasons, making the use of analog position detectors advantageous. A reliable output of these signals and the continuous evaluation of the position can be critical to ensuring patient safety.

Future outlook

New control concepts can facilitate completely new ophthalmic treatments, as well as successful and reproducible refractive surgeries. Such concepts provide more reliable position signals and an extended set of additional status signals that can be used for system monitoring and overall patient safety. They also improve the dynamic performance by utilizing the full capabilities of the galvo motors.

By substituting the existing machine base with upgraded equipment, along with the development of new treatments, innovative scan control concepts that enable increasing productivity and reliability have a high potential of success in this growing market.

Surgical suites are trending toward combining multiple diagnostic and surgical devices on one platform for end-to-end patient care, greater efficiency, higher flexibility, and a smaller footprint for the ophthalmologist, enabling the best patient treatment strategy. The described control concept can be employed in various ophthalmic procedures that require high scan fidelity. It could also be used in the manufacture and correction of intraocular lenses, either in situ or in vivo.

The complexity of laser scanning tasks will grow, with ever-growing precision and throughput requirements, combined with the need to control the laser properties exactly over time and space. Introducing software-based technologies, such as pre-planning of motion profiles, and information exchange plus synchronization with other hardware devices, will be part of the solution for handling the complexity of next-generation medical laser scanning systems.

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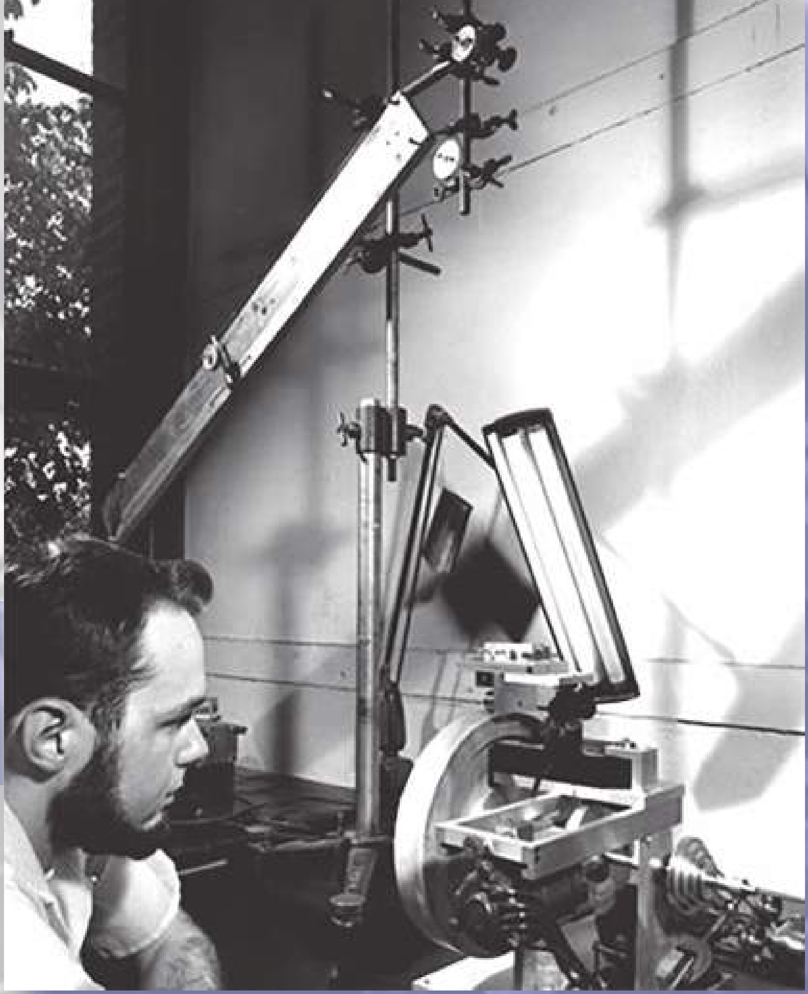

Figure 1. Larry Curtis of the University of Michigan draws the first optical clad fiber by the rod-in-tube method, for use in a medical endoscope. Courtesy of Abraham Katzir.

Optical Fiber Provides Real-Time Diagnostic Guidance

Robust physical properties and enabling capabilities make optical fiber-based sensors attractive for biomedical applications ranging from light delivery and imaging to robotic procedures.

BY ALEXIS MÉNDEZ
MCH ENGINEERING LLC

The biomedical community recognized the advantages of optical fibers long ago, accepting them even before their adoption for long-haul telecommunications[1]. Early research on the light-guiding properties of fibers in the late 1920s was aimed at applications in medical imaging. The first clad optical fiber was drawn on December 8, 1956, by Larry Curtis (Figure 1), a graduate student under Basil Hirschowitz at the University of Michigan. The technology was used in a multifiber bundle for a fiber endoscope, which Hirschowitz first tested on himself[2].

Optical fibers are attractive for biomedical applications because they are thin, flexible, dielectric (nonconductive), immune to electromagnetic interference, chemically inert, nontoxic, and lightweight. They can also be sterilized using the standard medical sterilization techniques: steam heat, radiation, or dry gas.

Their adoption in the medical field has expanded widely since the first endoscope, from imaging and analyzing biological functions to enabling rapid advancements in newer medical procedures, such as minimally invasive and robotic surgery (Table 1).

Fiber optic sensors compete with a limited number of conventional electronic devices in biomedical applications. Their primary advantage is the electrical isolation provided by the dielectric optical fibers, which enables safe use without risk of electric shock to a patient. Fiber optic sensors can also be used safely while patients undergo MRI, CT, or any other type of electromagnetic scan, without risk of inducing an electric current or generating heat from the large magnetic fields. Their small size — which enables integrating the sensors along small needles, catheters, and surgical tools — is another key advantage.

These factors make fiber optic sensors ideally suited for a broad variety of invasive and noninvasive applications in the life sciences, clinical research, medical monitoring, and diagnostics. As shown in Table 2, biomedical optical sensors can be categorized into four main types: physical, chemical, biological, and imaging.

Optical fibers for imaging

Imaging sensors encompass both endoscope devices for internal observation and imaging, and more advanced techniques — such as optical coherence tomography

Table 1.
Medical Industry Trends Promoting Increased Use of Optical Fiber

Trend	Requirement
Minimally invasive surgery	Disposable probes and catheters
Automation and robotics	Instrumented catheters
MRI, CT, and PET imaging; Ablative treatments using radio frequency or microwave radiation	Fiber sensors
Increased use of lasers	Fiber delivery devices
Optical imaging and scanning	Fiber OCT probes

Figure 2. Fiber optic Fabry-Pérot medical pressure and temperature sensors. Courtesy of Abraham Katzir.

(OCT), photoacoustic imaging, and others — where internal scans and visualization can be made nonintrusively.

Endoscopic imaging remains the most successful biomedical application for fiber optics.

Optical fibers can also be used to transmit light to tissue regions of interest, either to illuminate the tissue for inspection or to directly cut or ablate it (with a higher-powered laser). Hence, they are used extensively as laser-delivery probes, as well as imaging conduits for diverse illumination applications, either alone or integrated into medical instruments such as otoscopes and laryngoscopes.

Fibers are also used as scanning probes in advanced imaging applications such as OCT and confocal microscopy. And when fused together as plates or tapers, they are used as light-guiding components in digital x-ray devices to guide the light image from a scintillator to an electronic CCD detector array.

Physiological measurements

Physical sensors are used to measure a broad variety of physiological parameters, such as body temperature, blood pressure, respiration, heart rate, blood flow, muscle displacement, and cerebral activity.

Biomedical sensors using external-cavity Fabry-Pérot interferometers, fiber Bragg gratings, and fiber spectrometers based on light absorption and fluorescence are among the fiber optic sensors most commonly developed into commercial products, with temperature and pressure being the most popular parameters. The unique size benefits provided by fiber optic sensors can clearly be appreciated in the pressure and temperature Fabry-Pérot probes shown in Figure 2.

Some of the earliest fiber optic physical sensors date back to the early 1980s to such pioneering companies as Camino Laboratories, FISO Technologies (now part of Resonetics), and Luxtron (now part of Advanced Energy). In 1984, Camino introduced an intracranial pressure sensor based on an intensity-modulating fiber optic device using a miniature bellows as the transducer. FISO of Canada supplies OEM medical fiber optic pressure and temperature sensors based on external-cavity Fabry-Pérot interferometers interrogated with white-light interferometry. OpSens and Neoptix in Canada and RJC Enterprises in the U.S. are other long-standing developers and OEM manufacturers of temperature and pressure fiber optic sensors.

Chemical and biological analysis

Chemical sensors rely on fluorescence, spectroscopic, and indicator techniques to measure and identify the presence of chemical compounds and metabolic variables such as pH, blood oxygen, and glucose. These sensors detect specific chemical species for diagnostic purposes, and they monitor the body's chemical reactions and activity for diagnostic and therapeutic applications.

Biological sensors tend to be more complex and rely on biologic recognition reactions — such as enzyme-substrate, antigen-antibody, or ligand-receptor — to identify and quantify specific biochemical molecules of interest. One prospective implementation of such sensors is the so-called lab on a fiber[3] that combines optical fiber coatings with micro- and nanosize functionalized materials that react to specific physical, chemical, or biological external effects, creating multifunction, multiparameter sensing devices (Figure 3). Light remotely excites the functionalized materials embedded in the fiber's coating. These materials, in turn, react to specific biological or chemical substances (analytes) and induce an optical signal change proportional to the analyte concentration.

Biomedical sensors (fiber optic or otherwise) present some unique challenges[4]. Sensors must be safe, reliable, highly stable, biocompatible, amenable to sterilization and autoclaving, and not prone to biologic rejection. And they must not require calibration, or they must at

Table 2.
Classifications of Biomedical Optical Fiber Sensors

Physical	Chemical	Biological	Imaging
Body	pH	Antigens	Endoscopy
Temperature	pO_2	Antibodies	Optical coherence tomography (OCT)
In vivo pressure	PCO_2	Electrolytes	Optical acoustic tomography (OAT)
Blood flow	Oxymetry (SaO_2, SvO_2)	Enzymes	Confocal microscopy
Heart rate	Glucose	Inhibitors	
Force	Bile	Metabolites	
Position	Lipids	Proteins	
Respiration			
Shape sensing			

least be capable of maintaining calibration for prolonged times. Sensor packaging is critical. Small size is highly desirable for these sensors, particularly if they are intended for implanting or indwelling.

Sensors help guide surgery

Developments in minimally invasive surgery and remote robotic surgery have widened the market for medical sensors, adding position and force requirements to the sensing regime.

In minimally invasive surgery, surgeons avoid cutting open patients and instead perform small cuts and incisions through which a variety of surgical instruments and catheters are inserted. For remote robotic surgery, the surgical catheters must be fitted with sensors that provide both three-dimensional position information and force (haptic) feedback to the surgeon controlling the robot.

Optical fiber sensors are ideal for this application because they can be easily integrated inside the slender robotic catheters, and, by using multicore fibers inscribed with arrays of fiber Bragg grating strain sensors, it is possible to perform in situ and real-time 3D shape and position sensing. As the fibers bend, twist, and rotate, the fiber Bragg gratings detect the induced strains in the fiber. Specialized algorithms process the data to deliver inverse kinematics of spatial position in real time.

One system using such technology is Philips Healthcare's Fiber Optic RealShape (FORS). Other companies — such as FBGS in Belgium, PhotonFirst in the Netherlands, Intuitive Surgical in the U.S., and Fibercore in the U.K. — are actively working on this type of biomedical fiber optic sensor solution.

Another related innovation is the use of fiber Bragg gratings or Fabry-Pérot elements as force-sensing devices. The functionality of many drug-delivery, therapeutic, and medical device systems relies on a change in force. Force sensors can measure changes in force and relay this information to the clinician and/or patient for adjustments. Fiber optic force sensors, such as Abbott's TactiCath ablation probe, are available for radio frequency or laser-based ablation devices for treating atrial fibrillation.

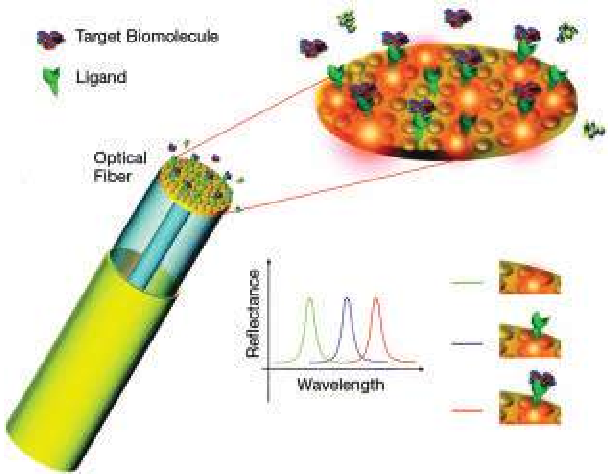

Figure 3. An illustration of the concept of a biomedical lab-on-a-fiber multianalyte sensor. Courtesy of Andrea Cusano

Along similar lines, Often Medical in Italy has developed an epidural anesthesia kit based on a fiber Bragg grating force sensor. The system enables real-time monitoring of epidural catheter placement and provides guidance of the needle until it reaches the epidural space, where the incorporated fiber sensor verifies the correct placement of the catheter.

Trends and commercial outlook

Optical fibers — and photonics technologies in general — represent a set of very powerful and versatile enabling technologies for medical devices, instrumentation, and techniques for diagnostic, therapeutic, and surgical applications. With a growing population requiring health care and increasingly sophisticated diagnostic tools, clinicians worldwide rely more and more on advanced biomedical instrumentation and sensors as necessary and effective tools for diagnosing, monitoring, treating, and caring for patients.

Future trends include the development of increasingly small and thin medical probes and catheters and a proliferation of laser-based treatments and therapies that require fiber optic delivery systems. OCT is also poised to become as common as conventional ultrasound scanning.

Endoscopy will continue to evolve as smaller and more sophisticated devices combine more advanced functions — beyond the standard illumination and visualization — such as direct tissue analysis and laser treatment. Optical imaging techniques will continue to advance, with digital x-rays making noninvasive examination and diagnosis safer and faster due to greater resolution and pinpoint accuracy.

The biomedical sensing market represents a lucrative and growing opportunity for fiber optic sensors, particularly for large volumes of disposable sensing probes. And there is also an unquestionable opportunity for fiber optic sensors to be used as electromagnetic-interference-compatible sensors to monitor patients' vital signs during the use of MRI (and related techniques) and radio frequency treatments, such as atrial fibrillation ablations. As costs drop and new sensing techniques are developed, the number and diversity of biomedical fiber optic sensors will increase.

Meet the author

Alexis Méndez, Ph.D., is president of MCH Engineering LLC. He received a doctorate in electrical engineering from Brown University and has 30 years of experience in optical fiber technology, sensors, and photonics.

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4. É. Pinet and C. Hamel (2007). True challenges of disposable optical fiber sensors for clinical environment. Presented at the Third European Workshop on Optical Fibre Sensors. *Proc SPIE*, Vol. 6619.

The *BioPhotonics* Conference Places Biomedical Imaging and Medical Laser Innovations at the Fore

Leading industry players converge to discuss recent advancements in spectroscopy, OCT, deep learning, and more.

BIOPHOTONICS
BRINGING LIGHT TO THE LIFE SCIENCES®
CONFERENCE
October 25-27, 2022

Photonics Media's second annual online *BioPhotonics* Conference, highlighting the latest advancements in optical biomedical and life sciences technology, will run Oct. 25-27. Attendees can expect an expansive lineup of presentations detailing the cutting-edge research and innovative technologies that are leading to improved diagnostics, treatments, and heightened understanding of the biophotonics field.

Top minds from academia and industry will present keynotes and lectures spotlighting topics such as OCT, live-tissue imaging, microscopy, artificial intelligence in imaging, and biomedical lasers. The free, three-day online conference features over 35 presentations across seven tracks. Sessions can be viewed on demand following their broadcast.

Aydogan Ozcan, head of the Bio- and Nano-Photonics Laboratory at UCLA, will deliver the keynote presentation for the Microscopy track, in which he will discuss deep learning-enabled computational microscopy and diffractive imaging. Ozcan will provide an overview of his lab's recent work using deep neural networks to advance computational microscopy and sensing systems, and he will cover the networks' biomedical applications, including the virtual staining of label-free tissue. Additionally, he will discuss diffractive optical networks designed by deep learning to all-optically implement various complex functions as the input light diffracts through spatially engineered surfaces.

Stephen Boppart, principal investigator at the Beckman Institute for Advanced Science and Technology and Abel Bliss Professor of Engineering at the University of Illinois at Urbana-Champaign, will present the keynote for the OCT track. He will discuss how OCT can be used to image biofilms — which are believed to be involved in nearly all chronic bacterial infections in humans — to better understand the role biofilms play in infectious disease.

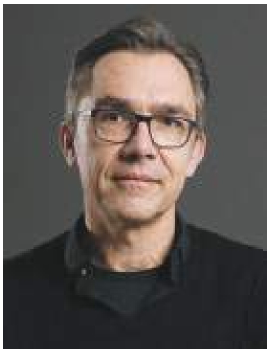
Laura Marcu, professor of biomedical engineering and neurological surgery at the University of California, Davis (UC Davis), will deliver the keynote for the Biomedical Imaging track. She will review the development of clinically compatible fluorescence lifetime imaging (FLIM) technology and its applications in surgical oncology. Marcu will also discuss how the technology can be integrated into the surgical workflow, and, more specifically, into the da Vinci surgical platform.

In the Spectroscopy track, Jürgen Popp — chair of physical chemistry at Friedrich Schiller University Jena and scientific director of the Leibniz Institute of Photonic Technology — will present the keynote, in which he will discuss the use of Raman spectroscopy for analysis in biomedical research and clinical diagnostics. Popp will provide selected examples to illustrate the potential of linear and nonlinear Raman spectroscopy for biomedical and life science analysis. Examples that he will cover include

Aydogan Ozcan, Chancellor's Professor and Volgenau Chair for Engineering Innovation and head of the Bio- and Nano-Photonics Laboratory at UCLA. Courtesy of Aydogan Ozcan.

Stephen Boppart, principal investigator at the Beckman Institute for Advanced Science and Technology at the University of Illinois Urbana-Champaign. Courtesy of Stephen Boppart.

Laura Marcu, professor of biomedical engineering and neurological surgery at UC Davis. Courtesy of Laura Marcu.



Jürgen Popp, chair of physical chemistry at Friedrich Schiller University Jena and scientific director of the Leibniz Institute of Photonic Technology. Courtesy of Jürgen Popp.

Marco Arrigoni, director of marketing at Coherent. Courtesy of Marco Arrigoni.

microbial diagnostics; the visualization of metabolic, defense, and chemical communication processes; on-site environmental and soil monitoring; and disease diagnostics.

The keynote for the Lasers & Therapeutics track will be delivered by Marco Arrigoni, director of marketing at Coherent. He will discuss the various applications of lasers in biology and medicine and categorize them by the type of process involved and the most significant trends. With an industry focus, he will cover applications such as laser-based diagnostics and treatments.

The other two tracks will cover Photoacoustic Imaging and Flow Cytometry.

Science and industry highlights

Attendees of the conference will hear about the ideas and technologies driving innovation in biomedical technology and get a comprehensive view of the burgeoning marketplace. Among the notable themes this year is the convergence of research and business.

Speakers from Olympus, Columbia University, UCLA, Colgate-Palmolive, Hamamatsu, the University of Texas, MKS, and other companies and universities will deliver their perspectives, discussing topics such as flow cytometry, laser biopsy, and more.

Viewers will have the opportunity to ask questions during a Q&A period after each talk.

Registration for the conference is free. For more information, visit **www.photonics.com/bpc2022**.

MICROSCOPY (TUESDAY, OCT. 25)

KEYNOTE:
Deep Learning-Enabled Computational Microscopy and Diffractive Imaging
Aydogan Ozcan (UCLA)

Applications of Multimodal Multiphoton Imaging Techniques in Preclinical and Clinical Pharmacological Studies
Aneesh Alex (GSK Center)

MediSCAPE Microscopy Enables Label-Free, 3D Histological Imaging in Vivo
Malte Casper (Columbia University)

Multi-Immersion Lenses for Cleared-Tissue Imaging
Jon Daniels (ASI)

Multiorgan COVID-19 Autopsy Findings Using 3D Virtual Histology
Guang Li (Tulane University)

Probes Provide Supermultiplexed Imaging of Tissues and Systems
Wei Min (Columbia University)

Selecting the Right Optics for Ultrafast Microscopy
Olivia Wheeler (Edmund Optics)

Semantic and Instance Segmentation of Microscopic Images Using Pretrained Neuronal Networks
Mike Woerdemann (Olympus)

OPTICAL COHERENCE TOMOGRAPHY (TUESDAY, OCT. 25)

KEYNOTE:
Optical Coherence Tomography and Multimodal Characterization of Bacterial Biofilms in Humans and Their Implications for Disease
Stephen Boppart (University of Illinois at Urbana-Champaign)

Computational 3D Microscopy with Optical Coherence Refraction Tomography
Kevin Zhou (Duke University)

Multimodal Functional OCT for Clinical Assessment of Oral Soft and Hard Tissue Conditions
Hrebesh Molly Subhash (Colgate-Palmolive)

OPTICAL COHERENCE TOMOGRAPHY (TUESDAY, OCT. 25)

RCM-OCT Enhances Skin Cancer Diagnosis and Therapy Guidance Through Hand-Held Imaging
Nicusor Iftimia (PSI Corp.)

BIOMEDICAL IMAGING (WEDNESDAY, OCT. 26)

KEYNOTE:
FLIM in Surgical Oncology
Laura Marcu (UC Davis)

BabyGlucoLight Uses Diffuse Optics to Link Glucose Levels at Birth with Early Brain Development
Sabrina Brigadoi (University of Padova)

Fiber-Based Spectrally and Time-Resolved Mapping of Tissues
Julius Heitz (Becker & Hickl)

Fluorescence Techniques Help Preserve Parathyroid Function During Thyroid Surgery
Frédéric Triponez (Hôpitaux Universitaires de Genève)

Macroscopy FRET FLI Monitors Cancer Drug-Target Engagement in Vivo
Margarida Barroso (Albany Medical College)

Multiphoton Imaging in Neuroscience
Joseph Mastron (TOPTICA)

Optical Technologies Are Poised to Guide Cancer Surgery in Low- to Middle-Income Regions
Jenna Mueller (University of Maryland)

Scientific CMOS Drives Discovery in Live-Tissue Applications
Brad Coyle (Hamamatsu)

PHOTOACOUSTIC IMAGING (WEDNESDAY, OCT. 26)

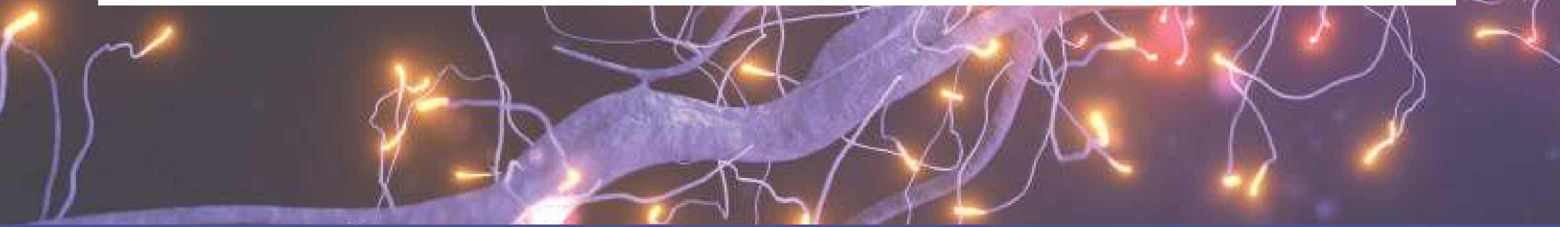
Emerging Clinical Applications of LED-Based Photoacoustic Imaging
Mithun Singh (Cyberdyne)

Photoacoustic Remote Sensing: A New Absorption-Based Microscopy for Assessment of Subcellular Structures
Parsin H. Reza (University of Waterloo)

FLOW CYTOMETRY (WEDNESDAY, OCT. 26)

Algorithms Al Fresco: Challenges in Visualizing High-Dimensional Flow Cytometry Data
David Novo (De Novo Software)

Time-Resolved Flow Cytometry Unlocks Simplified Workflows and Higher Sensitivity
Giacomo Vacca (Kinetic River)



SPECTROSCOPY (THURSDAY, OCT. 27)

KEYNOTE:
Raman Spectroscopy Provides Vital Analysis for Biomedical Research and Clinical Diagnostics
Jürgen Popp (Leibniz Institute of Photonic Technology)

Analysis of Common Dyes Using Steady-State and Time-Resolved Spectroscopy
Derek Guenther (Ocean Insight)

Cutting-Edge 3D Raman Imaging in the Life Sciences
Ievgeniia Iermak (WITec)

Hyperspectral Time-Resolved Compressive Sensing Spectrometer
Mamadou Diop (Lawson Research Institute)

Neuro-Monitoring with Diffuse Optical Methods
Maria Angela Franceschini (Harvard Medical School)

LASERS & THERAPEUTICS (THURSDAY, OCT. 27)

***KEYNOTE*:**
Specialized Laser Probes Capture Fluorescence Detail and Drive Therapy
Marco Arrigoni (Coherent)

Femtosecond Lasers Capture Details for Diagnosis
Ian Read (MKS)

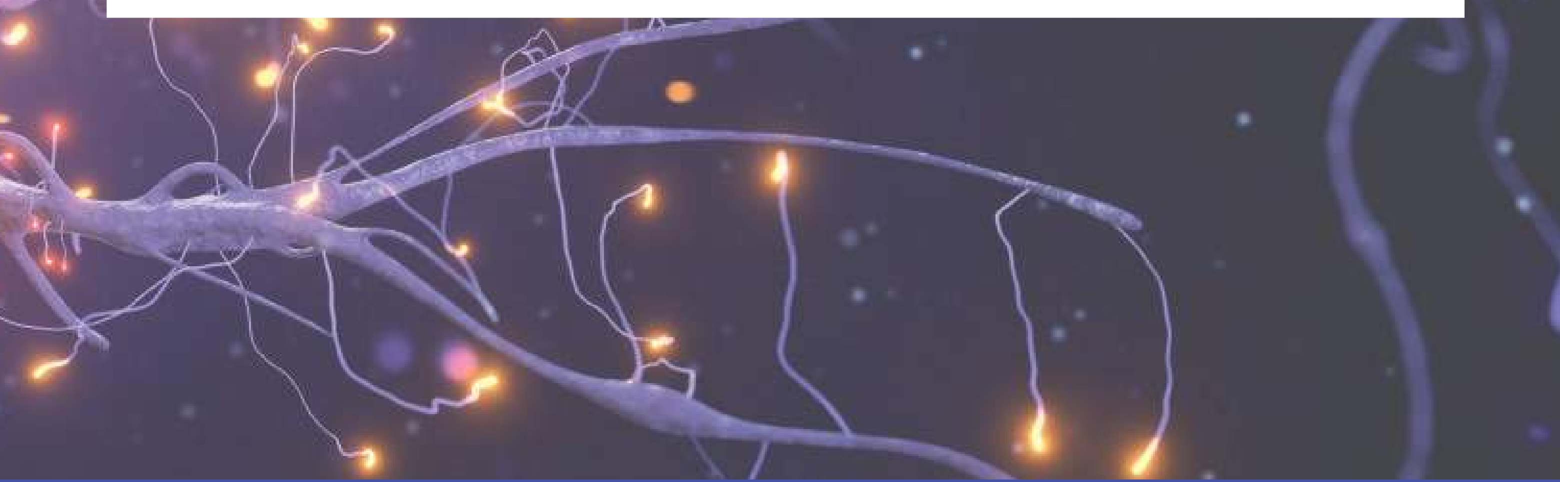
Laser Microbiopsy Could Provide Detailed Pathological Data with Limited Sample Damage
Jason King (University of Texas)

Lasers Aid in Cancer Treatment and Monitor Drug Delivery in Real Time
Zoe Ylöniemi (Modulight)

Multiline Lasers Help Simplify Systems Based on Light-Sheet Microscopy for Clinical Applications
Melissa Haahr (HÜBNER Photonics)

Photodynamic Therapy as a Cancer Technology for Global Health
Jonathan Celli (UMass Boston)

Reconstituted Beam Helps Classify Cancerous Tissue in Space-Time Light-Sheet Method
Mbaye Diouf (Brown University)



SciX to Explore Innovations in Diagnostics and Therapy at the Cellular Level

Attendees at the SciX 2022 conference, which will be held Oct. 2-7 in Covington, Ky., will hear from expert researchers about everything from the use of surface-enhanced Raman spectroscopy in drug discovery to machine learning's capability to capture biological and chemical changes in the body. The exhibit floor will offer insights into the latest developments in scientific analysis and laser-enhanced therapy, from major companies such as Avantes, Bruker Optics, Coherent, DRS Daylight Solutions, Edinburgh Instruments, HORIBA Scientific, Ibsen Photonics, OptoSigma, Teledyne Princeton Instruments, TOPTICA Photonics, and WITec.

Organized by the Federation of Analytical Chemistry and Spectroscopy Societies (FACSS), SciX will be held at the Northern Kentucky Convention Center.

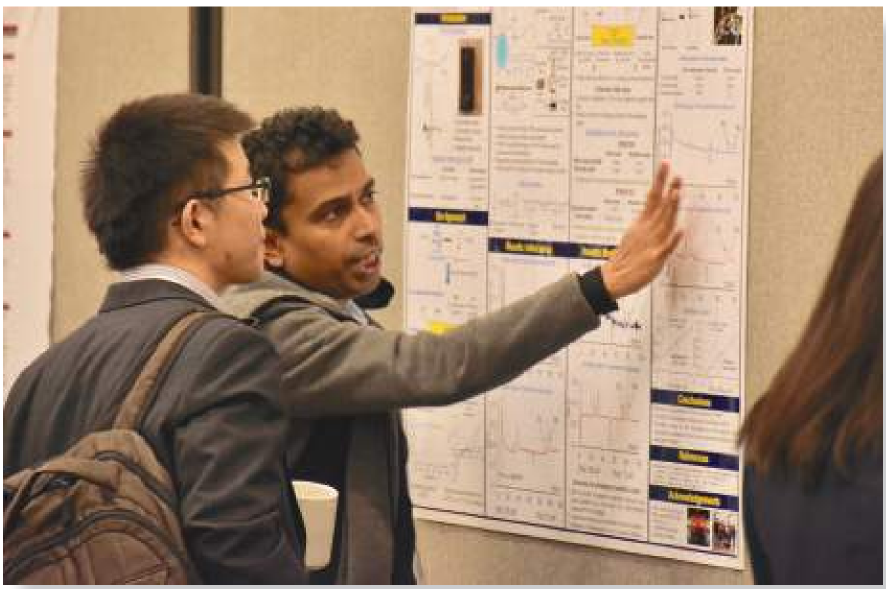
Robert Lascola, senior fellow scientist at Savannah River National Laboratory, will chair the program, which will include sections pertaining to biomedical and bioanalytical analysis, forensics and security, pharmaceutical analysis, Raman spectroscopy, and plasmonics.

"An area of interest is the interaction of artificial intelligence and deep learning toward improved methods for bioimaging and diagnostics," Lascola said. "For example, where intelligent analysis informs real-time measurements, pixel-specific spectroscopic imaging can be made more efficient, resulting in faster and more accurate diagnoses. Similarly, AI helps bring advanced analytical methods to the point of care, reducing or eliminating laboratory turnaround times, providing faster treatment and enhancing outcomes."

The Biomedical and Bioanalytical track will cover a variety of topics, including nanotheranostics and spectroscopy of living cells. The track is co-chaired by Jürgen Popp, scientific director at the Leibniz Institute for Photonic Technologies, and Fay Nicolson, a research fellow at the Dana-Farber Cancer Institute and Harvard Medical School.

"'Biophotonics Technologies Fighting Infections at the Point of Care' will bring to you innovative approaches at the threshold of translation," Popp said. "Fast and efficient diagnosis comes within reach for the detection of bacteria and their antimicrobial resistances but also for the characterization of the host response to infection when focusing on immune cells. Miniaturization plays an important role for sensitive malaria detection."

The Pharmaceutical Analysis track will cover topics such as chirality in pharmaceuticals and spectroscopic techniques in process analytical technology. It is co-chaired by John Wasylyk, associate sci-



A researcher interacts with an attendee during a poster session at a past SciX conference.

Audience members listen to a scientific program session at a past SciX conference.

Images courtesy of FACSS.

entific director at Bristol-Myers Squibb, and Katherine Hollywood, who is on the Faculty of Life Sciences at the University of Manchester.

"We have several sessions of interest," Wasylyk said. "Specifically, 'SERS for Drug Discovery' — which has talks covering 3D tissue models, drug detection in living cells, and machine learning using Raman for medical diagnostics — and 'Bioprocess Materials and Methods,' covering raw material and cell productivity using vibrational spectroscopy and analysis of adeno-associated virus."

The keynote presentation will be given by Amanda Hendrix, a senior scientist at the Planetary Science Institute in Boulder, Colo. She will speak on "The Analytical Chemistry of Space Exploration" and how UV-visible spectroscopy has been used to examine solar system surfaces and space weathering effects, and how the technology will guide both human and robotic exploration of the cosmos in the future.

"I will talk about the importance of the wide range of types of measurements, including sample studies, analog studies, ground- and space-based telescopes, deep-space probes, and human missions," said Hendrix.

Award recipients honored

Several awards will be presented throughout the program, including:

- Karen Faulds, professor of pure and applied chemistry at the University of Strathclyde, will receive the Royal Society of Chemistry Analytical Division Mid-Career Award for performing sensitive and selective bioanalysis using SERS and SESORS.
- Martin Zanni, principal investigator in the Department of Chemistry at the University of Wisconsin-Madison, will receive the SAS Ellis R. Lippincott Award for his work in advancing interfacial and voltage-gated two-dimensional infrared spectroscopy.
- Lu Wei, assistant professor of chemistry at the California Institute of Technology, will receive *Spectroscopy* magazine's Emerging Leader in Molecular Spectroscopy Award for utilizing stimulated Raman imaging for complex subcellular bioanalysis.
- Igor Lednev, distinguished professor of chemistry at the University at Albany, State University of New York, will receive the FACSS Charles Mann Award for Raman Spectroscopy for using Raman and machine learning for medical diagnostics and forensic purposes, the latter in conjunction with state crime laboratories.
- Wei Min, professor of chemistry at Columbia University, will receive the Coblentz Society Clara Craver Award for his work on stimulated Raman scattering imaging.
- Igor Gornushkin, senior scientist at the BAM Federal Institute for Materials Research and Testing, will receive the SAS Lester W. Strock Award for his work with multifaceted laser-induced plasma.
- James Piret, professor in the Department of Chemical and Biological Engineering at the University of British Columbia, will receive the SAS and Applied Spectroscopy William F. Meggers Award for his work in the process analytical utility of Raman microspectroscopy for cell therapy manufacturing validation.
- Joseph Loo, professor in the Department of Biological Chemistry at UCLA, will receive the ANACHEM Award for his work using mass spectrometry as a tool for structural biology.
- Aditya Khair, a professor of chemical engineering at Carnegie Mellon University, will receive the AES Electrophoresis Mid-Career Award for his work on nonlinear electrophoresis of colloidal particles.

The FACSS Innovation Award winner will be announced on the final day of the conference.

For more information, visit scixconference.org.

BREAKTHROUGHPRODUCTS

◀ UV Lasers

The OBIS XT series of compact, smart UV lasers from **Coherent Inc.** features extended powers, integrated controllers, and low heat dissipation for flow cytometry. The lasers are offered with 20 or 40 mW of true continuous-wave output. The OBIS 349 XT and OBIS 360 XT lasers are available with 150 mW of output at wavelengths of 349 and 360 nm, respectively. The 349-nm wavelength has become a dominant choice for UV counting and sorting.
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Cell Sorter ▶

The FACSDiscover S8 Cell Sorter from **Becton, Dickinson and Co.** features CellView image technology and combines spectral flow cytometry with sort-capable image analysis. The system is designed for research and cell-based therapeutic development across a range of fields, such as virology and oncology, as well as numerous disease states. The technology captures images of individual cells flowing through the system and sorts them based on detailed microscopic image analysis of each one at high sort speeds. This combination enables scientists to gain more accurate insights on cell populations and characteristics that can be visually confirmed in real time, and to interrogate and sort cells that could not previously be identified.
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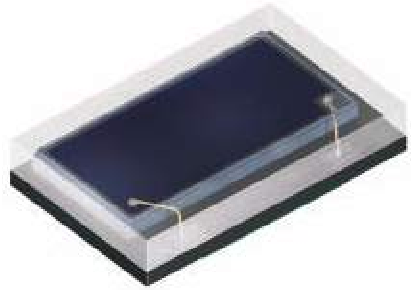

Photodiodes ▲

The SFH 2705 and SFH 2706 photodiodes from **ams OSRAM GmbH** demonstrate ~27% improved relative sensitivity at 530 nm green, and ~8% improved relative sensitivity at 660 nm red, providing a higher signal at these wavelengths. This allows customers to optimize power budgets and extend battery life for applications such as health monitoring by reducing LED driving current. With a package of 2.0 × 1.8 × 0.6 mm, the photodiodes are integration-compatible to their predecessors. The SFH 2705 features a square form factor to allow even more flexible placement of photodiodes next to LEDs in the system, such as in smartwatches.
sensors@ams.com

Laser Imaging Microscope ▼

The HYPERION II FT-IR Laser Imaging Microscope from **Bruker Corp.** combines Fourier transform IR (FTIR) microscopy with quantum cascade laser (QCL) IR imaging for R&D purposes, including tissue analysis and drug development. The system provides transmission, reflection, and attenuated total reflectance modes. Intuitive software allows seamless switching between FTIR and QCL technology. With an imaging speed of 6 sq mm/s, the system sets benchmarks in vibrational microscopy.
productinfo@bruker.com

Nanocytometer ▶

The Delaware Flow NanoCytometer from **Kinetic River Corp.** is designed for sensitive detection of submicron particles, including extracellular vesicles and tumor-derived exosomes, in flow cytometry. The system provides detection and characterization of biological and nonbiological nanoparticles. Based on a modular, customizable Potomac architecture, the NanoCytometer incorporates design modifications that enhance nanoparticle sensitivity without compromising throughput. The Delaware's high-power lasers provide up to five excitation wavelengths — 375, 405, 488, 532, and 640 nm — and a proprietary high-NA collection lens, to deliver maximum sensitivity. It offers two scattering channels, up to eight fluorescence detection channels, and >50-nm sensitivity.
info@kineticriver.com

Cooled CMOS Camera ▲

The ChemiMOS 9.0 cooled CMOS camera from **Atik Cameras Ltd.** is optimized for long-exposure imaging. Zero-amp glow and a low-noise design make hours of exposure time possible. The square-format, K-grade sensor is guaranteed for continuous use, while the 3000 × 3000 resolution and 3.76-μm pixel size are useful for multiple scientific applications, including chemiluminescence, Western blotting, and gel documentation. Benefits include very low read noise of <2 e^- and deep pixel full well of >50,000 e^-. Cooling is optimized to minimize the dark current to around 0.005 e^-/p/s, without the need for extreme temperatures.
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The FLEX PRO UV-VIS-NIR microspectrophotometer from **CRAIC Technologies** is a multifunctional tool that can acquire microscale images and spectra from the deep UV to the NIR. It is capable of transmission, reflectance, fluorescence, Raman microspectroscopy, and many other features. The system is tailored for cost-effective spectroscopic analysis of many types of microscopic samples, and it is designed to acquire spectra and images from the samples via absorbance, reflectance, fluorescence, and emission.
sales@microspectra.com

Slide Scanner

The C13220-21MDEU NanoZoomer S360MD slide scanner system from **Hamamatsu** is a high-throughput, in vitro diagnostic regulation (IVDR)-compliant model for use in hospitals and clinical laboratories. The whole-slide scanner for in vitro diagnostic use scans up to 82 slides per hour. Up to 30 slides can be loaded in one cassette, and up to 12 cassettes can be mounted in a system, for a total of 360 slides that can be scanned automatically in one batch. Automated correction maintains image quality and color balance.
photonics@hamamatsu.com

Particle Measuring System

The Ultra DI 20 Plus model from **Particle Measuring Systems Inc.** features laser optics and sensors to perform particle matching at concentrations <10 particles per milliliter, and it is optimized for increased confidence in reported data differences between particle counters, regardless of location. The system was built for low zero count and large sample volume while monitoring ultrapure liquids at a flow rate of 75 ml/min. It provides a sensitivity of 20 nm. With real-time particle measurement and benchmark detection, it enables an immediate response to detected contamination of bacteria and obtains statistical data for process management.
info@pmeasuring.com

AI Microscope

The APEXVIEW APX100 All-in-One Microscope from **Evident Corp.** provides publication-quality images for life science research. Featuring Olympus optics, intuitive software, and AI with a suite of smart features, the system is designed for labs and imaging core facilities. Its small footprint, built-in anti-vibration, and light-shielded optics enable the system to be placed anywhere, even in a brightly lit room. The imaging system automatically acquires an overview macro image while the built-in AI locates and displays the samples on the monitor so that the user can immediately begin capturing images. A gradient contrast method makes it possible to capture sharp, high-contrast images of live cells or thin, unstained tissue sections, without the need for specialized differential interference contrast or phase contrast optics.
info@evidentscientific.com

APPOINTMENTS

SEPTEMBER

18th Confocal Raman Imaging Symposium 2022 (Sept. 26-28) Ulm, Germany.
Contact WITec GmbH, +49 731-140-70-0, press@witec.de; www.raman-symposium.com.

BIOMEDevice 2022 (Sept. 28-29) Boston.
Contact Informa Markets, +1 310-445-4273, registration.ime@informa.com; www.biomedboston.com/en/home.html.

World Molecular Imaging Congress 2022 (Sept. 28-Oct. 1) Miami.
Contact the World Molecular Imaging Society, +1 310-215-9730, wmis@wmis.org; www.wmis.org.

OCTOBER

● **SciX 2022 (Oct. 2-7) Covington, Ky.**
Contact FACSS, the Federation of Analytical Chemistry and Spectroscopy Societies, scix@scixconference.org; www.scixconference.org.

● **Frontiers in Optics + Laser Science (FiO LS) 2022 (Oct. 16-20) Rochester, N.Y.**
Contact Optica, +1 202-223-8130, custserv@optica.org; www.frontiersinoptics.com/home.

CALL FOR PAPERS

Biophysical Society Annual Meeting 2023 (Feb. 18-22) San Diego
Deadline: Abstracts, Oct. 1
Contact Biophysical Society, +1 240-290-5600, society@biophysics.org; www.biophysics.org/2023meeting/abstracts.

NOVEMBER

● **Neuroscience 2022 (Nov. 12-16) San Diego.**
Contact the Society for Neuroscience, +1 202-962-4000, meetings@sfn.org; www.sfn.org/meetings/neuroscience-2022.

DECEMBER

● **Cell Bio 2022 (Dec. 3-7) Washington, D.C.**
Contact ASCB, The American Society for Cell Biology, +1 301-347-9300, ascbinfo@ascb.org; www.ascb.org/meetings-events/future-ascb-meetings.

JANUARY

● **SPIE BiOS 2023 (Jan. 28-29) San Francisco.**
Contact SPIE, +1 360-676-3290, customerservice@spie.org; www.spie.org/conferences-and-exhibitions/photonics-west/exhibitions/bios-expo.

● **SPIE Photonics West 2023 (Jan. 28-Feb. 2) San Francisco.**
Contact SPIE, +1 360-676-3290, customerservice@spie.org; www.spie.org/conferences-and-exhibitions/photonics-west.

FEBRUARY

● **SPIE Medical Imaging 2023 (Feb. 19-23) San Diego.**
Contact SPIE, +1 360-676-3290, customerservice@spie.org; www.spie.org/conferences-and-exhibitions/medical-imaging.

MARCH

● **SPIE Smart Structures + Nondestructive Evaluation 2023 (March 12-16) Long Beach, Calif.**
Contact SPIE, +1 360-676-3290, customerservice@spie.org; www.spie.org/conferences-and-exhibitions/smart-structures-nde/program.

● **LASER World of PHOTONICS China 2023 (March 22-24) Shanghai.**
Contact Messe München Shanghai Co. Ltd., +86 21-2020-5500, info@mm-sh.com; www.world-of-photonics-china.com/en.

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Wildlife tracking takes to the trees

Endangered animals, quite understandably, do their best not to be found. So it took the aid of sophisticated imaging and recording technology for a team of researchers from Finland and the U.K. to capture the habits and movements of tree hyraxes in the mountains of Kenya.

Tree hyraxes, mainly found in Africa, are nocturnal mammals with a guinea pig-like appearance that, as their name suggests, spend a lot of time in trees.

Takeaways from the researchers' study included: the higher in trees the better for an individual animal's survival, and the bigger the forested areas the better for providing food and shelter to tree hyrax communities. The animals also know not to talk until the lights are out.

The habitat of the tree hyraxes was studied in the fragmented forests of the Taita Hills in southeastern Kenya. There, the researchers determined that the animals seek cover that provides both protection and a potential escape route, and that the animals also reserve much of their audible communication for a limited number of hours in the middle of the night, when they stand the best chance of eluding predators or poachers.

A tree hyrax. The animals dwell in the shrinking forests of the mountains of Kenya. Courtesy of Hanna Rosti.

The scientists tracked the creatures not with a keen nose or a decoy, but via an array of high-tech modalities. They used audio recorders to capture the sounds made by the tree hyraxes. They used red beam flashlights to find the animals in the tree canopy, and a thermal imaging camera to determine the density of the population once it was discovered. To determine the size and structure of the forest canopy that the animals call home, the team analyzed lidar data that had been collected using an airborne sensor five years earlier.

The animals prefer to live in and eat from montane, or cool and moist forests with tall, canopied trees. In the study, the tree hyrax population thrived the most in three specific areas where the forest landscape was large and undisturbed, and the researchers urged conservation efforts to preserve these areas.

"[Tree hyraxes] prefer certain tree species. In Taita Hills, they like *Tabernaemontana*, *Macaranga*, and *Pauteria* (among others)," said Hanna Rosti, a doctoral candidate in wildlife biology research at the University of Helsinki, and a principal author of the study. "These trees often grow very large, and they provide nice platforms where [the animals] can rest. Tree hyraxes rest and sleep a lot, and their ecological niche is the same as in koalas in Australia and sloths in South America. Also, woody lianas, creepers, form dense nests around the trees. Tree hyraxes feed on these climbers and they also find safe sleeping sites inside the climbers. These are like tree hollows that are also used by tree hyraxes."

A spectrogram was used to distinguish between the calls of individual animals, she said, so that the hyraxes' communication could be isolated. Red light was used instead of white to avoid disturbing or scaring them. A wide angle on the thermal imaging camera enabled the researchers to scan the canopy as thoroughly as possible.

Despite the high-tech arsenal that the team entered the forest with, proper observation still took time. "In recordings, we get long-distance communication," Rosti said. "And from this long-distance calling, it is often impossible to know what they are exactly communicating about. However, we have been to the forest for months and have seen and heard many things. For example, when a predator approaches tree hyrax juveniles, there is a clear alarming, warning pitch in the calls. We have also heard and recorded trees falling, which results in an elaborate calling that has a concerned pitch."

The lessons learned in the study were simple: There is safety in numbers, and tone of voice matters when addressing each other.

The team's efforts could lead to more effective conservation of tree hyraxes by shining more light on the type of environment needed to ensure their survival.

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