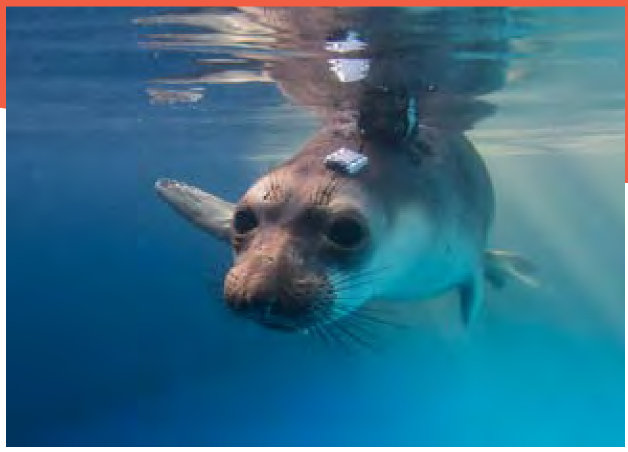
PHOTONICS WEST SHOW DAILY



Sealed and delivered

A wearable sensor reveals smart bloodflow when a harbor seal makes a long dive.

page 9

SPIE and University of Central Florida announce $650,000 scholarship fund

At Monday night's UCF CREOL alumni and associates event, SPIE announced the establishment of the SPIE-Glebov Family Optics and Photonics Graduate Scholarship Fund for the University of Central Florida (UCF) College of Optics and Photonics (CREOL). The $325,000 in funding from SPIE will be matched in full by the College's Research Foundation and the Glebov family, to create scholarships for graduate students at CREOL.

(L-R) David Hagan, John Greivenkamp, Alexei Glebov, and Kent Rochford. Credit: SPIE

"The generosity of Leonid Glebov and Larissa Glebova ensures promising opportunities for graduate students studying optics and photonics at UCF CREOL," said SPIE CEO Kent Rochford. "We are delighted to join with the Glebovs in creating a scholarship fund that will exist in perpetuity to help support the next generations of scientists and engineers who will create the future using optics and photonics."

Leonid Glebov, a research professor, and his wife, Larissa Glebova, a retired research scientist, are longtime members of UCF

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Eric Betzig has not been resting on his laureate

"If you want to understand any dynamic system, no matter how good your information is about its components, no matter how good the static images of the components, it's not enough to understand that system," noted Eric Betzig at the BiOS Plenary Session on Sunday, where he talked about "the secret life of cells" and his work involved in discovering that secret life.

To help explain the issue, Betzig discussed earlier microscopy tools and showed a slide of a BMW engine with all its parts laid out. "If I had no prior knowledge of how combustion works, or how the gears or the crankshaft works, it would be damned difficult for me to reverse engineer that," he said. "Many of the tools I just described don't give a comprehension of all of the parts, so you're missing many of the parts. If you're doing biochemistry over express, now you have three crankshafts and 18 pistons and you're wondering how that's going to work. Starting in the 1980s optical microscopy would start

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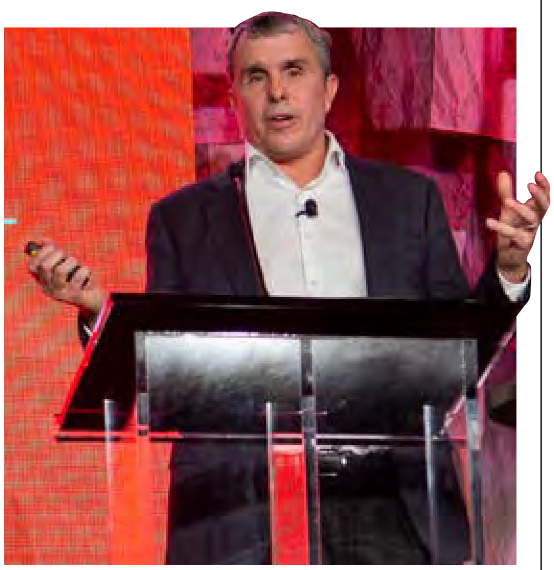


What's his secret? Eric Betzig tells all. Credit: SPIE

DON'T MISS THESE EVENTS TODAY.

PLENARY SESSION
NANO/BIOPHOTONICS
10:30 – 11:30 AM, Rm 207, So. Level 2

INDUSTRY EVENTS
JOB FAIR
10 AM – 5 PM, Hall C, (Exhibit Level)

PHOTONICS WEST EXHIBITION
10 AM – 5 PM, No. and So. Halls

AR/VR/MR EXPO
10 AM – 5 PM, RM 204, Level 2 Moscone West

EQUITY, DIVERSITY, AND INCLUSION LUNCH & LEARN: Creative, Inclusive Cultures
12 – 1 PM, Industry Stage, Hall DE (Exhibit Level)

BUILDING AN INDUSTRY: The Commercialization of Quantum Technology
1:30 – 4:30 PM, Industry Stage, Hall D/E (Exhibit Level)

INVESTING IN PHOTONICS PANEL DISCUSSION
2:45 – 3:45 pm, RM 2020/2022, Level 2 Moscone West

OPTICS AND PHOTONICS TECHNICIAN SHORTAGE: Solutions and Opportunities
5:15 – 6:30 PM, Marriott Marquis Hotel, Golden Gate C

LASE POSTER SESSION
6 – 8 PM, Level 3 Moscone West

For the full schedule, see the technical program and exhibition guide or download the SPIE Conferences app. Some events require registration. Read daily news reports from Photonics West online: spie.org/PWnews

IN THIS ISSUE.

And the $5,000 winner is: Tao Zhan, of CREOL

Turn a bunch of brilliant students loose on AR/VR and what happens?

Well, for Tao Zhan, from CREOL, at the University of Central Florida, it meant a $5,000 check as winner of the 2020 Student Optical Design Challenge.

In his project, “Planar Optics Enables Chromatic Aberration Correction in Immersive Near-Eye Displays,” he used a Pancharatnam-Berry phase lens to correct chromatic aberrations in VR displays by up to 93 percent.

Augmented bank account: Christophe Peroz (L) and Bernard Kress (R) with optical design winner Tao Zhan. Credit: SPIE

Why did he win?

One judge, Zhujun Shi, a Harvard student and the first Challenge winner, in 2018, said: “His solution was very practical. He wasn’t trying for a big breakthrough. He identified the practical challenge in chromatic aberration, for imaging systems in general, and he proposed a liquid based planar lens to solve this problem.”

Another judge, Jessica Degroote Nelson of Optimax Systems, in Ontario, NY, said of the winning talk, “Tao Zhen made novel use of a lot of technologies. It was a neat concept. I’d love to see him back here as a professional one day.”

About 50 teams sent in papers, and the finalists made eight minute talks before a mostly industry jury.

Second prize, a $2,500 check, went to Wei Lun Huang, of Johns Hopkins University. His team proposed “A Portable Projection Mapping Device for Medical Augmented Reality.” They designed a hand-held laser projector to track medical targets in real time, projecting patterns on a surface, and demonstrated its use in single stage cranioplasty.

Third prize, a $1,500 check, went to Praneeth Kumar Chakravarthula, of the University of North Carolina at Chapel Hill, for “Computing High Quality Phase-Only Holograms for Holographic Displays.” He used “deep learning metrics” in compact near-eye displays for AR and VR to address the Vergence Accommodation Conflict. He suggested an algorithm to compute phase-only holograms, using complex Wirtinger derivatives.

Other finalists included: Lantian Mi, from Shanghai Jiao Tong University, in China, with “A Retinal-Scanning-Based Near-Eye Display with Diffractive Optical Element” for AR devices; and Jie Chen, also from Shanghai Jiao Tong. In his talk, “A Foveated Intraocular Display on Contact Lens for Augmented Reality,” he described using vertical-cavity surface-emitting laser diodes on the contact lens with pixel density matching the density of cones on the retina.

Bernard Kress, of Microsoft HoloLens, a cochair of the new self-standing AR/VR/MR conference, was impressed by their ideas to reduce size of display engines, putting more pixels in the old spaces, and efforts to increase field of view, or FOV, with greater resolution.

Another judge, Hong Hua of the Wyant College of Optical Sciences at the University of Arizona, said, “Some had good ideas, but they were not practical for implementation today.”

FORD BURKHART

Panel guides you from startup to success

Business-minded: (L-R) Farzin Samadani, Zack Helft, Brit Berry-Pusey, Oliver Hvidt, Ryan Shelton, and Adam Wax. Credit: Matthew Peach.

It was standing room only at the BiOS Healthcare Founders Panel on Saturday, when a group of successful startup company founders revealed their experiences and gave their tips on how to turn biophotonics ideas into successful businesses.

Guided by moderator Farzin Samadani, from the National Instructor for the US NSF I-Corps Program that helps scientists become business people, the panelists gave a range of valuable insight into how startups can succeed – and how to avoid the pitfalls.

The panelists – Zack Helft, Co-founder, C-Light; Brit Berry-Pusey, founder, Avenda Health; Oliver Hvidt, CEO and co-founder, NorLase; Ryan Shelton, CEO and co-founder, PhotoniCare; and Adam Wax, Founder, Lumedica – also shared the experience of having been successful in various recent SPIE initiatives, such as the Startup Challenge and Prism Awards.

Helft commented, “SPIE has a great environment for startups. We took part in the Startup Challenge and were Prism Award finalists. The cash prize helped us to go to a bunch of events over the course of several years and the networking opportunities there really paid dividends. Berry Pusey’s Avenda Health won the competition in 2019: “That was a great experience for us, not least the cash award, worth $15,000. But what I really took away from it was the great community around this.”

Samadani asked what the panelists would have done differently if they knew what they now know. Wax said that academia could benefit from a more business-like approach: “Academics could use a bit more training, such as how to manage a lab and how to manage grants to develop the business culture.”

Ryan joked, “Not everybody out there thinks that your intellectual baby is as cute as you do, so rather than presenting the middle-of-the-night problem version, you need to work on posting an Instagram version of your idea.”

Helft’s advice was “You need to ask yourself ‘so what’ five times to take you away from your great idea in order to understand what the market’s questions might mean for taking it into the real world.”

Wrapping up, Farzani asked each panelist to give one short piece of advice to the next wave of biophotonics entrepreneurs. Wax suggested “going to the Startup Challenge”

Shelton said, “play hooky from the technical program and look and see who the panelists are at events like this and come talk to us.” Hvidt advised buying as many cups of coffee for industry people as possible, while Berry-Pusey recommended putting together “a great team, not just internally, but also your external vendor network.”

Helft offered, “If you have a problem or an idea then socialize it!”

MATTHEW PEACH

Photoacoustics selects best kidney for your transplant

A clinical trial starting in Toronto, Canada, this spring will look at the effectiveness of photoacoustic imaging for assessing the quality of donor kidneys, with the goal of better matching each donated kidney to the patient.

Ryerson University researcher Eno Hysi reported on pre-clinical studies of the potential application during the weekend’s Photonics plus Ultrasound conference sessions. He explained that the growing incidence of hypertension and diabetes is increasing demand for kidney transplants. It means that demand greatly outstrips supply, while patients do not always receive a well-matched replacement organ.

That’s partly because of the nature of the current gold-standard “punch” biopsy approach, which presents a risk of bleeding and is only able to sample 1% of the tissue in the organ before a transplant is carried out. Results can be misleading because one of the important features to look for in a donor kidney is the extent of fibrosis – an adverse build-up of collagen.

Using a photoacoustic unmixing approach incorporating a new wavelength-selection algorithm, Hysi and colleagues imaged a series of samples including mouse, pig, and human kidneys, finding a “remarkable correlation” between the imaging results and histology analysis.

“Photoacoustics can quantify human intra-renal collagen variations,” Hysi concluded, before revealing news of the trial with St. Michael’s Hospital in Toronto, a center of excellence for organ transplants in Canada.

MIKE HATCHER

Quantum leaps in Earth imaging

Landsat 9: Engineers work on the newly integrated Landsat 9 satellite in a cleanroom at the Northrop Grumman facility in Gilbert, Arizona. Credit: Northrop Grumman

Stunning images of giant fires in Australia, India, and Brazil, taken by Landsat 8 from space, proved the progress of NASA Goddard's teams, advancing from early days of a single pixel image to 1k x 1k scenes. That was just part of an opening day session of SPIE's Quantum Sensing and Nanoelectronics and Photonics conference.

New imaging devices use a hard-to-fabricate 4 to 6 million transistor integrated circuit to readout the current detector array signals, explained Murzy Jhabvala, of NASA Goddard's Space Flight Center in Greenbelt, Maryland. He spoke on Sunday at the Moscone Center in San Francisco.

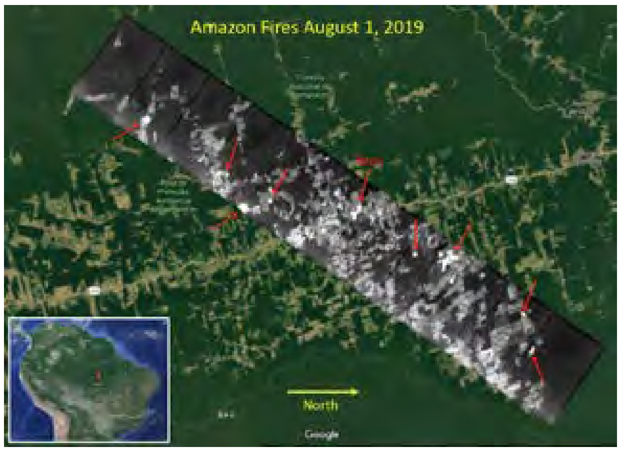
Murzy's team has pushed the frontiers for more than 30 years, from the gallium arsenide devices of the 1980s, when a one pixel image was an initial goal to now, with 4 million pixels as the newest goal.

These days, he said, "the entire world relies on Landsat data."

He described the some of the latest challenges facing NASA and Department of Defense, saying "new redesign techniques can minimize radiation effects."

He reviewed progress of QWIP – quantum well infrared photodetector – and SLS – strained layer superlattice – devices for the Landsat 8, and the Landsat 9, to be launched this year, and for the International Space Station. As NASA Goddard built the new thermal instruments in collaboration with QmagiQ, LLC, and Northwestern University, by 2011, the arrays got much bigger, with more broadband spectral response. "It all worked," he said.

NASA also works on devices with JPL and the Army Research Lab, in Adelphi, Maryland.



Amazon fires as seen by Landsat 8. Credit: NASA

"The SLS technology is very promising for monitoring global fires and thermal infrared earth science climate parameters," he said.

In the Mojave Desert, the NASA Goddard team tested the capability of QWIP-based cameras, to find even small caves in a desert. In caves, temperatures are at times colder than the outside air, and other times warmer. "If we can detect the caves on Earth, maybe we can use this technology to look for caves on Mars," he said.

The team also took the technology, including a 640 x 512 pixel camera, to Kitt Peak National Observator, near Tucson, Arizona, to perform thermal infrared solar imaging. "We unexpectedly imaged a sunspot that produced a flare," he said. "It was astounding. That hadn't been done before, to see a flare with the infrared. It was quite a bonus."

Now, the team is trying to evolve the technology for space as well as earth science. "Space science is tougher. The QWIP's are low efficiency," he said. They have goals of looking with infrared at Jupiter, Mars, Mercury, and Venus. "This is fun, too."

In a dramatic slide of farms, Jhabvala showed images taken from 2,300 feet that showed amazing detail, including even power lines and road signs.

At one point, NASA asked for at least one image from a test flight. The team produced 15 million images, at 80 meters per pixel.

"It was great," Jhabvala concluded.

FORD BURKHART

Eyes turn to lidar in MEMS conference...

The hot industry topic of lidar in autonomous vehicles was high on the agenda on Saturday, with James Jung from AEye giving an invited talk on optical MEMS devices in high-performance systems.

Jung, director of MEMS technology at the venture-backed San Francisco startup, avoided revealing specific details of AEye's approach, instead discussing the advantages of MEMS-based lidar.

The "point-scan" approach MEMS supports offers significantly better range than alternative approaches like flash or line-scan lidar, although that can lead to enormous data demands to operate with the kind of low computing latency necessary for safe driving at speed. More obvious advantages incude the small form factor of MEMS and the ability to scale volumes for cheap production, although packaging still presents some challenges.

AEye, which raised $40 million in a series B venture round in late 2018, is tackling that with its proprietary "iDAR" technology. It is based on scanning more intelligently, rather than simply using more photons and data points to produce more detailed point-clouds.

Jung said that the approach has proved successful in a number of hazardous "edge case" driving scenarios where the agility of lidar is critical – for example identifying road debris, or spotting "hidden" pedestrians where they would be invisible to cameras or radar.

He added that biaxial architectures, where the transmit and receive optical paths are independent and can be developed and designed in a modular fashion, suits the MEMS approach best.

Based around 1550nm laser sources, which take advantage of more relaxed eye safety regulations than at 905nm to allow deployment of more photons, AEye's lidar systems are said to achieve ranges in excess of 300 meters.

Jung said that the company had focused on redefining the three "Rs" of lidar – rate, resolution, and range – to produce a technology capable of long-distance object classification combined with the low latency and resolution requirements needed for safe autonomous driving.

MIKE HATCHER

...and Waymo wants better lasers for automotive lidar

Waymo hardware developer David Schleuning addressed a packed session on Sunday, discussing the Silicon Valley company's exploits in autonomous vehicle development – and the need for higher-performance lasers in lidar systems.

"We're at a very exciting time, and a time of rapid technology development," Schleuning told attendees during the High-Power Diode Laser Technology XVIII session dedicated to lasers for 3D sensing and lidar.

He discussed the possibilities of increasing intensity on the facet, for example by adding junctions to the semiconductor laser structure. High-power VCSELs may offer another option for lidar developers, he added.

Meanwhile, visitors to the Photonics West exhibition can check out a compact new automotive lidar system developed by Boulder-based Insight Lidar, a subsidiary of Insight Photonic Solutions at booth #3127.

Unveiled to the public for the first time in San Francisco this week, the technology is adapted from the parent company's earlier work on optical coherence tomography (OCT) subsystems. CEO Michael Minneman and head of development Chris Wood believe that for vehicles to become truly autonomous, they will need to adopt the frequency-modulated continuous-wave (FMCW) version of lidar, rather than the more common pulsed time-of-flight systems that have dominated the scene thus far.

So far, Insight's all-chip, no-moving-parts approach has culminiated in the development of a paperback-sized unit. The unit has a claimed range of 300 meters, and is said to be particularly good at perceiving so-called "edge-case" scenarios that autonomous vehicles typically struggle with.

MIKE HATCHER

Insight Lidar's compact unit, on show for the first time at Photonics West. Credit: Insight Photonics Solutions

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FEATURES

- Total Power **>20W**
- External Triggerable **1-80MHz**
- Wavelength **430-2400nm**
- Internal Repetition Rate **0.01-200MHz**
- Pulse Energy **>1.5uJ**
- Single-Mode Output

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APPLICATIONS

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- **Two/Three Photon Imaging**
- **OLED Dicing**
- **Glass/Sapphire Drilling&Dicing**
- **Thin Metal Drilling&Dicing**
- **OPO/OPA/OPCPA Pumping**

FEATURES

- Average Power **100W**
- Pulse Duration **~300fs-10ps**
- Peak Power **>500MW**
- Repetition Rate **25-5000KHz**
- Pulse Energy **>200uJ**
- 515nm/343nm Available

A broader spectrum, a bigger picture

SPIE CEO Kent Rochford welcomes all delegates to this year's expanded Photonics West.

For us in the photonics world, *Happy New Year* is synonymous with *get ready for Photonics West,* and for us at SPIE, in 2020, it meant *to organize the largest Photonics West ever.* I think we succeeded, and after the week is over, I hope you agree that it was the *best Photonics West ever.*

As we kick off a new decade, it seems that we are getting closer and closer to living in the future that many of us envisioned as we watched the first generations of Star Wars or Star Trek. Much of this future is built on optics and photonics, by the people in the Moscone Center this week. Everyone you pass in the halls or sit next to at a presentation is building or enabling some part of our technological future.

Kent Rochford

Connecting ideas is vital to progress, and some of the most valuable outcomes of Photonics West are new connections and new ideas.

From advancements in healthcare to the infrastructure of next-generation networks, from advanced manufacturing and quantum technologies to sensing, imaging, and displays, from autonomous vehicles to space exploration, literally everything in our future technology ecosystem, is here this week. Whether being presented in a conference room, showcased on the exhibition floor, discussed on a panel, taught in a short course, or debated at a reception, you can learn about the latest in just about everything photonics related somewhere at Photonics West.

2020 brings the most complete industry program to date. With separate tracks running the entire week, we are striving to offer a valuable program to every stage of the market. Whether you are C-level executive of a multi-million dollar company, an investor looking for your next unicorn technology, or a post-doc commercializing a successful project from the lab, there is something for you. Hopefully, all three of you bump into each other at one of the many networking events scheduled and make history.

Happy anniversary

We will also celebrate the 10th year of the SPIE Startup Challenge this week, and I look forward to seeing the look on the winner's face Wednesday afternoon when we hand them the giant check. Between now and then, all of the companies will be busy polishing their pitches with help from experienced veteran entrepreneurs and investors during the semi-finals and related workshops.

We made big changes to the ever-popular AR/VR/MR program. This year we have an entire 3-day conference co-located with Photonics West held over at Moscone West. With many of the leading hardware designers and visionaries in attendance, the rooms are sure to be packed once again with the buzz of a burgeoning industry. It's all included in your Photonics West technical pass..

A growing pain of our industry, achieving a trained workforce, will be addressed at a Tuesday evening event aimed to pair technician training programs with industry for deeper collaboration between the two. If you are hiring technicians or want to help inform future technician curriculum, please attend. Working alongside the photonics industry to help foster a growing and healthy photonics ecosystem is core to the mission of SPIE.

We were proud to announce our Endowment program and its first partner at last year's Optics + Photonics, and we were equally pleased to announce our second gift to endow the SPIE-Glebov Family Optics and Photonics Graduate Scholarship at the University of Central Florida College of Optics and Photonics at CREOL's reception last night. Giving back to our community is ingrained into SPIE's mission and supporting optics and photonics professors and graduates will benefit us all as they build the next generation of our future.

Equity and diversity

Equally important is helping foster an equitable and diverse industry. Please come to one of the many Equity, Diversity, and Inclusion events held during the week and learn how you can help in making our community more welcoming and prosperous to everyone.

Connecting ideas is vital to progress, and some of the most valuable outcomes of Photonics West are new connections and new ideas. I know many of us attend with a plan – who to meet, which presentations to listen to, which booths to visit, but be sure to try something new. Go to a presentation outside of your focus, strike up a conversation with a stranger, visit a booth of an unfamiliar company, or come to one of the many non-technical offerings throughout the week.

You will benefit significantly by learning new things and meeting new people, as will others benefit from your attendance or welcoming gesture. No one person can see it all, but most of us will try to see as much as we can. Pace yourself – the week is long, but Thursday is only three days away!

KENT ROCHFORD

A team from the University of St Andrews and Artinis Medical Systems attached an adapted version of the company's "PortaLite" NIRS sensor to harbor seals, finding that the aquatic mammals are able to use cognitive control to re-distribute blood around their bodies shortly before diving below the water for long periods. Copyright: Jessica Kendall-Bar.

Wearables get wet as physiology meets photonics

Portable biophotonics technology is now able to monitor vital signs in synchronized swimmers and free divers – and has even shown how seals control blood flow in advance of long dives.

Have you done your ten thousand steps yet? Well if you've been traipsing around the Moscone Center today, the answer to that question is almost certainly "yes." By now most of us are familiar with wearable health monitors – most obviously the watches and wristbands from household brands like Apple, Garmin, and Fitbit that record your heart rate, daily steps, and more.

The photonics technology in those products is pretty basic, typically limited to some green LEDs to track your pulse, and maybe some red or near-infrared emitters to measure blood oxygen saturation. But biophotonics has the potential to do much more than that, and a brand new conference within this year's BiOS Symposium is dedicated to advancing the utility of photonics-based health monitoring. The inaugural *Biophotonics in Exercise Science, Sports Medicine, Health Monitoring Technologies, and Wearables* conference took place over six sessions on Saturday and Sunday morning, covering topics ranging from diabetes monitoring to quadricep muscle oxygenation dynamics in trained cyclists.

Many of the applications presented in San Francisco this weekend are based on near-infrared spectroscopy (NIRS). The technique generally relies on a pair of near-infrared emitters at different NIR wavelengths, to monitor levels of oxyhemoglobin and deoxyhemoglobin. Unlike the basic pulse oximeters found in most wearables, the more sophisticated approach is able to measure oxygen saturation in a specific muscle, or potentially any tissue type – including the brain, other vital organs, and even bones.

Critically, NIRS yields the ratio of oxygenated blood to total blood in the target tissue. This figure is known as the "tissue saturation index," and quoted as a percentage. Measurable in real time, in simple terms it tells us how much oxygen is in the tissue under test.

In recent years several companies have sprung up to sell NIRS-based oximeters, initially with benchtop equipment aimed at research laboratories. But that technology is now being shrunk into wearable form factors, and aimed largely at applications in sports science. One company that sells both types of equipment is Artinis Medical Systems, based in The Netherlands. It was co-founded over 15 years ago by Willy Colier, a member of the program committee overseeing the new BiOS conference. Wout Kregting is the firm's product manager for wearables, and during his five years with the company has seen it grow from just seven employees to around 40.

"A decade ago we only had basic devices; now have intelligent systems capable of multi-channel measurements," he says, adding that as well as selling systems to university hospitals and research groups, Artinis is increasingly targeting the biomedical sector, and looking to extend its wearables product line into the commercial arena.

Seals and swimmers

Something that owners of wearable monitors will be all too familiar with is that most current products work a lot better on dry land than when they get wet. That's partly because of the way that light is scattered and absorbed by water, making oximetry measurements a lot less reliable in the water. But in the past few years Artinis has found ways to adapt its technology for aquatic applications – first in swimmers, and more recently in free divers and even seals.

continued on page 11

Wearables get wet continued from page 09

Back in 2014, a team led by Chris Cooper from the University of Essex in the UK used a waterproofed "PortaMon" device from Artinis to track changes in muscle oxygenation in swimmers. A similar approach was then applied to Olympian synchronized swimmers, including the multiple gold-winning Russian pairing of Natalia Ishchenko and Svetlana Romashina.

Kregting says that the results of those studies were remarkable, opening up a whole new level of understanding about changes in blood oxygenation and specific muscles when humans are under the water and holding their breath. More specifically, they suggest that the athletes' spleens play a crucial role in providing a kind of "reserve tank" of oxygenated blood that can flow into the brain. In the case of Ishchenko, whose performances showed an incredible awareness of the movements of her partner Romashina, her spleen was shown to change in size by almost 60% – giving her a significantly larger oxygen reserves than all the other competitors.

After synchronized swimmers, Artinis' technology was applied to another group of mammals known for an extraordinary ability to hold their breath while diving – seals. Carried out in collaboration with a University of St Andrews team led by Chris McKnight, these experiments found that – unlike the synchronized swimmers – the seals do not rely on the same spleen effect.

But perhaps even more remarkably, it appears that seals have developed the ability to prepare for a long dive by using cognitive control to increase the volume of blood in their brains around 15 seconds before each submersion. Then, during the dive, they are able to further increase brain blood oxygenation. We know this because the researchers were able to adapt a "PortaLite mini" device from Artinis, and fix it to the slippery skin of the four seals to monitor blood characteristics in their blubber and brains.

Counter-intuitively, the skull does not present any great obstacle to accessing brain tissue. "Since near infrared light is mainly absorbed by blood, and the skull does not contain much blood, the skull is relatively transparent in the near infrared range," explains Mathjis Bronkhorst, a project leader at Artinis who worked on the seal project. "In practice, it is no problem to measure through the skull. [Although] on the head it is sometimes necessary to move hair out of the way, since hair absorbs near-infrared light."

Currently accepted theory dictates that NIRS yields a maximum penetration depth of approximately half the distance between the receiver and the transmitter element of the oximeter's optodes. In the seal monitoring experiments the team used three different distances, accessing a maximum depth of approximately two centimeters. "This is enough to reach the neocortex or the outer layers of the brain of the seals," said Bronkhorst, adding that employing a three-channel optode design allowed them to apply spatially resolved spectroscopy. "In this way we can measure the oxyhemoglobin and deoxyhemoglobin ratio in living tissue."

"The success of NIRS in such an extreme environment highlights its potential for observing physiological processes in real-world contexts in the wild and in aquatic environments," concluded McKnight and colleagues in their paper on the work, published in June 2019.

Brainwave: Netherlands-based Artinis offers NIRS equipment in both a high-specification benchtop format and increasingly wearable form factors. Research applications in cerebral hemodyamics – monitoring blood volume in the brain – is among the major growth areas. Photo: Artinis Medical Systems.

Healthier aging

While the utility of wearables in sports science is clear, it's important to note that the technologies under discussion in the Moscone this week are not just for elite athletes or the middle-aged-man-in-lycra brigade. With an aging population, there is a desire to extend not just our sheer life spans, but the amount of that time we spend in good health. Biophotonics-based monitoring may have the potential to help spot the early signs of cardiovascular disease and osteoporosis, and could even give us a better understanding of the relationship

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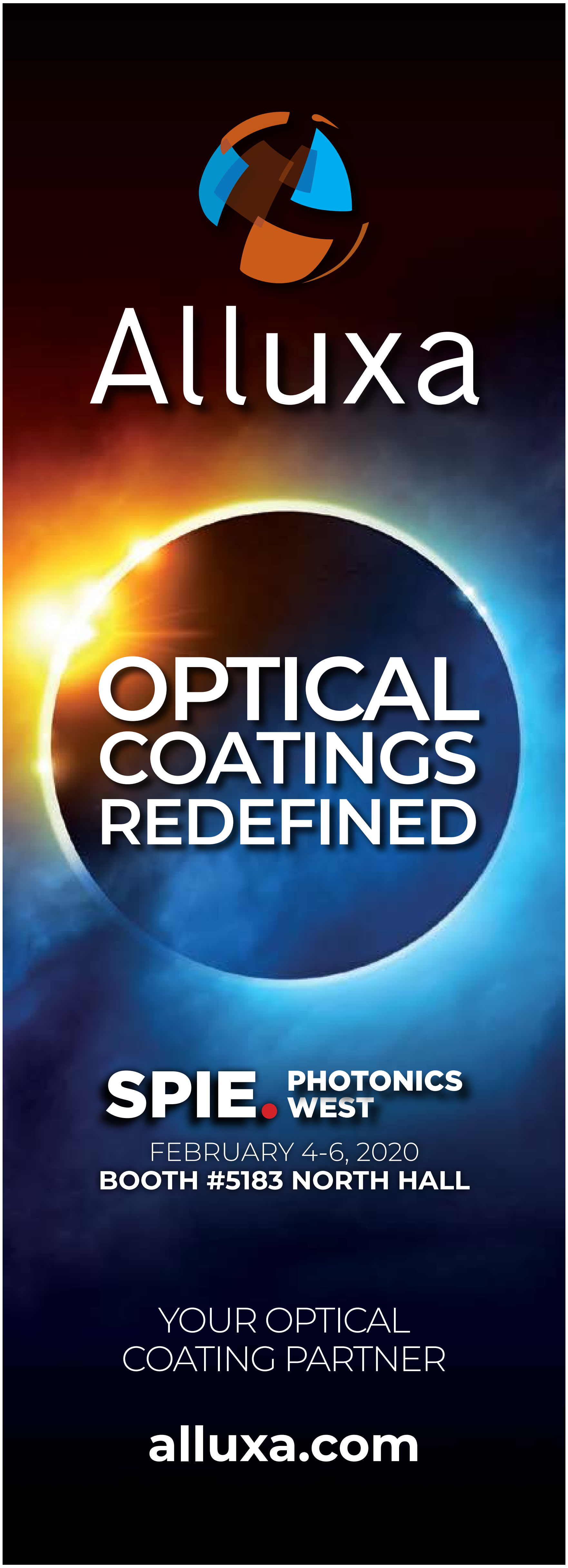
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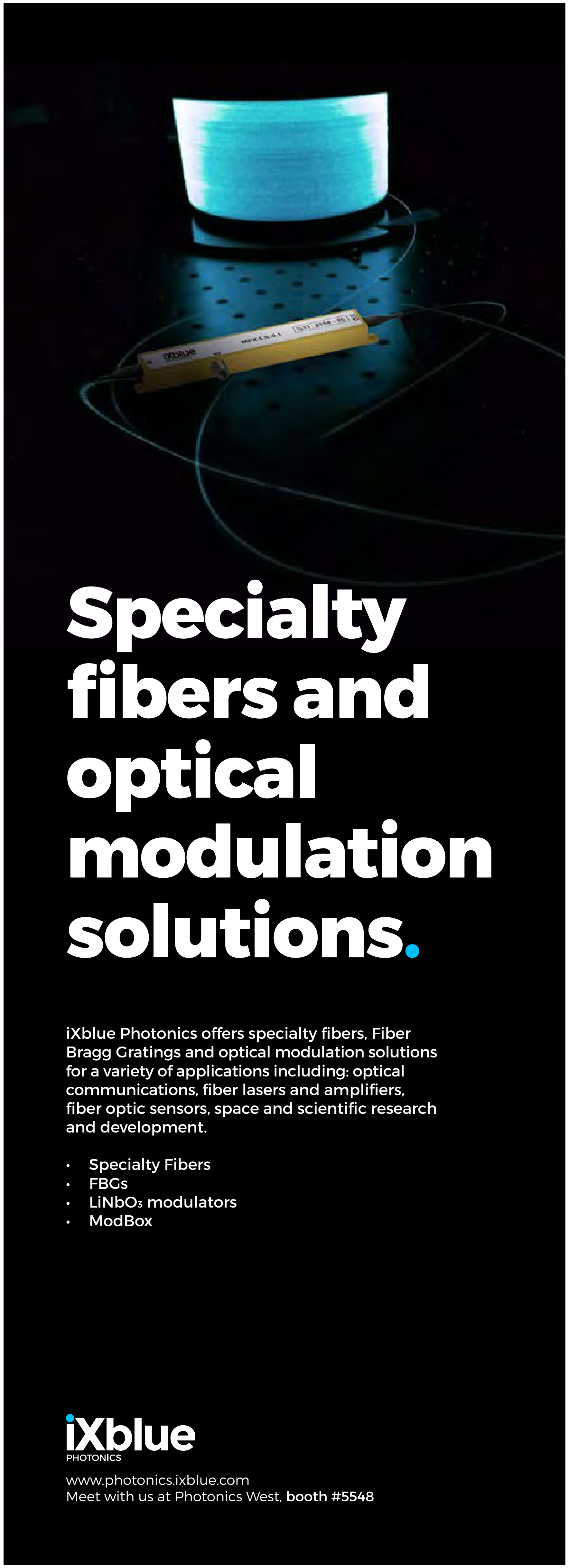
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Wearables get wet continued from page 11

between blood oxygenation in the brain and the effects of dementia.

Luke Harris is an Associate Professor in the School of Health Sciences at the University of Northern British Columbia in Canada. His team is presenting four papers on NIRS applications at BiOS, with a focus on developments ultimately aimed at increasing the "health span."

One of those studies looked for any effects that respiratory endurance training had on blood oxygenation in the brain. And it seems to have produced some intriguing results. As Harris explains, subjects in the study had their brain hemodynamics tested one month apart – before and after a training program designed to strengthen the muscles used in respiration.

The tests, which took the subjects to exhaustion, showed only a small improvement in respiratory performance after the month of training. However, the subjects' own perception at the end of the training period was that they were now able to complete the test more easily. Now, here's the interesting part: NIRS results showed that before the training program subjects' blood volume was much higher in the left side of the pre-frontal cortex. But after the month of respiratory muscle training, it was blood in the right pre-frontal cortex that became dominant.

"It appears that the difference is in the brain's perception of how hard the body is working, and that a switch from the left to right cortex [in terms of brain blood volume] is connected," Harris observes.

Other studies from the Harris group being presented this week looked at the effects of moderate exercise on cognitive function; optimizing the doses of *botulinum* toxin used to treat muscle stiffness in stroke patients; and the ability of NIRS to probe blood perfusion in bones – all of which may end up helping us age more healthily.

Harris says he was inspired to work in the field in part by the exploits of Rick Hansen, the Canadian Paralympian whose foundation is at the forefront of researching treatments for spinal cord injuries. And he sees Babak Shadgan, co-chair of the new BiOS conference alongside Amir Gandjbakhche, as one of the pioneers in the field. A principal investigator at International Collaboration On Repair Discoveries (ICORD) in Vancouver, Shadgan uses NIRS to study spinal cord injuries and also in sports medicine.

Luke Harris from the University of Northern British Columbia demonstrating the "SpiroTiger Smart" breathing apparatus, a respiratory muscle endurance training (eRMT) instrument. BiOS presenter Johnna Somerville used the equipment in her study of eRMT effects on cerebral hemodynamics and self-reported effort perceptions. Photo: Luke Harris / UNBC.

Credibility

While the potential of NIRS is clear, and its applicability is growing as more wearable versions of the technology emerge, there still seems to be something of a credibility problem. Considering that the technique was first reported more than forty years ago, that seems surprising. Part of the issue, says Harris, is that compared with, say, magnetic resonance imaging, NIRS is a difficult technique for physiologists to identify with. A lack of standardization has also made NIRS validation more of a challenge. Harris believes that the new BiOS conference is unique in its aim to bring together optics specialists and physiologists under the same roof – and that, with time, it ought to help improve that credibility.

Bronkhorst has some ideas about how photonics technology development might help advance wearable health monitoring. "The challenge in our field is that light dissipates approximately a factor of ten with every half-centimeter of measuring depth," he explained. In theory, this can be addressed by deploying either a higher optical output power or a more sensitive detector. But in reality there are practical limitations associated with LEDs.

Vertical-cavity surface-emitting lasers (VCSELs) could offer a new option here. "VCSELs have a narrow-wavelength spectrum and arrays can increase the amount of receiver-transmitter combination that can created," Bronkhorst told Show Daily.

He says that any technique that increases optical power without increasing the surface temperature of the LED or VCSEL emitter would improve measurement depth. "This can also be applied on the receiver side, where a photodiode with an increased sensitivity and low noise in the range of 700-900 nm would be greatly beneficial for the wearable NIRS field," he added. "Another interesting development is small-package LEDs with multiple wavelengths. In our case 760 and 850 nm are used, but additional wavelengths allow the measurement of extra chromophores."

* The BiOS conference on Biophotonics in Exercise Science, Sports Medicine, Health Monitoring Technologies, and Wearables took place Saturday and Sunday in Room 159, Upper Mezzanine South of the Moscone Center.

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Multiphoton microscopy: deeper, wider and faster

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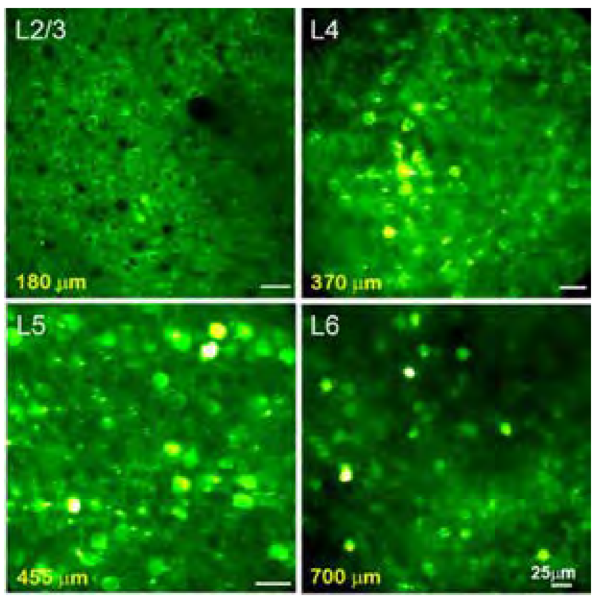
The remarkable capabilities of optical microscopes that can obtain high-resolution mouse brain images directly through the surrounding skull promise to transform how we understand ourselves. Chris Xu, whose team at Cornell University, in Ithaca, US developed the technique, explains that the capability arises from multiple photons simultaneously interacting with molecules in the brain. Together they excite and make the molecules fluoresce. Each photon can therefore be lower energy, and therefore longer wavelength, than if a single photon was causing the fluorescence. "This allows you to penetrate better," Xu explains. "This is the same logic why the sky is blue, and sunset is red, right? Long wavelengths scatter less, including in tissue and bone."

Penetrating skulls is therefore just one of the many breathtaking capabilities two- and three-photon techniques offer, steadily driving their adoption. In fact, multiphoton microscopy can be applied even without adding colored or fluorescent molecules to enable cells to be imaged like many other approaches do, Xu explains. Instead, intense infrared multiphoton excitation makes molecules fluoresce that are naturally found in cells, like the key metabolic cofactor NADH. Xu and other pioneers in the field will be announcing the latest frontiers such methods have reached at Photonics West 2020.

The most commonly-used technique is two-photon excited fluorescence. The probability of two photons reaching a molecule and being absorbed by it to produce excitation is low, and therefore the fluorescence signal is relatively weak, Xu explains. "To make it practical for biological applications, a femtosecond laser must be used," he says. "You bunch photons in time so when the laser is on, so it's extremely bright. By doing so you can enhance this nonlinear excitation probability." Other approaches exploit scattering rather than absorption, for example second harmonic generation analysis of collagen, which has been used in cancer diagnostics, Xu notes, and third harmonic generation, which is useful for looking at myelin in the brain.



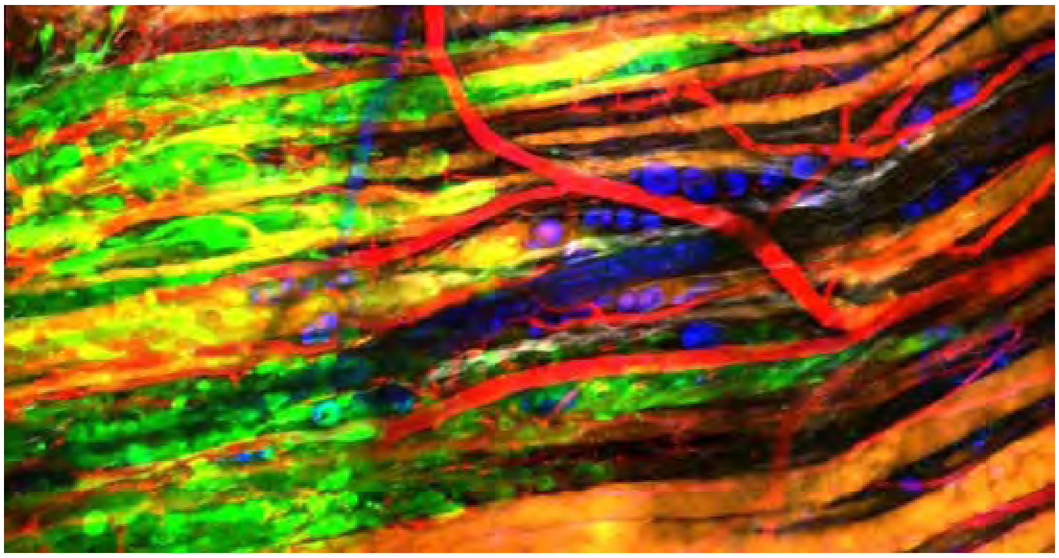
Na Ji's team uses multiphoton microscopy to image neurons from L2/3 to L6 of the primary visual cortex in the brain of a mouse. Credit: Na Ji/University of California, Berkeley

Multiphoton microscopy is a powerful tool for high resolution imaging in a 3D sample that is optically opaque, echoes Na Ji from the University of California, Berkeley, US. This includes most biological tissues. "The fluorescence signal is only generated at the focal spot of the microscope due to the very small cross-section of multiphoton excitation," she says. "As a result you just need to focus your light at a particular position in the sample and collect all the fluorescence photons coming out." To generate a large image involves scanning the laser focus at very high speed across the sample and record the fluorescence brightness at each position.

Darryl McCoy from Santa Clara, US, headquartered Coherent Inc. stresses that restriction of absorption to the focal point is only practical with femtosecond lasers. Femtosecond technology also has advantages beyond providing high peak powers that enable multiphoton absorption in relevant fluorescent probes, McCoy adds. Femtosecond sources also "provide that peak power without raising the average heat output, preventing thermal damage to biological samples," he says. The long wavelengths used also help further reduce scattering, enabling penetration even deeper into tissue.

Putting disease in the picture

McCoy's colleague Marco Arrigoni adds that the largest consumer of multiphoton microscopy is neuroscience, due to the relatively large amount of funding available. "The brain is actually a friendly or-



Multi-wavelength two photon excitation microscopy of tumor cells, produced using Coherent's Chameleon Ultra II laser and Compact OPO products. It shows melanoma cells (green) invading skin tissue. The cells are guided by structures such as muscle fibers (orange), nerve fibers (blue), collagen (grey) and blood vessels (red). Credit: Courtesy of Bettina Weigelin and Peter Friedl, Radboud University Nijmegen.

gan to look at, because the tissue of the brain is more transparent," he says. And three-photon microscopy is pushing brain studies further, going 1.5-2 times as deeply as two-photon approaches, he adds. Such capabilities are enabling potential future directions, such as improving or replacing current histopathology methods to tell whether tissue is cancerous using multiphoton microscopy together with computer algorithms. Arrigoni also raises the potential that multiphoton microscopes could be used in surgery. "People would look with multiphoton microscopes at the tissue being operated on, for example, for brain cancer," he says.

Michelle Digman, from the University of California, Irvine, US takes multiphoton microscopy in yet another direction: making it more accessible to non-experts. She highlights that multiphoton microscopy is interesting in many biologists without deep knowledge of its technical basics, because it excites autofluorescent components without exposing samples to harmful UV light. Exploiting how long the fluorescence signal or photon from two-photon excitation microscopy is emitted in fluorescence lifetime imaging microscopy (FLIM) is a powerful way to investigate complex biological systems non-invasively, Digman says.

Building on this, Digman and her University of California, Irvine colleague Enrico Gratton co-developed phasor-FLIM analysis. This can identify fluorescence lifetime signatures from multiple molecule types in an image, she explains. Conventional FLIM uses fitting techniques that identify the different molecules by the extent to which two-photon excited autofluorescence signatures in biological samples decay. By transforming the histogram of time of arrival of photons into a polar coordinate system, Digman does away with the need for fitting. Because phasor-FLIM is a fit-free method, it does not require an expert to analyse the image, which makes it more accessible and more robust to observer-induced biases or artefacts. It is also easier to calculate the fraction of different fluorophores in any given pixel of an image.

Researchers are therefore using this approach to study metabolism in various parts of the body such as the liver, kidneys and intestines. "It's becoming a very useful way to both characterize cells or tissues in response to drugs, or in diseased cells," Digman says. "We've looked at Huntington's disease, and we've seen cells that have actually aggregated this protein called huntingtin, they form these plaques. They've actually have shifted the metabolism within the cell. Across the spectrum in neurons, in cancer biology – FLIM is a very useful tool to look at metabolism in almost any disease."

Digman's talk at Photonics West took place Sunday, February 2 in session 4 of Multiphoton Microscopy in the Biomedical Sciences XX. "The work we are presenting at Photonics West is using FLIM to determine what's happening in the development of embryos in a label-free, fit-free way. Now we have a way to characterize

continued on page 21

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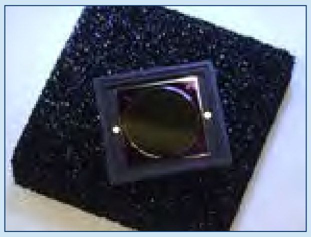

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Microscopy continued from page 15

the signatures of healthy embryos at any embryonic stage," she says. This can be used to predict the best developmental potential in pre-implantation embryos for in-vitro fertilisation. Her team has also used two-photon microscopy to induce double-stranded DNA breaks. "We've been able to show that there is a pro-survival response to DNA repair activation through a change in cellular metabolism, which is proving to be critical in discovering new potential protein targets for treatment and for the understanding of genetic and carcinogenic consequences of diseases," Digman explains.

Pushing limits

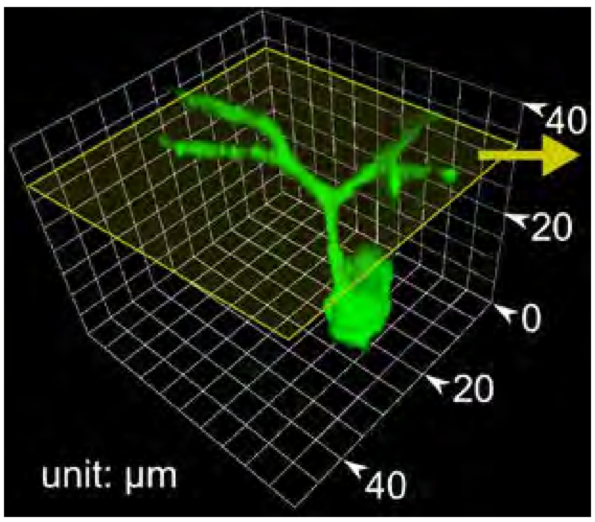
Implementing the phasor approach is easy, asserts Digman, which microscope makers are aware of, and exploiting. Phasor-FLIM is therefore fairly widely used by groups she has never even talked to or heard of. "We're happy that other people are using it," Digman says. However she would like Phasor-FLIM to be far more widespread. Digman suggests that the software that groups use should be updated as improvements are consistently being made in identifying fluorophore lifetimes in mixtures. Currently the approach can distinguish two or three fluorophores. "The question is, can we start unmixing four, five, six fluorophore lifetimes that could be within that same pixel," Digman says. "We are now making efforts in that regard to unmix those possible lifetimes."

Na Ji is likewise pushing the limits to increase scanning speed for 3D imaging using multiphoton microscopy. By scanning long, thin Bessel beams through a sample in 2D, signals are generated across the length of the beam, she explains, which changes the 2D frame rate of microscope capture into a "3D volume rate." Samples being studied are kept perfectly still, Ji says. "We know where everything is exactly, we just need to look at how the signal changes with time," she adds, with these changes reflecting ongoing activity of the neurons in the brain. Newton, US-headquartered optical equipment company ThorLabs has licensed the approach from Ji's team to make add-on units for its commercial two-photon microscopes.

In session 2 of Multiphoton Microscopy in the Biomedical Sciences XX, Ji will present a collaboration with Kevin Tsia at the University of Hong Kong. Tsia has developed a "super-fast way of scanning a focal point in one dimension, so you can scan eight million lines per second," Ji says. "We can image samples at 3000 frames per second," she adds. They have used the work to image membrane potentials arising from electrical signals within the brain.

Yet data handling for this ultrafast raster scanning approach is a big challenge. A few seconds of imaging generates "a huge amount of data" Ji says. Ji and Tsia are collaborating with the Paninski lab at the statistics department at Columbia University, in New York, US, among others, to develop techniques to resolve the issues. "It will probably be five to ten years before you can see an easy-to-use commercial product for biologists," she says.

The approach is part of the three biggest trends that Ji sees in multiphoton microscopy: improvements in speed, resolution and depth of imaging. Speed is important because some of the biological processes being investigated happen on a millisecond scale, Ji says. "This requires kilohertz imaging, with speeds of one image per millisecond," she says. "The higher resolution part is where adaptive optics is, I believe, essential, to correct for sample-induced distortion of the excitation light. And Chris Xu has developed this three-photon excitation microscopy, which is really pushing the limit of how deep we can image."

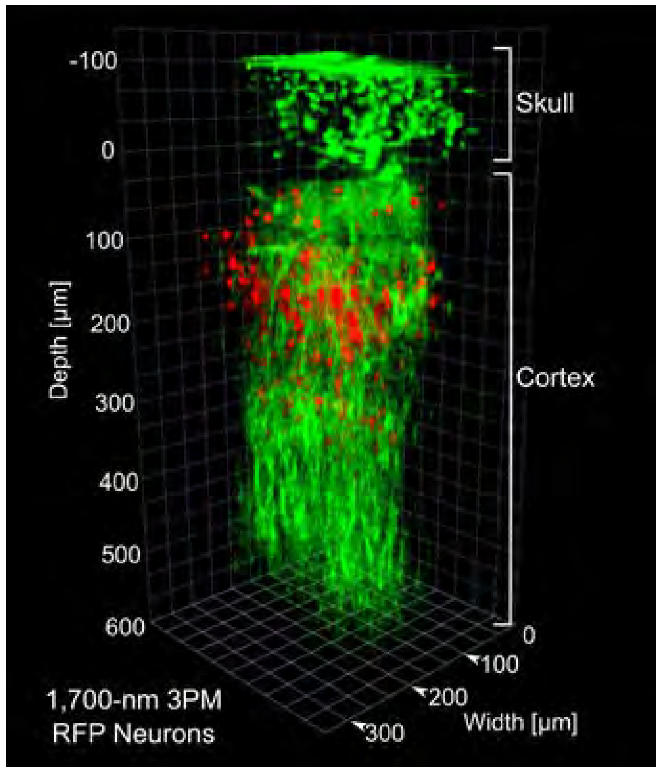


3D reconstruction of a labeled neuron located about 140 microns below the cortical surface in a mouse imaged by three photon microscopy. Credit: Chris Xu/Cornell University

In his talk, also in session 2 of Multiphoton Microscopy in the Biomedical Sciences XX, Xu will be presenting in line with his slogan, "Imaging deeper, wider, and faster," he says. "For imaging deeper, we are pushing the three-photon, longer wavelength approach," Xu explains. "Wider imaging is to build large area imaging microscopes. For imaging faster, we are presenting a new laser source that we have developed that increases photon efficiency. We want to make sure every photon we put in the brain is doing work for us, not just heating up the brain."

Wide-ranging usefulness

Xu adds a further important trend beyond deep imaging of intact tissue, which is translation of the technology to biological and clinical applications. Deep imaging allows the imaging of biological processes in their natural environment, he stresses. "If you take a neuron out of the brain, you can look at it very carefully, but it's probably not very meaningful," Xu says. Yet this requires a laser, which is ultra-fast, with the right wavelength, pulse energy, and right repetition rate among other factors, Xu adds. That brings one of multiphoton microscopy's key challenges in the cost of lasers with these capabilities, which begin at $20,000 and go up to $500,000.



3D reconstruction of three photon microscopy through-skull imaging of a cortical column of neurons in a mouse, with different proteins labeled red and green. Credit: Chris Xu/Cornell University

Coherent's McCoy says that serving a range of "who want huge amounts of flexibility and performance from the laser, to customers that are really focused on price and size' isn't straightforward. 'We have to create a suite of femtosecond lasers that from the outside is very biologist friendly and yet on the inside integrate quite complicated laser techniques and technology,' he says. 'In general that means that you have challenges in creating lasers that are small enough and cheap enough to really expand the market."

The two multi-photon products that Coherent will be presenting at Photonics West are the Axon series of single wavelength femtosecond solutions, and the Chameleon Discovery NX. "The Axon series has been developed for the main popular fluorescent probes at 920nm and 1064nm, with other wavelengths on the way," comments McCoy. "The Chameleon Discovery NX offers industry-leading power, pulse width and modulation capability in a single one-box flexible platform. We'll also display lasers for advanced imaging techniques such as deep imaging using three-photon excitation, that employ high energy fiber-laser technology and optical parametric amplifiers." Coherent will demonstrate these products at BIOS booth #8322, and Photonics West booth #4845.

Yet adoption of femtosecond lasers and multi-photon techniques outside universities is slow, Arrigoni adds. Replacement of conventional histology with lasers is still far away, due to the entrenchment of the incumbent technology. "Our part in this is to develop laser sources that are more compact, more reliable and more effective, like the Axon family," he says. "Most of the activity right now is academic research with longer-term horizon of addressing neurodegenerative diseases and some types of cancer."

Nevertheless, Xu highlights the importance of the relationship between academic groups and laser producers in bringing multiphoton microscopy to the mainstream. "When we started three-photon imaging about seven, eight years ago, we worked with commercial companies," he says. "Now these lasers are commercially available from a minimum of six companies. They're actually pretty fast coming online."

Xu adds that he feels this synergistic relationship will continue, "because it's very fruitful so far for all of us. It is estimated that there are 4,000-8,000 two-photon microscopes across the world, so it's not a niche any more," he says. "For the three photon imaging techniques, 40-50 groups are using it, it's remarkable really given that lasers were commercially available only a few years ago. Most of the technologies developing in the multiphoton field are reasonably translatable. You can buy a multiphoton microscope, do your favorite experiments, and write great science with it. It's interesting – this whole field has only taken thirty years from initial demo to many people doing imaging with this technology."

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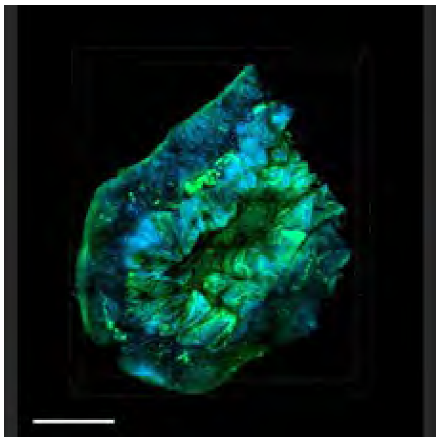
Rising star Barton anticipates a galaxy of new tools in 2020s

Co-chair of BiOS Jennifer Barton reveals her great expectations for new decade.

To unwind, Jennifer Kehlet Barton likes to visit a small, remote observatory to do some astrophotography near the border with Mexico in the Patagonia Mountains, using a digital deep-space CMOS camera. "This is just fun. We are definitely amateurs," she says, musing on the Orion Nebula, the Pleiades and such places that may well hatch a few new stars.

As a professional, Barton watches over the 300 or so stars, top faculty scientists, at the BIO5 Institute in central Tucson, AZ. And for her, that too could not be more fun. Since 2015, she has directed BIO5, a University of Arizona center for futuristic bioresearch on disease, hunger and the environment, connecting five disciplines: agriculture, engineering, medicine, pharmacy and science.



Jennifer Barton is researching ovarian tumors in mice to develop the first effective screening method for the disease. (Photo courtesy of the National Cancer Institute)

This year at Photonics West, she will again be blending work and play, beginning a term as new co-chair of SPIE's BiOS Symposium. Barton, who works on early cancer detection in her own BIO5 lab, says she looks forward to learning at a few PW industry sessions how to turn lab breakthroughs into successful market products.

We asked Barton to take us on a conceptual tour of BIO5, pointing out hot topics from Photonics West that are being explored by these labs:

Medical imaging and microfabrication

Barton said the tour could start with Judy Su, more formally Tsu-Te, who does microfabrication of nanostructures. "She makes incredibly sensitive detectors of biomarkers in the body. One of her big areas is looking at Alzheimer's disease."

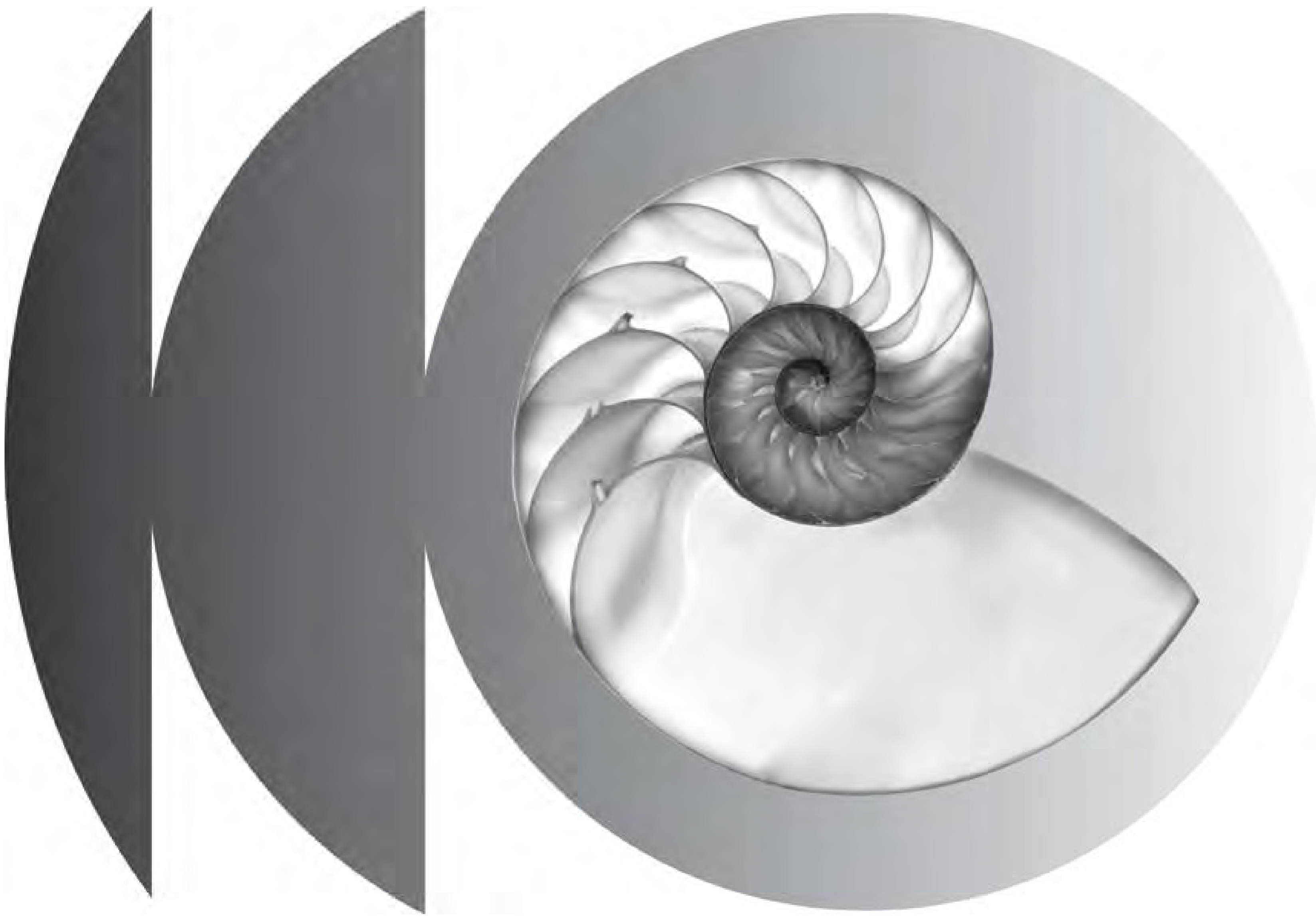
Su's team is putting photonics technology into a biosensor that could become a useful diagnostic. It uses microtoroids with which a light can be directed to travel around a sample and find very small particles – in the attomolar range, at a concentration of ten to the minus eighteen moles per liter – of the protein biomarker being flowed past the sensor.

"She needs to fabricate these devices and then we need to test them, to make sure they are useful as a diagnostic. Su works with the physicians and brain scientists here in the Bio5 Institute to make sure her biophotonic device works for this medical problem."

Optomechanics

The work of Dongkyun Kang, known as D.K., is an ideal example of "where optics is going," Barton said. In the past, a visitor might see optical research tables full

continued on page 25



Photonics superstar continued from page 23

of lasers and mirrors and fancy tools of optomechanics. "And that's a fine place to start," Barton said, "but that's not going to be useful in the medical community. D.K. is taking, in his case, the confocal microscope and turning it into a portable handheld device that can go into rural areas, including rural Arizona, into developing countries, to diagnose cancers that affect a lot of people."

Kang calls it "stopping cancer with a smart phone."

The commercial confocal microscope is a large device that can cost upwards of $100,000. "And that's not something that most people can afford," she said. Kang is taking that capability and making sensors that are portable, highly sensitive, and at a cost goal of $5,000.

"This is all because of advances in photonics," Barton said. "You can use a small laser diode and implement it in the imaging and diagnostic devices that we are building. Today you can manufacture small optics at a reasonable price."

Translational imaging

We asked Barton to visit her own lab where work with spotting ovarian tumors is unfolding. She is developing what would be the first effective screening method for ovarian cancer. And that, she says, illustrates BIO5's ability to carry out fabrication and imaging using high-resolution optical techniques.

"If you want to look at cells or tissue microstructure, you can't image very deeply. You end up needing to build endoscopes," Barton said, "And I do that."

Her microendoscopes provide nonsurgical techniques for looking into the body's tissues.

The body has many natural orifices needing study, Barton said, "and the same advances in photonics and materials allow us to make tiny, flexible endoscopes that can go all kinds of places in a body, in a pretty minimally invasive manner."

Barton's work, funded by a Department of Defense Ovarian Cancer Research Program grant, has involved placing the devices in the fallopian tubes where they can do imaging below the surfaces to a depth of about a millimeter, several times the width of a human hair (up to 250 microns), with noninvasive optical coherence tomography, or OCT.

In the past, technology could only take white light images on the surface.

"We are now going to create images as your eye would see if it could get in there," Barton said.

In addition to OCT, Barton's wandlike microendoscope uses fluorescence imaging and multiphoton microscopy.

Multiphoton microscopy is a "great example" of Barton's future goals. "People started out doing multiphoton microscopy with a titanium-sapphire laser (or Ti:sapphs, in the 200 nm bandwidth, for the wavelength of 700 to 900 nm). They were expensive, still are. And when they first came out, you had to have a laser tech there always, to keep the laser running."

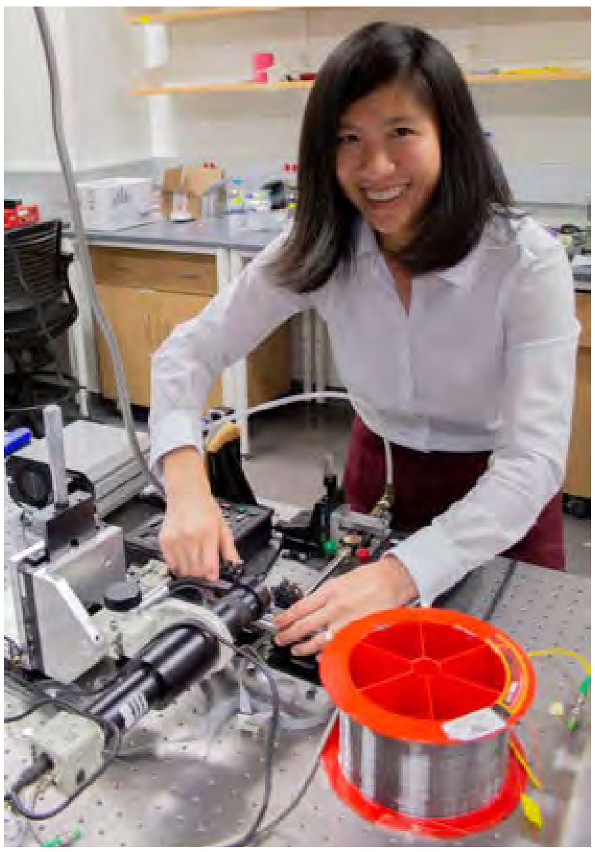
"Today, the market offers a shoebox size fiber laser that puts out the needed femtosecond pulses that you need for multiphoton microscopy. It's just a little turnkey shoebox with a fiber coming out that you can plug into your endoscopes."

Her lab is now manufacturing endoscopes between 0.8 and 3 millimeters in diameter. "Which gets you into just about all the holes in the body," Barton said.

In the years ahead, her goals are to make such procedures simple enough to be done in an office. "My big themes," she says, "are tiny, portable and inexpensive."

Her own technology, which Barton said is still about seven years away from becoming a market product, will add capability to look for cancer below a surface with OCT, and to look at cell functions and metabolism with fluorescence, and to look at cell structure with microscopy. "We are adding a great deal of extra capability to what the medical community has had in the past."

Jennifer Barton in the lab at BIO5, University of Arizona. Credit: Deanna Sanchez.



Judy Su of BIO5, whose group is putting photonics technology into a biosensor. Credit: BIO5, University of Arizona.

Microscopy

BIO5 is responding to stepped up market demand for improved contrast agents for human cells.

"If you wanted to have a contrast agent that targeted, say, cancerous cells, there's nothing approved right now," Barton said.

"A lot of FDA approved drugs happen to fluoresce and the drugs are highly targeted," Barton said, "and BIO5 is working on using microdoses of an approved drug, ones that have no therapeutic effect, as a contrast agent."

Because skin cancer is a particularly big deal in Southern Arizona, BIO5 has a strong skin cancer-imaging program.

Its labs are looking at how to use tissue optics to diagnose skin cancer, which often involves taking a biopsy. "How can you diagnose skin cancer without having to take a biopsy?" Barton said. "Melanoma of course is the killer, but how do we figure out the hallmarks of whether tissue is benign vs. a melanoma?" BIO5 also studies how to treat the cancers with photodynamic therapy. Work done by Clara Curiel, a dermatology professor, centers on diagnosis and treatment for squamous cells and basal cells, which represent a huge public health cost burden in Arizona and Australia.

Optogenetics

"If you do optogenetics, you need some way of delivering the light to the optogenetically encoded cells," Barton said. A BIO5 biomedical scientist studies just that. He's Philipp Gutruf, who has invented soft miniature tools, without batteries or wires, which use oxide based stretchable sensors and photonics.

"You often see pictures of experiments with rats or mice with this big thing coming out of their head, tethered to a cable that goes back to the laser," Barton said. "That's not very realistic. You don't get normal behavior. How can we make microelectronics that harvest the body's own motion for power? Or use very low power LEDs?"

"That's another whole area where BIO5 is going," Barton said.

Overall, BIO5's 180,000 square foot Keating Bioresearch Building, which opened in 2006, houses some 40 PI's and labs, and its new 150,000 square foot, $107 million Bioscience Research Laboratories, which opened last year, houses about 50 PI's and labs with nearly 400 researchers, including about seven grad students per lab.

Business focus in 2020

This year, PW will have an expanded entrepreneurship track. "They are doing a really good job," Barton said, "of bringing the medical device industry together with investigators like myself who are developing new devices, and talking about how you commercialize, how you define your markets, and get FDA approval."

"What I'm most excited about is that this whole series on industry and entrepreneurship basically goes all day. It's almost a parallel track to the scientific sessions," Barton said. "I need to split myself into thirds, so one third can go to the industry and entrepreneurship track, so I can learn how to take my devices and turn them into a successful product, which is something we don't learn in school.

"Then I need another clone of me to spend all day long in the technical sessions," Barton said. She would start with the new conference called "Biophotonics and Exercise Science: Sports Medicine, Health Monitoring Technologies and Wearables."

Overall, for the decade ahead Barton predicts "an explosion of new technologies coming on the market. I think we are finally there in terms of products that are truly useful, can truly help patients, and are inexpensive enough to have good market penetration. That's the difference between the $100,000 device for confocal microscopy and the $5,000 device."

FORD BURKHART

Free-space optics beginning to achieve real-world value

Free-space optical technologies continue to occupy a position at the cutting-edge of global communication systems – and their importance looks set to continue growing.

The key recent trends and themes in the development of FSOC technology over the past year or so have been efforts focused on "moving out of the lab and into practice." In Kane's view, the RF spectrum is "limited and already crowded, and there's only going to be more demand as 5G expands and the Internet-of-Things takes off," according to Tim Kane, Professor of Electrical Engineering at Pennsylvania State University

"Free-space optical communications will never replace RF, of course, but will serve in a complimentary position, especially in RF crowded or denied environments. This will be enabled by continuing improvements in FSO communication rates, reliability and adaptive network design," he says.

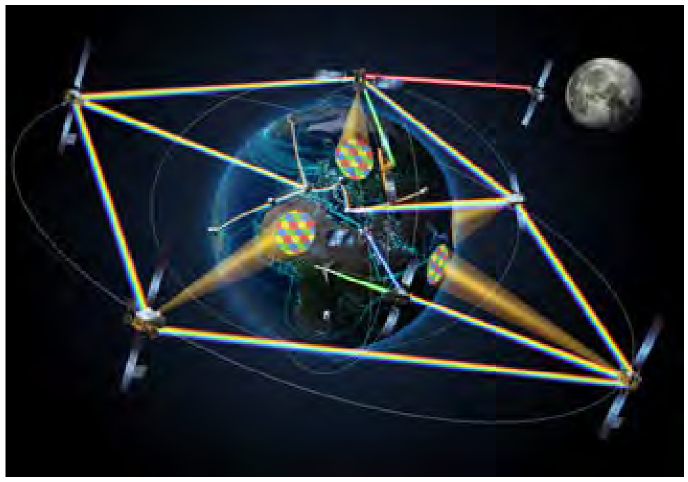
This week, Kane is presenting the results of his teams' work on acquisition, tracking and pointing for reconfigurable free space optical communication systems in RF challenged environments [LASE poster session this evening, Tuesday]. As he explains, some of the teams' current work applies real-time image recognition and tracking to the estimation of relative position and heading between optical transceivers in the 10s of meters range.

"The primary challenge is in reducing latency – that is, how long it takes to lock-on and communicate, while retaining reliability. We are beginning to explore applications in vehicle-to-everything (V2X) communication, robotic navigation, as well as undersea. In the future, satellite-to-satellite comms is an exciting and crucial area of interest," he says.

As part of this work, Kane's team has custom built its own transceivers, supplemented with image tracking using COTS (Commercial-Off-the Shelf) components and algorithm development, as well as MEMS-based fine-tuned beam steering mirror arrays.

Looking ahead, Kane also predicts a number of key innovations and trends in the development of free space optics communication systems over the coming few years. In particular, he argues that, at the most basic level, several key innovations must include the development of high-precision low-latency pointing, acquisition and tracking systems and low-cost, high-reliability optical transceivers, as well as advanced modulation and coding schemes and advanced FSO network topologies.

"The latter two, especially, are necessary for improved capabilities in turbid environments – think haze or fog – as well as intelligently integrating into existing RF networks," he adds.



The proposed Hydron program at the European Space Agency.
Image: ESA

Crowded space

Elsewhere, Jim McNally, Vice President for Strategic Development at Applied Technology Associates (ATA), observes that the key recent developments in this space have been advances in solid state lasers and commercial fibre-optic communications hardware, as well as the development of lower cost, high-speed rad-hard ADCs, DACs, and rad-hard FPGAs.

"The community is developing SW-based modems and the continued development of these over the past few years has really been enabling for small, highly-capable FSOs. Market pull has driven the industry to mature the needed technologies for widespread implementation of FSOC. There are planned large LEO constellations requiring communications links between each platform," he says.

Meanwhile, McNally's colleague, John Garnham, reveals that the issues caused by 'spectrum contention' as the RF communications spectrum continues to get more and more crowded, as well as the 'insatiable demand from consumers for more and more bandwidth,' are also driving the industry towards FSOC.

Both Garnham and McNally have recently been engaged in work on the use of position and time information via FSOC. As part of this work, ATA has employed advanced platform stabilization technologies and detection techniques for its cutting edge FSOC terminals – as well as advanced laser beam stabilization and tracking technologies that permit small size, weight and power terminals to be employed.

McNally predicts two different major trends. The first is small, low-cost cross-links between satellites (or UAVs) for moderate data transfer and command and control, with a large emphasis on small and low-cost, which will require the implementation of photonic integrated circuit technologies for the terminals and overcoming challenges relating to the need to develop rad-hard optical amplifiers. The second is large, very high throughput FSO links to act as major feeder links for geosynchronous communications satellites.

"The challenges for the wide implementation of FSOC terminals for GEO backhaul communications constellations will be to drive the costs of the terminals down," adds McNally.

Meanwhile, Zoran Sodnik, Head of the Opto-Electronics Section: TEC-MME at the European Space Agency, reveals that the main recent trends in FSOC, at least at ESA, are: cost efficient optical terminals for inter-satellite communication in

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Free-space optics continued from page 27

constellations, small direct-to-ground optical communication terminals for Cubesats, optical feeder-link technologies for terabit data rates, quantum key distribution from LEO (and GEO), cost-efficient optical ground stations and networks, PICs and technologies, standardisation of optical communication technologies.

"My section deals with the development of optical communication and quantum key distribution systems and their testing and commissioning once launched. To do so we run ESA's optical ground station in Tenerife," says Sodnik. "The European Data Relay System (EDRS) also runs the only commercial optical inter-satellite link worldwide."

Generally speaking, Sodnik believes that space-based optical communication is "ideal" because of the absence of clouds and atmospheric turbulence and, in order to exploit these advantages, EDRS is using a coherent modulation scheme at a wavelength of 1064 nm. ESA is also developing optical communication technologies in the 1550 nm wavelength spectral band.

Zoran Sodnik in his office at the European Space Agency. Image: ESA

Looking ahead, Sodnik predicts that the key trends moving forward are "clearly the development of reliable links through atmospheric turbulence and efficient switch over between optical ground stations in case one is clouded over."

Elsewhere, Prof. Manijeh Razeghi, Director of the Center for Quantum Devices at Northwestern University, observes that one of the benefits of research in free space communications is the fact there are "so many ways to tackle the same problem." From her perspective, current themes in the development of free space optics technology are split into two key foci: the communications system and the solid-state engineering behind the laser and detector.

"The work on communication systems seeks to maximize symbol rate in a given frequency window and apply high order modulation formats. The optics work is focused on atmospheric attenuation, spatial multiplexing, and the potential of MWIR and LWIR frequencies," she says.

Some of the other trends Prof. Razeghi has noticed are spatial multiplexing, MIMO systems to mitigate atmospheric effects, and a shift in focus "towards novel modulation techniques rather than increasing system speeds."

In Razeghi's view, the uniqueness of the development of high-speed free-space optical communications stems from "a desire to minimize the atmospheric loss due to carbon dioxide absorption," which "can be done by shifting the operating wavelength from the 1.55 µm to 1.6 µm window, where the majority of commercial FSOC systems operate, to the mid-infrared." In an effort to achieve this, she and her team have focused on the development of high-speed free-space optical communications based on quantum cascade lasers and type-II superlattice detectors.

Team member Emily Dial, an undergraduate student at Northwestern University, explains, "Quantum cascade lasers are a promising technology with the flexibility for application in numerous FSOC system types. They offer room-temperature continuous wave operation, high output power, intrinsic robustness against optical feedback, and large modulation bandwidth. Type-II superlattice materials, commonly used for imaging, are also capable of being effective detectors for FSOC systems."

"Mercury cadmium telluride detectors are currently the prevailing technology; while promising, they have large dark currents and require cooling. T2SL detectors have lower dark current and can operate uncooled. The design, fabrication, and implementation of these innovative quantum devices has allowed the CQD to produce high-speed MWIR free-space communications," she adds.

Infrared advantage

In Razeghi's view, the uniqueness of this system is that it operates in the mid-infrared, taking advantage of the atmospheric window, where scattering due to carbon dioxide is decreased – a feat the team accomplishes by utilizing the CQD's quantum cascade lasers and type-II superlattice photodetectors. An FPGA also receives a data stream and encodes it with Manchester encryption, before sending the data to a PCB laser driver that directly modulates the QCL, transmitting a continuous bit stream. A single aspheric lens is then used to collimate the QCL beam. After passing through a Fresnel lens atop a T2SL photodetector, the data is decoded via FPGA and sent to a computer for viewing.

Rendering of the SOCOM CubeSat from the team at ATA. Image: ATA.

"FSOC technologies are useful for their high security, high bandwidth, and portability. For example, a university or business located in a metropolitan area that desires a secure, high speed communication link between buildings may employ an FSOC system, as it requires much less infrastructure to set up than a fibre optic link at comparative speeds," says team member Stephen Johnson, also an student at Northwestern.

"The security aspect of FSOC is especially useful for military applications, for, due to the point-to-point nature of the technology, the beam cannot be intercepted without a loss of power at the receiving end. And as autonomous vehicles and satellite communications increase in ubiquity, the need to communicate rapidly through free space creates a need for robust FSOC technologies," he adds.

Looking ahead, Razeghi points to "many exciting areas of research" in the field of free-space communications, with potential innovations tending to fall into either increasing the speed and/or the distance of the FSOC link. As RF and fibre communication speeds increase, in parallel, she reveals that FSOC technologists are also beginning to push toward terahertz operation, a feat he points out will require 'novel encoding schemes, modulation techniques, and high-speed nanotechnologies.

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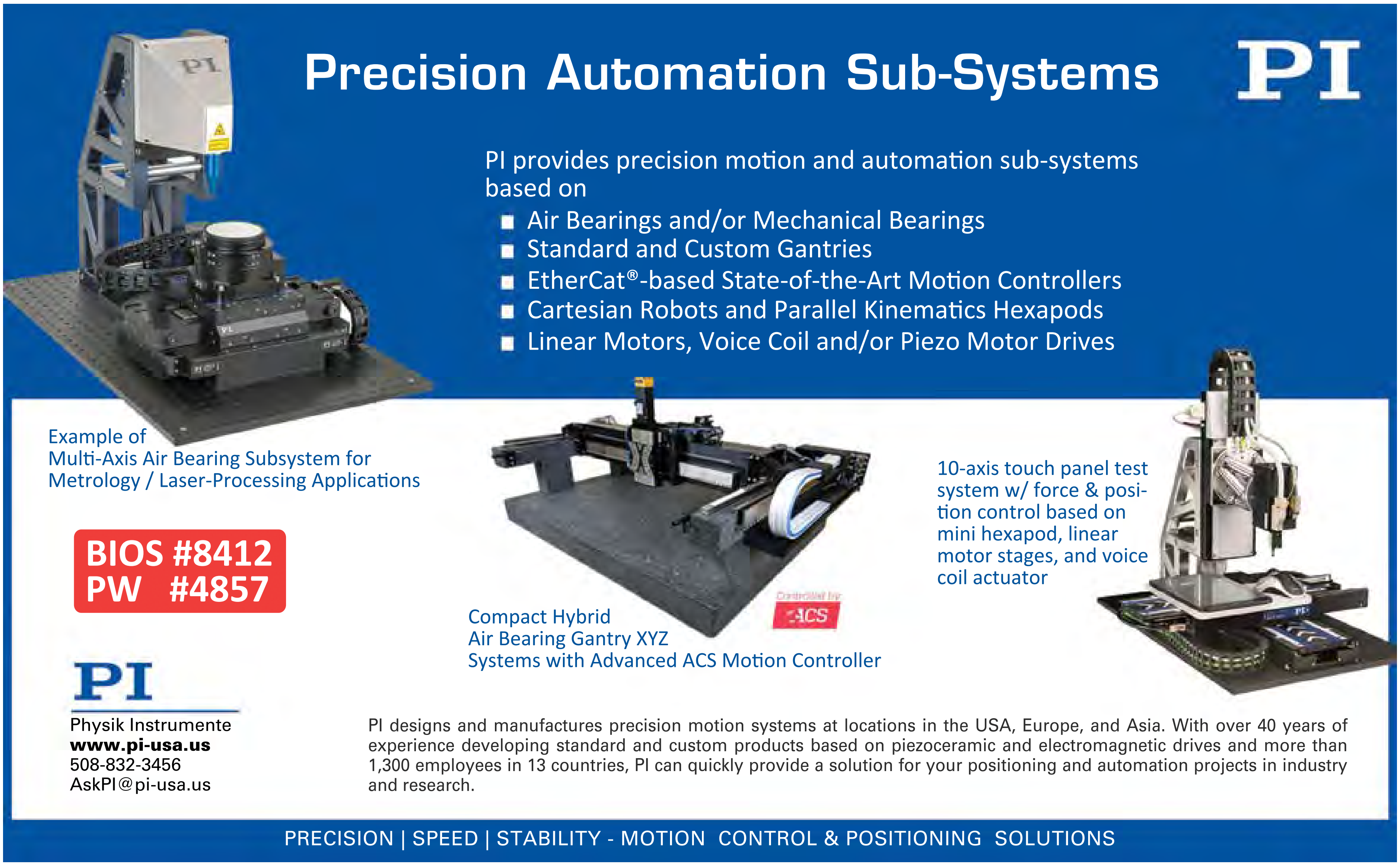
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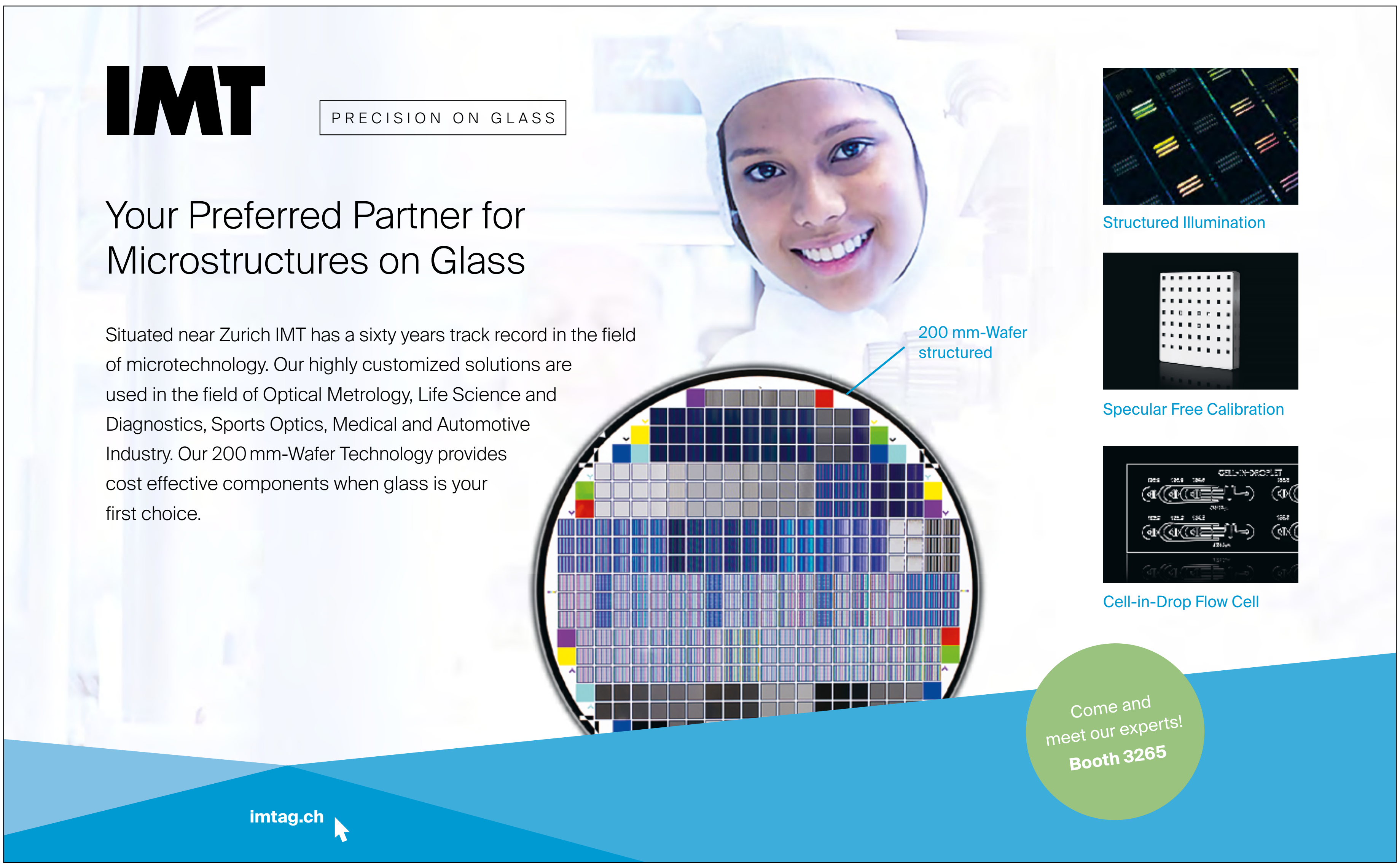
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Light-scattering technologies ready to make clinical impact

Adam Wax co-chaired the milestone tenth BiOS conference on biomedical applications of light scattering, which, he says, could include cancer diagnosis and neural imaging.

Adam Wax: "We deliver low-cost biomedical imaging and make it more accessible."

Scattering of light can be problematic in many imaging scenarios, but also offers the ability to characterize biological tissues in ways that either cannot be achieved by direct optical imaging, or not carried out to the same resolution. This makes it a potentially disruptive technology for cancer diagnosis and other biomedical challenges.

Adam Wax of Duke University, who is co-chairing the tenth BiOS conference on Biomedical Applications of Light Scattering alongside Vadim Backman from Northwestern University, believes that the field is now thriving, thanks to a combination of smart technological innovation and an increasingly smooth path for translation into clinics.

"It really shows the staying power and strength of interest in biomedical applications of light scattering that we have got to a tenth meeting on the topic," commented Wax. "We had a hiatus for a couple of years, but have brought it back for 2020 to discuss some of the most significant current work in the field."

Like many of the early researchers into biomedical light scattering, Wax initially became interested in the technique's potential to detect and characterize cancerous tumors, after initial clinical trials in the late 2000s showed that the early stages of the disease could be identified in this way.

Subsequent studies have honed the technology into a versatile means of gathering information about other forms of tissue as well, often exploiting the improved signal-to-noise ratio that can result when the angular distribution and scatter of light returning from a target is detected, rather than the smaller number of directly returned photons.

Some of these breakthroughs were featured in previous BiOS Hot Topics sessions as promising concepts, before now returning for discussion in the dedicated BiOS conference stream as diagnostic techniques, poised to make a clinical impact.

Among a high-caliber conference program, Wax highlighted a presentation by Paul Campagnola from the University of Wisconsin-Madison, describing optical methods to distinguish between healthy and diseased tissue through the combination of scatter and second harmonic generation emission. This could be valuable in the diagnosis of ovarian cancer, pulmonary fibrosis and osteoarthritis.

Another significant paper concerning cancer detection comes from Quing Zhu and Yifeng Zeng of Washington University in St Louis, who used OCT to reveal scattering signatures of human colorectal and ovarian tissues, for quantitative classification of both normal and malignant processes underway in the cells.

A third area of innovation involves the use of light-scattering techniques to study neural structures and brain behavior—a highly significant use for the technology, according to Wax.

"We have Daniel Palanker from Stanford University discussing interferometric imaging of neural activity, and how cellular deformations associated with changes of cell potential can reveal underlying physiological activity," he said.

"And Erin Buckley from Emory University has combined diffuse correlation spectroscopy with more traditional near-IR approaches, to visualize cognitive dysfunction after brain injury. This is very timely, in view of the current debate about how to effectively classify head injuries suffered during competitive sports, and preferably do so right there on the field of play."

Making technology widely available at lower cost

These research breakthroughs will need as smooth a translation as possible from laboratory to clinic, if their potential is to be fully realized, and Adam Wax believes that the path is becoming increasingly well understood, both by researchers and those in control of the funding mechanisms involved.

"After the initial clinical studies in the early 2010s, people were naturally excited to bring these to clinic," he said. "But some of the FDA regulatory approvals at the time proved to be difficult, and VCs had to be approached for substantial sums of money. Today we see a much more receptive FDA, which is turn makes the market more receptive to the idea of funding new technologies. You no longer need to raise millions of dollars to bring something new to market."

> Lumedica has developed a small ocular OCT scanner with a low cost and user-friendly design compared to conventional clinical OCT devices.

The US Small Business Innovation Research (SBIR) program, along with other governmental grant operations, has been particularly significant in reducing the sums of seed capital needed to develop devices for trials. Wax has personal experience of this improved climate through his position as co-founder and chief scientist at Lumedica, a 2014 spin-out from Duke University's Biomedical Interferometry Optics & Spectroscopy Lab.

Lumedica has developed a small ocular OCT scanner with a relatively low price point and a robust user-friendly design, compared to conventional large clinical OCT devices. The intention is to allow OCT to reach more patients in areas where access to clinical care may be limited, including several low-resource settings. The company exploited advances in 3D printing to design a device where the effects of expansion and contraction are carefully controlled, while keeping both cost and weight as low as possible.

"Our approach was to deliver low-cost biomedical imaging equipment to market and to make it more accessible, by adopting technology likely to be readily FDA approved and designing a device that was lightweight, robust and portable," noted Wax, who sees a parallel between the changed climate for innovation that has benefited Lumedica and that now available to developers of light-scattering technologies.

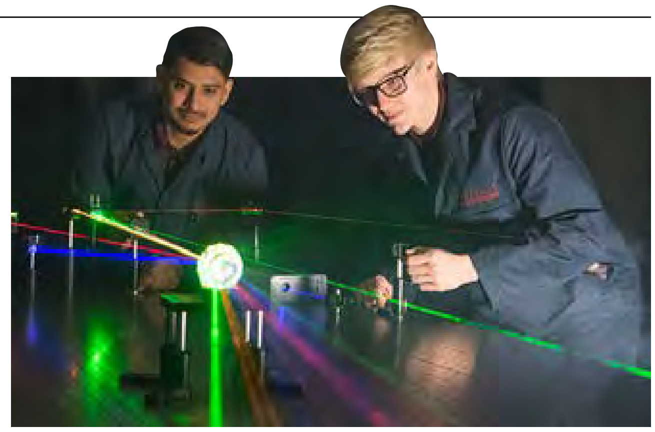
"For this field I would like to see the same kind of process, where we take these great technical advances by cutting-edge researchers, and enable them to become more broadly accessible. That might mean using 3D printing to help manufacture the relevant instrumentation, or perhaps new forms of fiber-optic probes used by the device. But the opportunity is there is to make these light-scattering technologies widely available at lower cost. Being able to deliver new technologies to market without multi-million-dollar VC investments and in devices costing perhaps hundreds, rather than thousands, of dollars would enable the technology to take leaps and bounds towards clinical translation."

In the meantime, SPIE Photonics West events such as the Startup Challenge, in which Wax competed in the past, along with the multi-disciplinary nature of the BIOS conference, will continue to spark the kind of connections through which the technology can progress.

"Advances are made when good researchers spot new technologies and see how their own projects might benefit," commented Wax. "Putting those ideas in front of people is the start of the whole ecosystem. And as a biomedical engineer, it's great when we can transcend the optics journals and reach the medical community. When we have the doctors talking about these light-scattering optical techniques, that is really exciting for me."

TIM HAYES

Industry event seeks to increase new-collar technician pipeline



In demand: lab technicians are the bedrock of our industry. Credit: Indian Hills Community College

Optical technicians and electrical engineers today are often referred to as new-collar workers. Their jobs bear little resemblance to the industrial assembly line manufacturing jobs of sixty years ago, because they are often skilled, rewarding, and well paid, with opportunities for advancement and continued training. But getting the word out about these technical career paths is a challenge.

Alexis Vogt, endowed chair and associate professor of optics at Monroe Community College Vogt advocates for parents and high school guidance counselors to encourage students and make optics part of student vocabulary. "The biggest obstacle is getting the word out," she says. "No high schooler is thinking 'I'm going to be an optics technician.'"

Vogt will be among a group of representatives at "Optics and Photonics Technician Shortage: Solutions and Opportunities," on Tuesday, February 4 at 5:15pm. This happy hour industry networking event will bring together employers interested in increasing the number of technicians in the pipeline and colleges with technician training programs.

Three speakers will open the session with short presentations on activities at their respective institutions that have successfully increased the technician pool.

Jim VanKouwenberg, training coordinator at Optimax, will discuss his company's high school and internship programs that include summer camps and other outreach programs.

Norman Hodgson, vice president for technology and advanced research at Coherent, will tell the audience how Coherent partners with the Laser Technology Program at San Jose City College where they help design the curriculum and donate equipment, such as breadboards and laser systems.

Trent Berg, president of the Montana Photonics Industry Alliance (MPIA), will discuss how the MPIA has worked to build a regional technician pipeline and student interest in the program.

The message about the technician shortage is not just aimed at high school and college students. The tech industry is also open to adults considering a career change, including veterans and immigrants, who would find a career as an optics and photonics technician an attainable option.

After the presentations, college representatives and technician program instructors will be available at information tables to network with participants. If your company is finding it difficult to hire technicians, come and learn from the success of others and help trainers and educators understand your needs.

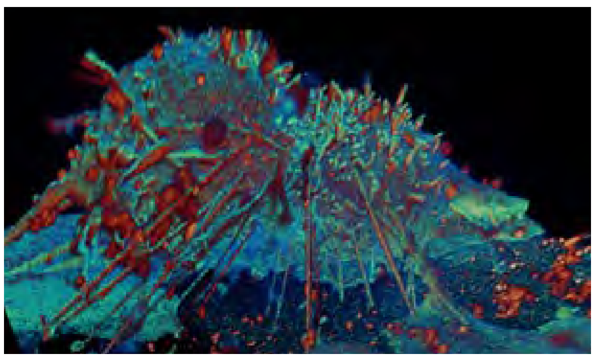
5:15 – 6:30 pm Marriott Marquis Golden Gate C

KAREN THOMAS

Betzig continued from page 01

to play a bigger role in in biology."

Betzig's work in this role in the 80s and 90s led to the 2014 Nobel Prize "for the development of super-resolved fluorescence microscopy," which he shared with Stefan Hell and William E. Moerner. Not one to sit back after recognition, Betzig is currently a Senior Fellow at the Howard Hughes Medical Institute's (HHMI), Janelia Farm Research Campus and a faculty scientist at University of California at Berkeley.



3D high-density localization microscopy. Credit: Betzig Lab

Journey to PALM

Betzig's career has three stages – the first began with near-field microscopy, which he began working on in 1982 as a graduate student at Cornell. By 1992, he had his own lab at Bell Laboratories where he built a near-field microscope, that he says was too slow and difficult to use. Frustrated with the project, Betzig quit Bell Labs in 1994. For the next eight years, he worked as vice president of R&D in his father's machine tool company where he developed a high-speed motion-control technology based on an electrohydraulic hybrid drive with adaptive control algorithms. The technology was a commercial failure, so he left the business. "You'll learn a hell of a lot more from a failure then you do from a success," said Betzig. "All my failures shaped my career. So, pain is the best teacher."

After a couple of months as a stay-at-home dad, inspiration for making his microscope finally work came as he was pushing his child's stroller. He and former Bell colleague Harald Hess worked on the concept of using stochastic photoactivation instead of color to isolate molecules. Their work led to the super-resolution technique of photoactivated localization microscopy (PALM).

"We were both unemployed, so we built it in Harold's living room," said Betzig "Since we knew zero biology, we contacted Jennifer Lippincott-Schwartz at NIH who had invented a photo-activatable fluorescent protein. Within a month of working with her, we improved the resolution."

As Betzig explained to *Show Daily*, even though the round, diffraction-limited spot representing the image of a single fluorescent molecule in a conventional optical microscope is 100 times larger than the molecule itself, it is possible to point to the center of the spot with much better precision than its diameter. The problem is that in most biological samples, the fluorescent molecules are so closely packed that their diffraction-limited images overlap, making it impossible to isolate each and localize their centers.

The trick in PALM is to use special molecules to tag the proteins of interest that can be "turned on" from a non-fluorescent state to a fluorescent one with a second color of "activating" light. By reducing the intensity of the activating light to a very low level, only a few molecules will be active at a given time.

This active subset will likely be well separated from others, and hence can be precisely localized to a small fraction of the diffraction limit (~10-20 nm). The active subset is turned off, and the cycle is repeated until most of the molecules in the sample are precisely located, creating the super-resolution PALM image.

It's a simple enough technique," says Betzig. "You can get 20 nanometer resolution in your living room, so as a result it took off very quickly and eventually led to Stockholm, to my still great surprise."

KAREN THOMAS

SPIE endowment continued from page 01

CREOL. "We are pleased to partner with SPIE and UCF CREOL to create an enduring scholarship for graduate students in the exciting field of optics and photonics," said Glebov. "Together, we are investing in new opportunities for talented young people, because talent does not correlate with the ability to pay for an education."

"With the matching funds from SPIE, the Glebov family's gift creates a fully endowed scholarship for our graduate students. The scholarship will have immediate impact for our current students and will help us recruit the brightest minds in optics and photonics. SPIE's support magnifies the impact of the gift," said Dr. David Hagan, Interim Dean of UCF CREOL.

The SPIE Endowment Matching Program, established in 2019, is a $2.5 million, five-year, educational-funding initiative designed to increase international capacity in the teaching and research of optics and photonics. SPIE supports optics and photonics education and the future of the industry by contributing up to

Donors: Alexei and Leonid Glebov. Credit: UCF

$500,000 per award to college and university programs with optics and photonics degrees, or with other disciplines allied to the SPIE mission. The initial SPIE contribution to the University of Arizona named a new endowed faculty chair, the SPIE Chair in Optical Sciences.

This program is in addition to over $5,000,000 provided in 2019 by SPIE to community support including scholarships and awards, outreach, travel grants, public policy, and educational resources.

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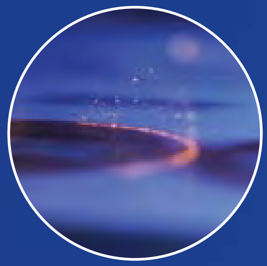
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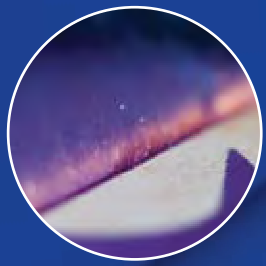
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