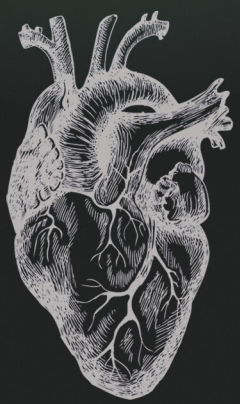
SPIE. Professional
October–December 2019



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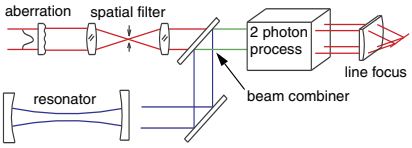

GLAD uses a general description of intensity and phase to perform full diffraction propagation through the most complex systems including detailed treatment of laser gain, nonlinear optics, stable or unstable resonators, diffractive optics, waveguides, fibers and coupling, fiber lasers, photolithography, excimers, optical integrators, etc.

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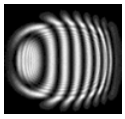
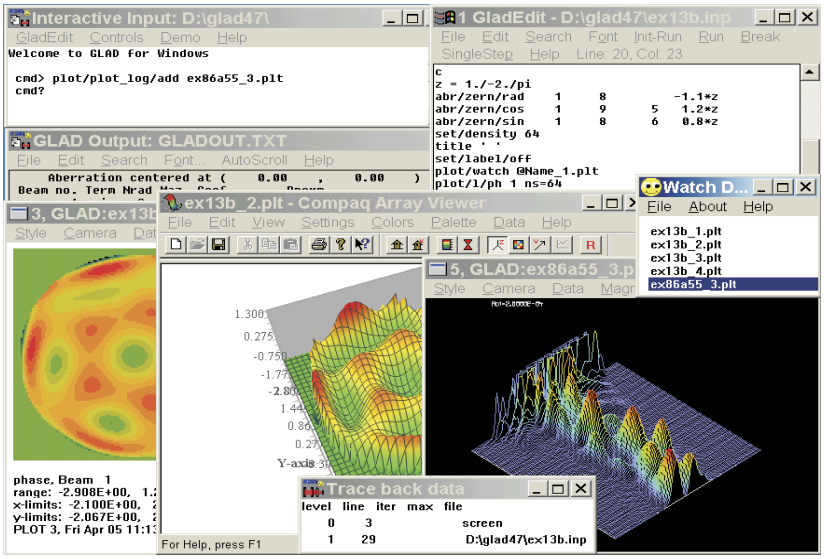
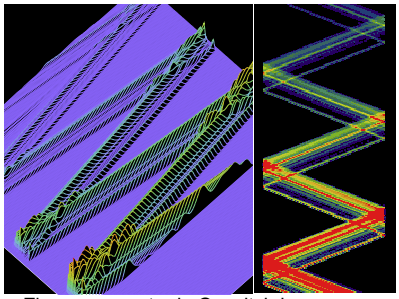
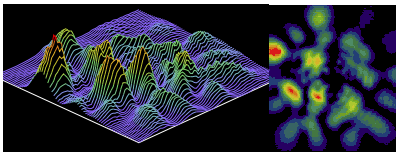


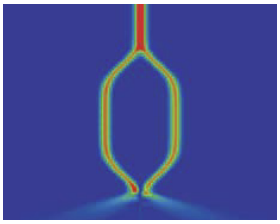




Zigzag resonator in Q-switch laser showing amplification from top to bottom and self-interference at side mirrors.



Transient Q-switch laser mode at 2ns



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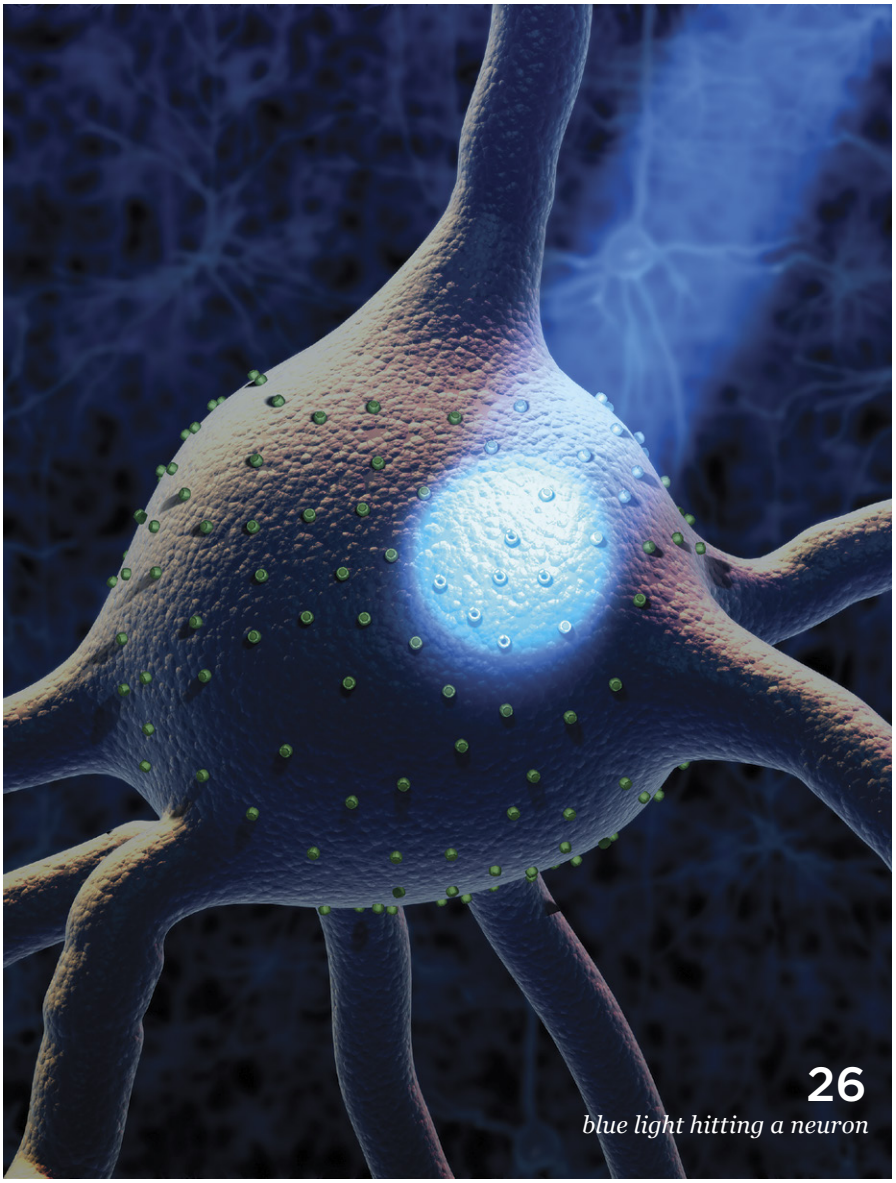
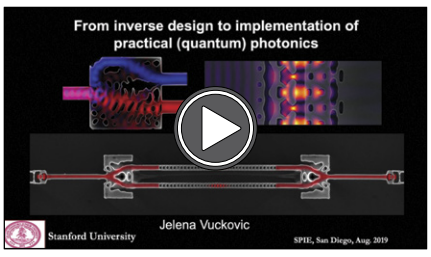


26
blue light hitting a neuron

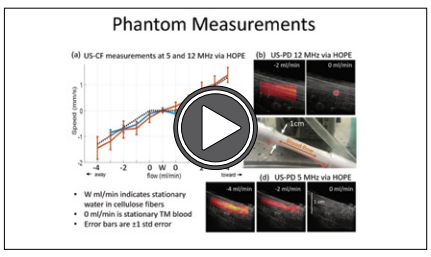
Credit: NASA

FEATURES

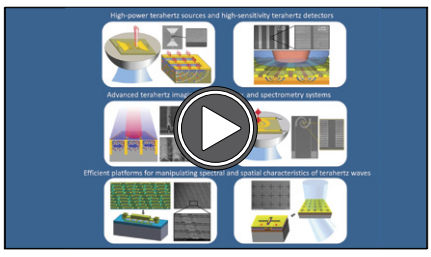
ONLINE OPTICS + PHOTONICS 2019 PLENARY RECORDINGS ON THE SPIE DIGITAL LIBRARY



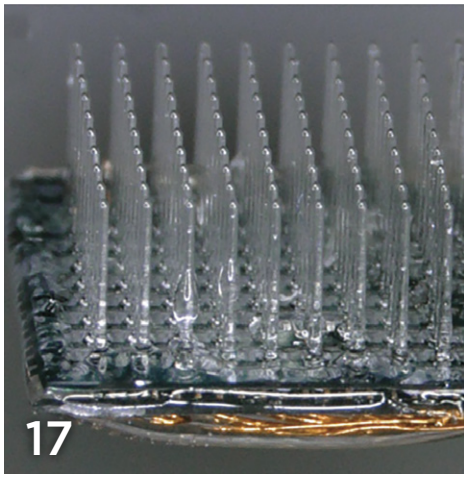
From inverse design to implementation of practical (quantum) photonics
Jelena Vuckovic
» spie.org/OP19_DL1



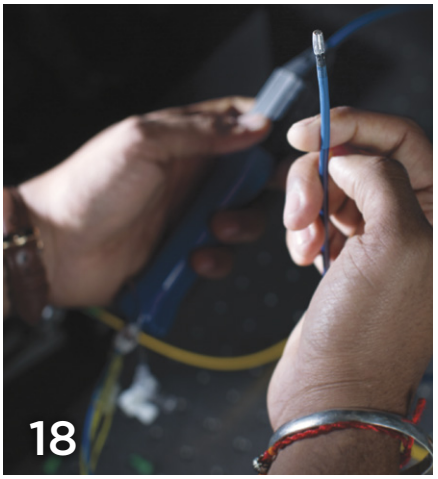
Exploiting data sparsity to enhance sensitivity in medical images
Michael F. Insana
» spie.org/OP19_DL2



Plasmonics-enhanced terahertz spectroscopy
Mona Jarrahi
» spie.org/OP19_DL3



Credit: Niall McAlinden



Credit: Christine Hendon, Columbia University

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SPIE Professional publishes stories about people and technology in the optics and photonics community. Stories should be engaging, creative, and noncommercial in nature. If you have a story idea that you would like to be considered for publication, please write a query letter containing a one-paragraph abstract of your proposed topic. Send the query and a one-page writing sample to **spieprofessional@spie.org**.

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ON THE COVER
Faces, Gettyimages; heart, brain, eye, Shutterstock.

Progress Includes Partnerships

In this final 2019 issue of *SPIE Professional* and the last quarter of my SPIE presidency, I'd like to highlight some of the many accomplishments we made this year. A key part of our effort includes collaboration and partnering to more fully achieve our mission and make a difference in the world. This year, we formed new partnerships with other organizations to leverage our mutual strengths and amplify our thoughts and ideas through our combined voices. I endeavor to give some concrete examples herein.

In the area of contractually expanded partnerships, two important examples come to mind. At the start of the year, we rolled out the BioOne Digital Library, which is built on the same platform as the SPIE Digital Library. This platform provides a very capable system that serves 15 publishers in the biology community, while our partner's contributions fund a portion of our Digital Library costs. SPIE has also benefitted from new ideas to improve our own digital platform and better serve our optics and photonics community as a result of the BioOne collaboration.

In June of this year, we announced that SPIE will acquire Xmark Media, organizer of photonics exhibitions and conferences in the United Kingdom (UK), including Photonex, the UK's largest optics and photonics exhibit. This combination will improve SPIE's service to the UK photonics community, and will allow us to provide more support to UK advocacy and industry groups working to promote our field.

In January, SPIE and the Australian Optical Society (AOS) agreed to merge two of our meetings that take place every other year in the same part of the world and at the same time. The new combined meeting is being run by SPIE for the AOS and takes on the AOS name, Australian New Zealand Conference on Optics and Photonics (ANZCOP) with SPIE and AOS conferences underneath. Topics covering biophotonics and astronomy are also being added to this event.

We also signed a new MOU with the Optical Society of Japan (OSJ) providing support for awards, leadership presence (at both OSJ and SPIE events), and agreement to find other collaborative activities of benefit to our communities. We are working on updates to similar agreements with other optical societies.

Previously developed work continued between The Optical Society (OSA), SPIE, and other groups in the areas of outreach, advocacy, and policies, such as:

- Joint SPIE/OSA Code of Conduct, which rolled out at all meetings in 2019
- OSA/SPIE Harassment Survey
- Continued multi-society support of the International Day of Light
- Continued support for the National Photonics Initiative.
- Arthur H. Guenther Congressional Fellowship
- Joseph W Goodman Book Writing Award
- Optics Education Directory

Building upon these collaborative efforts, we began a recurring "Meeting of the Optical Societies" gathering at venues where representatives of many other optics and photonics societies are in attendance. This year, SPIE hosted two such meetings with societies from around the world at SPIE Photonics West and the World of Photonics trade show. Ten societies were represented. We discussed issues from each country's perspective, shared examples of how we might help each other, and where we may collaborate. We discussed the OSA/SPIE Code of Conduct, the International Day of Light, and shared policy information that may help others. The intent is to find areas where our collective voices are aligned and can make a larger positive impact in our communities.

Lastly, leveraging upon our history of giving back to the community, we announced a $2.5 million program over the next five years to fund SPIE-named endowments such as scholarships, chairs, etc. at universities or like organizations that can match and manage these funds to provide support in perpetuity for educational purposes. The first recipient of funds from this new program was announced at SPIE Optics + Photonics 2019: The SPIE Endowed Chair in Optical Sciences at the University of Arizona (UA). SPIE donated $500,000 to the UA, which is being matched with $1.5 million from Jim Wyant (a 3:1 match), providing for this $2 million SPIE Endowed Chair of Optics and Photonics that will help fund top professors at the Wyant College of Optical Sciences in perpetuity.

As you can see we have had a very busy and fulfilling year, far beyond the usual exciting meetings, events, and publications! Still, there is much work to do and areas we need to improve. For example, we are increasing our efforts in diversity and inclusion. To show our commitment, SPIE appointed Allison Romanyshyn as Chief Inclusion Officer. This is a staff senior director position reporting directly to the SPIE CEO. However, we still need to diversify our pool of speakers, committee members, Fellows, and award nominees, and we hope to collaborate with you, our members, in this effort.

The Society is in great shape and we hope this renewed era of collaboration will better serve the broader community for many years to come.

Jim Oschmann, 2019 SPIE President

Science and Security

Rising Tensions Bring Policy Changes to US Institutions

In response to ongoing concerns regarding foreign scientists' access to critical research and technology being developed in the United States, US agencies are putting forward policy changes that will impact international collaborations.

DEPARTMENT OF ENERGY (DOE)

On 14 December 2018, DOE issued a memorandum titled "Department of Energy International Science and Technology Engagement Policy." The memo lays out a set of immediate changes related to foreign nationals' access to DOE laboratories, including enhanced vetting procedures. The memo also establishes a DOE Federal Oversight Advisory Body that is charged with developing an S&T risk matrix. The purpose of the risk matrix is to identify technology areas of national interest to the US, and to limit access to these technologies by certain individuals from countries deemed "sensitive."

Neither the list of technologies nor which countries would be considered as sensitive was listed in the memo. The memo also states that scientists performing research in a listed technology area from one of the sensitive countries will not be allowed access to DOE laboratories to perform activities regarding those technologies. DOE laboratories receive tens of thousands of foreign visitors a year, a large portion from China.

Additionally, DOE issued a memorandum on 31 January 2019 prohibiting DOE employees, contractors, or those performing work under a DOE grant or cooperative agreement from participation in foreign talent recruitment programs of countries deemed sensitive. The memo also does not specify what countries DOE deems to be sensitive. On 17 June 2019, DOE issued a directive adjusting the scope of the original memo to cover DOE employees and contractors, but plans to issue a separate memo regarding grant recipients.

NATIONAL SCIENCE FOUNDATION (NSF)

On 11 July 2019, NSF Director France Cordova sent out a Dear Colleague letter—an official correspondence between members of US Congress—announcing that NSF is putting forward a policy that prohibits participation in foreign talent recruitment programs by NSF personnel. In addition, the letter states that NSF has commissioned the independent scientific advisory group JASON to conduct a study to assess security risks and make recommendations to NSF on potential policy changes. Their report is expected by end of year.

In addition, NSF published a "Proposal and Award Policies and Procedures Guide" to provide clarity regarding disclosure requirements.

NATIONAL INSTITUTES OF HEALTH (NIH)

The National Institutes of Health sent out a notice on 10 July 2019 titled "Reminders of NIH Policies on Other Support and on Policies related to Financial Conflicts of Interest and Foreign Components." The notice details reporting requirements for "all sources of research support, financial interests and affiliations, both foreign and domestic, and to continue to support properly reported international collaborative research." Though the notice was presented as a clarification of existing policy, many see it as an expansion of NIH reporting requirements.

The notice comes on the heels of increased enforcement of existing NIH reporting requirements for disclosure. NIH concerns have grown out of numerous uncovered violations of the policies for disclosure of foreign ties, which has resulted in the dismissal of several NIH-affiliated scientists.

A DELICATE BALANCE

The difficulty of maintaining a correct balance between open science and national security is not lost on the leaders charged with promulgating these policy changes. In the NSF letter released in July, Director Cordova stated, "International collaboration is essential to pursuing the frontiers of science" and that a "great strength of the US research and engineering enterprise is the diversity of talent—both domestic and international." However, it is hard to deny that the totality of the increased scrutiny by US agencies, as well as the White House and Congress, has many foreign researchers working in the US on edge.

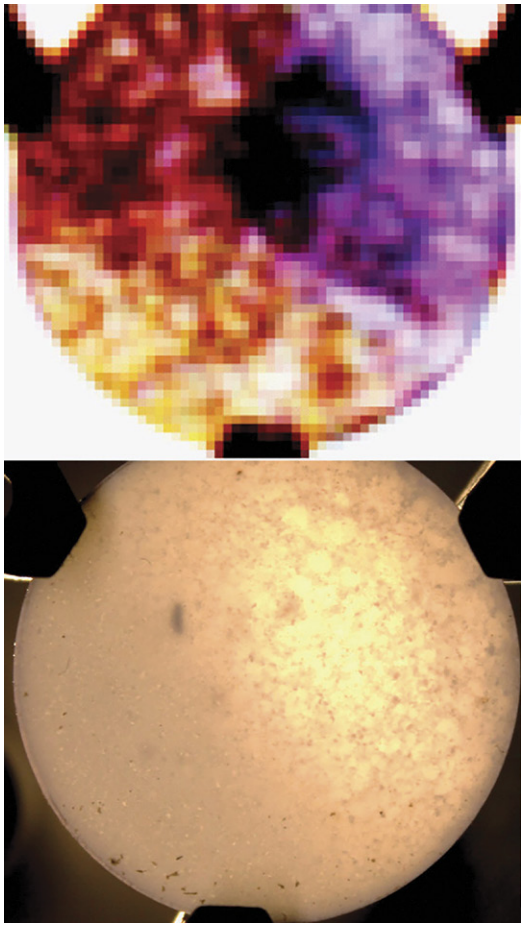
SPIE will continue to represent the optics and photonics community on these matters and serves as a resource to the US government in the ongoing decisions regarding securing scientific research.

SPIE supports policies that allow for the international mobility of scientists. Sharing knowledge and talent through collaboration has been core to scientific breakthroughs for over a century and will continue to be a vital element to innovation across the sciences. ■

–Jennifer Douris O'Bryan *is the SPIE Director of Government Affairs.*

For links to the memos and publications mentioned in this article, please view it online:* ***spie.org/science-security*

Imaging Spectroscopy Sheds New Light on Pill Production



Credit: Sterczewski et al./Optica

A novel terahertz hyperspectral imaging system based on THz quantum cascade lasers rapidly measures the chemical compositions of solids. A conventional image of a sample pill is shown above; below, looking at the same surface with terahertz frequencies reveals various ingredients as different colors. Such images would aid quality control and development in pharmaceutical manufacturing, as well as in medical diagnosis and treatment.

Tablet-based medical therapy dates back to about 1500 BCE, with the earliest pills apparently being made from bread dough, honey, or grease, with active ingredients (such as ground up medicinal plants) mixed in before being formed into little balls that could be swallowed. Today, "pills" have evolved into a sophisticated component of the medical therapeutics tool kit. They come in various types including tablets, capsules, and caplets. Tablets uniquely comprise a diverse set of categories including coated/uncoated tablets, modified and time-release tablets, and soluble, dispersible, chewable, and effervescent tablets. Mass-production of pills has grown into a significant global undertaking, with pharmaceutical giants like AstraZeneca of Cambridge, United Kingdom, producing more than 10 billion tablets and capsules annually.

While it may not be obvious to the outsider, photonics plays a major role in the production of all those tablets. Spectroscopy-based analytical quality control is a critical aspect of tablet manufacturing and is one of the key factors that ensures each unit is safe and effective by the time it reaches the consumer.

There are many analytical tools available to probe pharmaceuticals before, during, and after their manufacture. Most of them are spectroscopic in nature and the choice of method depends on the substances involved and the type of measurement desired. Raman spectroscopy generally outperforms near-IR with inorganic compounds, for instance, while near-IR spectroscopy easily differentiates cellulose and sugar-like compounds that can be difficult to differentiate using Raman spectroscopy.

Conventional pharmaceutical production is generally accomplished using batch processing with laboratory-based analytical testing conducted on samples taken from the production line to evaluate product quality. The testing technologies are often destructive: though tablets taken from a production line may be probed using spectroscopy, destructive testing, such as dropping, cutting, and dissolving the tablet is also involved.

Even for homogeneous tablets (as opposed to time-release or coated tablets), manufacturers must assess whether the correct amount of the active ingredient is present in a specific tablet, and that it is not only uniformly distributed within a tablet but also consistently across multiple tablets in a batch. Further, since most active pharmaceutical ingredients (APIs) are produced by crystallization, the phenomenon of polymorphism, whereby an organic molecule can adopt more than one crystalline form, is also an important aspect of product quality that must be monitored during the manufacture of tablets. The uncontrolled occurrence of multiple physical forms (polymorphs, solvates, salts, co-crystals, or amorphous) of an API can have significant effects on the performance of the medicine.

Several years ago, the US Federal Drug Administration (FDA) noted that the opportunity existed to improve pharmaceutical development and manufacture and released its Process Analytical Technology (PAT) guidance framework for industry. The guidance was intended to encourage the voluntary development and implementation of innovative pharmaceutical development, manufacturing, and quality assurance.

"The FDA has challenged companies to explore innovating and developing more efficient and more effective continuous manufacturing processes and implementing those with various types of looped, online systems where you can employ continuous process control and continuous sensing," explains Doug Kiehl, a Research Advisor at Eli Lilly and Company in Indianapolis, Indiana.

Two relatively recent additions to the spectroscopy toolset are hyperspectral

imaging, and terahertz imaging and spectroscopy. These can provide inline information such as spatial distribution and architecture of active ingredients that complements the compositional, quantitation, and structural determination available from other methods.

Terahertz technology, like hyperspectral imaging, is nondestructive—a key element of inline testing—and can estimate critical quality attributes in pharmaceutical products such as crystalline structure, thickness, and chemical composition. Terahertz systems maker TeraView of Cambridge, United Kingdom, is a leading manufacturer of systems for this market. The company has also produced 3D coating thickness maps for multiple coating layers and structural features models that allow better understanding and control of product scale up and manufacture.

There is, however, no silver bullet, explains TeraView CEO Dr. Don Arnone. "All these techniques are very complementary. What we have discovered with terahertz, or hyperspectral imaging, or Raman, or infrared is that there will be a class of APIs and/or excipients that work well with a certain technology but don't work well with others."

"Hyperspectral imaging is a very powerful technique," he says, "but one of the advantages that [terahertz has] over hyperspectral is that we can see through a complete tablet with a very negligible scattering from an imaging perspective, but from the spectroscopy perspective, that also enables us to get very clear spectra."

"Hyperspectral imaging can do a similar thing, but there will be some materials where it doesn't work well, due to absorption or scattering, and terahertz does work well," he says. There will be other applications where hyperspectral or infrared or indeed Raman techniques actually give you very accurate information, whereas terahertz is more limited."

In the pharmaceutical industry, Kiehl agrees that the physical and chemical attributes of the materials dictate what may work for some processes and might not work for others. "You still may need to implement a separate batch manufacturing process for some steps," he says. "It's case by case. Ideally, whatever is going to be simplest and whatever is going to address the immediate need most economically and most directly while maximizing attention on safety and quality is what's going to be employed," he says.

Arnone highlights two areas of current interest around terahertz spectroscopy. "One is in using terahertz spectroscopy, not to do polymorph detection, but actually to look at the amount of amorphous versus crystalline materials and drugs, and things like drug and API stability."

"If a certain polymorphic form is absorbed by the body—has high bioavailability—if that changes into an amorphous state, or indeed, if it changes into another polymorphic form, another crystalline state, then that actually affects the bioavailability," he explains.

The other area of current interest is tablet disintegration. "If you pass terahertz [radiation] through a tablet and look at the refractive index of the tablet, that refractive index actually correlates with the propensity of the tablet to disintegrate. So what we've got is a potentially very interesting technique for doing inline monitoring of the quality of tablets … whether they will stay intact as they make their way from a blister pack, or whatever the dispensing mechanism is, to the body," Arnone explains.

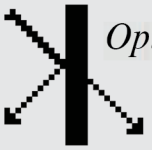
Looking to the future, it's clear that both hyperspectral and terahertz techniques will remain part of the overall landscape of tablet testing. "The key for terahertz," says Arnone, "is to move from being a development technique or tool, to more on the QA side of things."

Both Kiehl and Arnone also note the growing importance of portable and handheld technologies. "They are of very high interest in the pharmaceutical environment," said Kiehl, "because of the convenience and accessibility, especially in places like warehouses and loading docks."

So, while medicinal tablets may be "as old as the hills," the processes involved in making them continue to evolve are, in fact, very modern. As tablet production moves to inline processing to the extent possible, quality assurance protocols are continuously improving. They will likely involve photonics for the foreseeable future as evolving techniques like imaging spectroscopy shed new light on the quality of the end products. ■

***–Stephen G. Anderson** is the SPIE Director of Industry Development.*

TFCalc



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- electric field intensity
- equivalent index
- equivalent stack
- gain materials
- global optimization
- group optimization
- illuminants
- layer sensitivity
- local optimization
- material mixtures
- multiple environments
- needle optimization
- optical monitoring
- optical density
- phase shift
- psi
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How to Construct a Compelling Grant Proposal

Whether pursuing a career in academia or industry, a researcher's success and autonomy hinges upon skillfully crafted funding proposals.

Grant reviewers look for answers to six questions when appraising a proposal:

1. What is the problem the team wants to solve?
2. Why is that problem critical to the funding agency's mission?
3. What solution does the team propose?
4. What is the team's plan to implement or test its proposed solution?
5. Why is the team qualified to implement its plan?
6. How can the funding agency contribute to the project's success?

The most common mistake researchers make is spending too much time answering questions 3 and 6 but not enough time answering questions 2 and 4. To ensure that a proposal completely answers those six questions, follow this ten-step process:

1) **Highlight critical elements within the funding agency's request for proposal (RFP).** Identify everything in the RFP that is a priority for this specific funding opportunity. Some project requirements are expressed directly, but some must be inferred. For example, the agency may mention the importance of undergraduate participation but not mention it in the list of proposal requirements.
2) **Turn every highlighted element into a question.** To ensure that your project completely aligns with the funding agency's interests, create a questionnaire that addresses every highlighted point in the RFP. To extend the previous example, your list should include a question like "How will this project incorporate undergraduate participation?"
3) **Develop a project proposal that answers every question.** Use the questions as prompts to articulate your proposed project. Write thorough answers to every question. The more detailed you are now, the easier it will be to assemble the proposal later.
4) **Call the funding agency if possible.** Most RFPs include contact information for the topic author or expert. It is best to call, rather than email—a personal conversation is more efficient and establishes rapport. Explain your proposed solution and how it addresses the problem, then ask whether the project is, in proposal jargon, "responsive to the RFP." Listen more than you talk. These conversations often reveal unwritten priorities that you should address and will give you an advantage over other applicants.
5) **Create a project plan and schedule.** Create a week-by-week (or minimum month-by-month) schedule for the project. Some US agencies—especially Department of Defense and NASA—expect an enumerated work breakdown structure and an annotated schedule, and some expect only an outline. Regardless of what the agency requires, the process of creating a clear schedule is an essential tool for good project management.
6) **Establish a budget and cost justifications.** Every RFP has different rules for format, content, cost considerations, etc. As a researcher, the important thing is that you review your project plan and articulate what you need, in what time frame, and why. Too often applicants delay creating the budget until last, only to discover that the scope of the project is larger than the budget.
7) **Copy every answer from step 3 into the corresponding section of the proposal.** Find a home for everything to ensure that nothing critical gets lost. Some answers may fit in more than one section, which is fine. Thoughtful repetition will reinforce information.
8) **Make the proposal easy to skim.** Create a sequence of figures that provide a high-level visual explanation of the project. For every figure, write a caption that states the conclusion the reviewer should make. Use bullets, tables, italics, and bold fonts to draw attention to important information.
9) **Fill in gaps and smooth transitions.** The reward for following all of the previous steps is that, in principle, the proposal, though disjointed, is now a complete and thorough rough draft. What follows is a very careful rewrite to improve clarity. Technical writing is a skill that only comes from practice, but books such as Michael Alley's *The Craft of Scientific Writing* can train you to write better, faster.
10) **Proofread.** Grammar, spelling, and punctuation errors are distracting, and the last thing you want is a distracted reviewer. Ask someone not involved in the project to read the proposal.

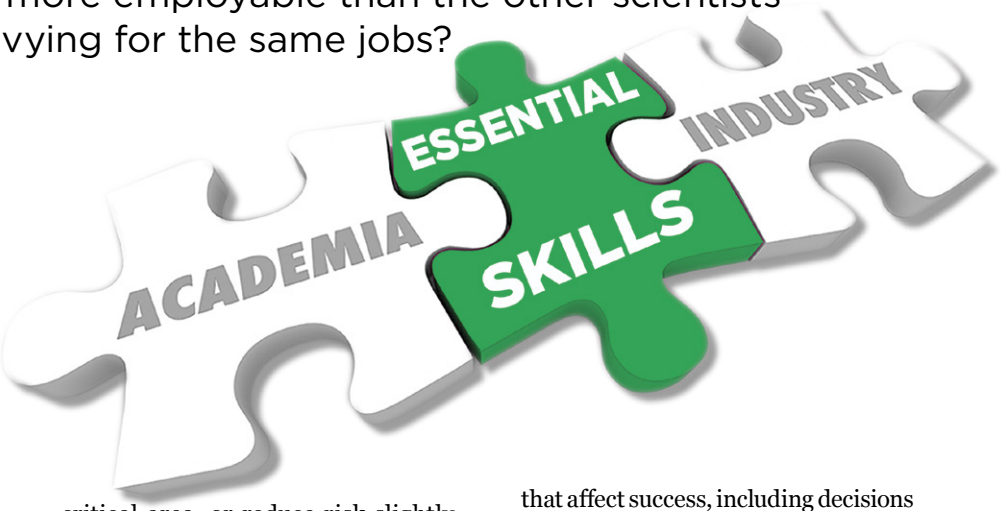
Following the above process guarantees that a grant proposal will be clear, complete, and well-structured. Reviewers will quickly find answers to evaluation criteria, thus reducing the chance that something important will be overlooked. Most importantly, this method puts central emphasis on why the project is important to the funding agency.

Nothing guarantees a proposal's success, but high-quality proposals always rise to the top. ■

*–**Damon Diehl**, PhD, is the Technology Program Manager at Luminate, the first optics-only startup incubator in the world. In addition to his grant-writing workshop, he also teaches the SPIE professional development class "The Very Least You Need to Know about Optics."*

Essential Skills for a Career in the Private Sector

What can you do to be more employable than the other scientists and engineers who are vying for the same jobs?



Completing our technical education and preparing to begin our careers in photonics can be one of the more exciting periods of our lives. For those of us who begin our careers in the private sector, the anticipation of getting to solve real-world problems can be particularly exciting.

However, despite the excellent technical skills we learn through our formal education, university doesn't generally teach us how to be productive in an industry environment. This is especially true if we have an advanced degree and spent several years in a research lab. Academic research is very different than product development, and many early-career scientists and engineers find that some of the work habits they picked up in academia don't serve them so well in their first industry job.

Their managers notice this as well. Many tech company managers describe the same set of academic habits that limit the productivity of their R&D staff members with advanced technical degrees. Learning to recognize these habits will make you more employable in the private sector:

1. **Make sure your work helps the company make money.** Spending time on an interesting problem may have been acceptable in the research lab where the goal was publication of novel results, but that will not earn your industry manager's approval. Companies need revenue to survive, so make sure you are working on things that will reduce costs, improve yields, or result in a new product with a clear market.
2. **Learn to figure out what matters and what doesn't.** Not every task that gets added to a project will end up contributing significantly to the desired result. Some tasks simply improve understanding in a non-critical area, or reduce risk slightly and make the development team feel better, but ultimately don't make a big impact on the outcome. These tasks take time and resources that could be better spent on more critical tasks. Learn to tell the difference and you will increase your value as a member of the technical team.
3. **Focus on being effective, not smart.** Of course, companies do need smart scientists and engineers to be successful, but their real goal is results. Our formal education taught us that we always need to know the right answer and be able to solve problems on our own. This approach is too slow for a company that is competing to win. Focus on getting results, even if it means admitting you don't know the answer and finding someone else who does. Points are awarded for fast and efficient results, not for being right.
4. **Learn to make decisions with "just enough" data.** In science and engineering, more data and more analysis typically result in greater certainty. The inability for early-career scientists and engineers to make quick decisions is one of the biggest complaints from industry managers. In an industry environment, there are many nontechnical factors that affect success, including decisions made by customers and vendors, personnel issues, and macro-economic influences. In this environment, progress requires making a decision for an important question even when there is no "right" answer, which can be a particular challenge for those of us who were trained to relentlessly gather data before making a decision. If you want a successful industry career, learn to make decisions with less data than you might like to have.
5. **Learn to persuade others to follow you and your ideas.** Academic research publications typically require enough data and analysis that the results speak for themselves. This is often not possible in a company environment (see skill #4). There might not be a "right" answer, and you may need to convince nontechnical people who wouldn't understand your proof anyway. Learn to be persuasive by being articulate and helping others see the value in your ideas, and you will be much more successful in your industry career. ■

*–**David M. Giltner** is a speaker, career coach, and founder of TurningScience, a company designed to teach scientists and engineers how to design rewarding careers in industry.* ***turningscience.com***

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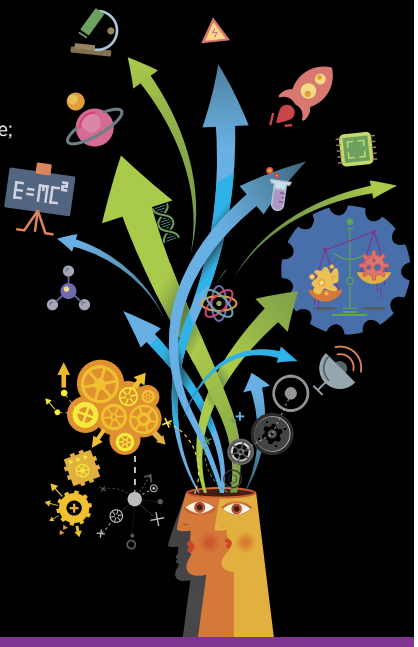

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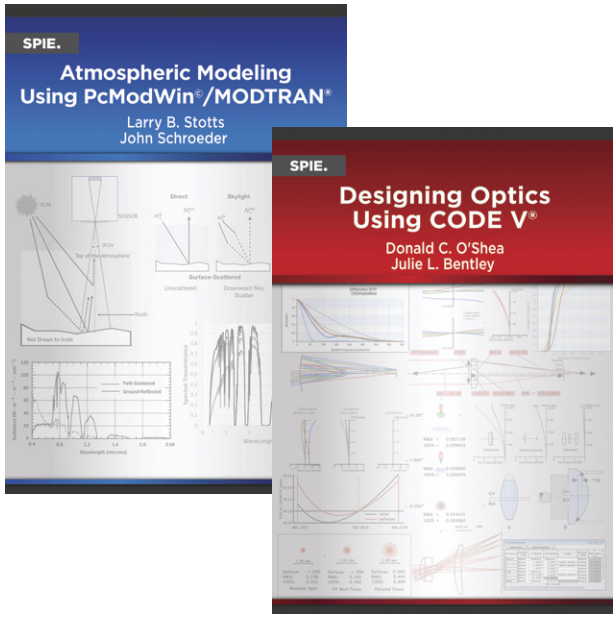

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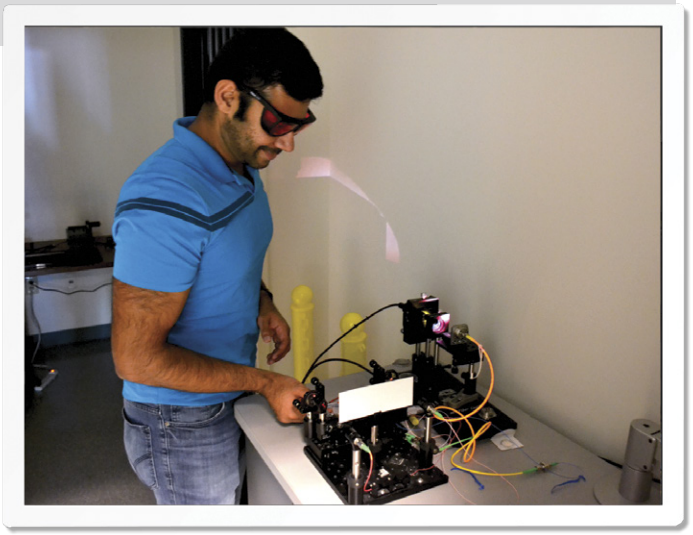
A Day in the Life of an SPIE Professional

In 2019, the #FacesofPhotonics series in *SPIE Professional* will focus on people who have taken different career paths in optics and photonics, from industry, to starting a new company, to academia, to government. These profiles will give SPIE members a glimpse at a day in the life of an SPIE Professional.

Nishant Mohan

Vice President of the OCT Division at Wasatch Photonics



Following his role as an optical engineer for Bausch + Lomb, SPIE Senior Member Nishant Mohan is now responsible for business strategy, new product development, product marketing, and product life-cycle management of the OCT Division at Wasatch Photonics, a company that designs and produces instrumentation for optical coherence tomography (OCT), Raman, and other spectroscopy techniques.

How did you end up working in the optics industry?

In graduate school, my thesis research was on an optical imaging technique primarily used for eye imaging. I was immediately fascinated by the relationship of optics to other signal analysis tools and the omnipresence of optics in our lives. After my postdoctoral study at Harvard Medical School, I joined the vision care division at Bausch + Lomb to apply different types of optical and imaging methods for contact lens development. I progressed into a management role, and to this day I am fascinated by optics and its role in medicine.

What type of education is needed to work in the optics industry at entry level?

The optics and medical imaging industries bring in individuals with a variety of backgrounds and education levels. We have people with associate's degrees in optics and lasers, bachelor's and master's degrees in a variety of engineering and management disciplines, as well as PhDs with a focus on specific applications.

What are three skills, technical or soft, necessary to do your job?

Problem Solving. In my role at Wasatch Photonics, I need to have a strong understanding of all aspects of technology and business, from computer-aided designs to customer satisfaction metrics. However, the fundamental skills needed are the ability to understand the bigger problem we are trying to solve, break it into smaller pieces, and then apply available tools to reach the desired goal.

Learning Capacity. This may not fall under most skill lists, but in my opinion is one of the key differentiating factors for professionals today. In a rapidly changing environment, it is imperative to constantly learn and evolve—a commitment that requires both desire and discipline.

Empathy. Whether we are developing a new product or communicating to customers, teammates, or investors, the most critical factor is being able to truly understand where our stakeholders are and where they want to be. Only then we can be sure that our efforts are truly headed in the right direction.

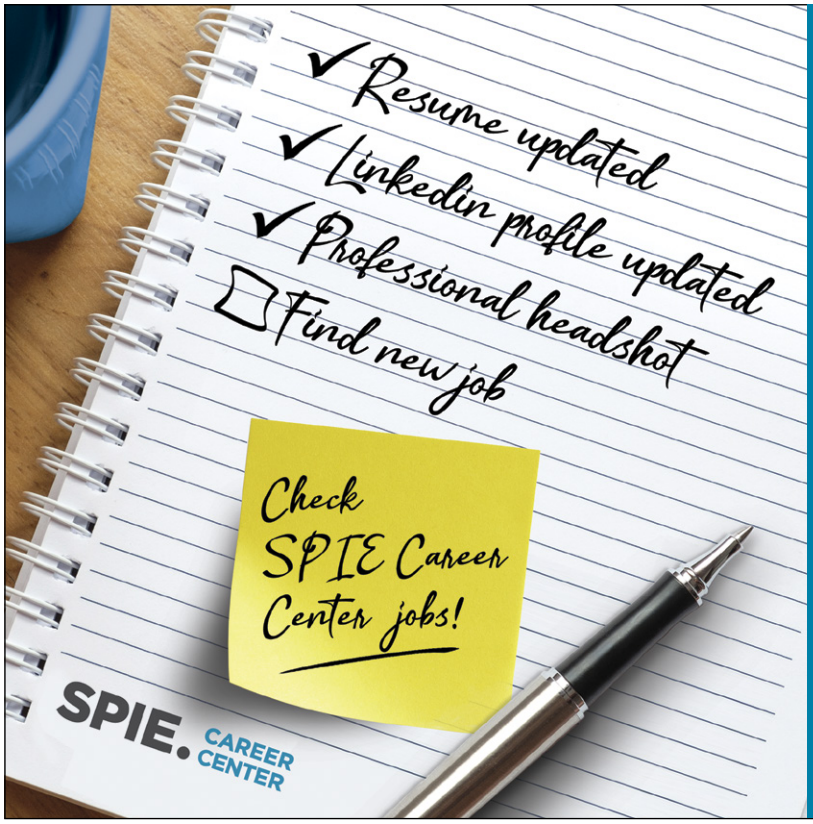
Describe a typical recent day at the office.

Before heading to our Morrisville, North Carolina, facility, I spent about two hours this morning focusing on items of long-term strategic importance and reviewed my calendar and goals for the day. Then, at the office, I responded to emails and delegated items as needed, followed by a meeting with one of my direct reports. I keep one hour per week for face-to-face conversation with all of my direct reports. We use the time to focus on problem solving and to plan for immediate actions. After this meeting, I worked on number crunching in preparation for a monthly meeting where I will present the state of the business to my team.

Next, I collected data for an image-processing problem my team is working on to improve image quality. In midafternoon, I took a call from one of our customers about the current state of their project and some critical future steps. This was followed by a discussion with our key technicians related to manufacturing builds on our production floor.

Towards the end of the day, I skimmed through a few abstracts from journal email alerts on topics of interest, and dug a little deeper into an interesting publication on intraoperative optical coherence tomography. Next, I organized my thoughts around how to lead an upcoming group discussion at the SPIE Optics + Photonics conference to be most productive for the audience. I like to spend time on volunteer work whenever possible, because it is always an extra boost of energy.

While there is no such thing as a typical day, I hope this gives a flavor of the interpersonal, technical, and business activities I engage in to encourage the growth of individuals and our business. ■



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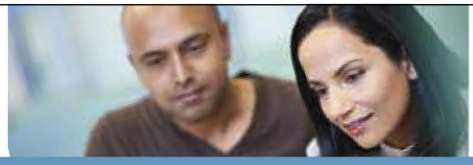

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MEMS-in-the-Lens Offers Miniaturized Laser Scanning Microscope

Montana State University integrates MEMS device into microscope objective for a high-NA platform

Smaller and more versatile laser confocal microscopy platforms would potentially be of great value for *in vivo* imaging of live biological specimens, in scenarios where the size of conventional platforms can be an inconvenience.

Miniaturization of the scanning mechanism itself would be an important step along this path, and current advances in the design and construction of microelectromechanical systems (MEMS) offer one route to achieving a reduction in both size and complexity.

A project at Montana State University (MSU) has now demonstrated a microscope objective lens that employs an integrated MEMS device within the objective to perform biaxial scanning, axial focus adjustment, and control of spherical aberration. The work was published in Nature's journal *Light: Science & Applications*.

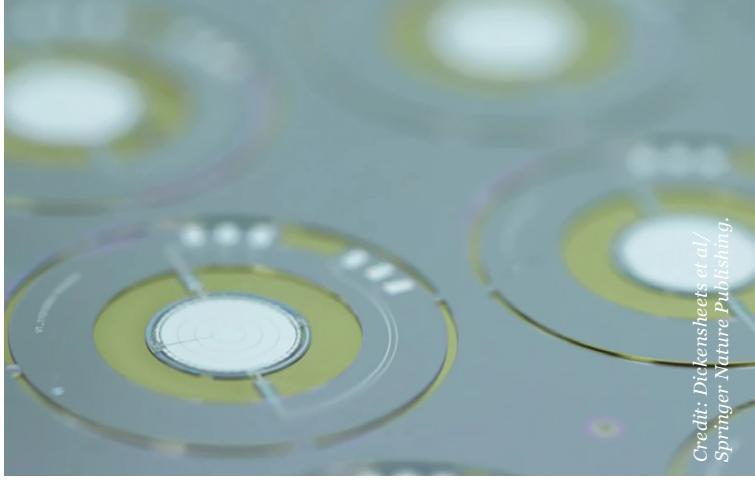
The new optical system places a 3D beam scanner within the objective, between a high-NA hyperhemisphere front element and a lower-NA back lens group. It employs a recently developed hybrid polymer/silicon MEMS three-dimensional scan mirror, according to the team, featuring an annular aperture that allows it to be coaxially aligned within the objective lens without the need for a beam splitter.

David Dickensheets of MSU commented that although "MEMS-in-the-lens" has been the subject of some prior research, a more common method has been to position a suitable MEMS device outside the objective, either before it or after it in the optical design.

"The usual approach has been a MEMS scanner positioned before the objective lens, taking the place of some other scanning method such as a galvo scanner," he said. "But the lens itself must then work well over a range of beam angles, corresponding to the field of view in the tissue."

Putting the MEMS after the objective lens instead does allow the lens to be small, and therefore simple, but then requires a long working distance between the lens and the tissue to insert the scanner. This can negate the advantage of a small lens in the first place and limit the numerical aperture of the system.

A MEMS element in the objective itself allows it to perform the lateral scanning needed to form the image; change the focus of the beam by adjusting its curvature; and make the fine adjustments needed to correct spherical aberration, which are the dominant optical aberrations at high NA.



MEMS devices, shown on-wafer following the release process.

"MEMS-in-the-lens is a compromise, with the MEMS scanner deflecting a converging beam—rather than a collimated beam—at low numerical aperture, followed by a final high-numerical-aperture lens that can be simpler and smaller," said Dickensheets.

"What makes this work well is the active surface of our MEMS scanner, which can correct for spherical aberration dynamically while it is scanning. Because the mirror can focus and adjust spherical aberration independently and quickly, it can take care of much of the work that a conventional microscope objective lens must do with extra glass elements. Putting the MEMS in the lens effectively means leaving glass out of the lens and leads to a more compact and versatile solution."

In bench-top trials, the objective was successfully used to demonstrate imaging of a structured high-reflectivity film, a sample of human cheek cells, and confocal sectioning of suspended polystyrene beads. The resolution and field of view were comparable to more conventional confocal microscopes with a similar numerical aperture, according to the project, and point towards the feasibility of a fully miniaturized platform.

The new architecture could prove valuable in several scenarios where high-NA microscopy is an advantage, such as the use of endoscopic microscopes for diagnosis of cancer, and there could be significant advantages to using architectures like the MSU device for optical biopsies in which tissues are examined without being removed from the body.

"Optical biopsies looking for skin cancer are today carried out using reflection confocal microscopy, eliminating the need for physical biopsy and delivering on-the-spot diagnosis," said Dickensheets. "But the instruments are large, so it doesn't translate well to the GI tract or other target tissues that we would use an endoscope to reach. This innovation can provide a path toward miniaturizing that equipment, while preserving and even enhancing its optical performance."

It may also encourage the tackling of fundamental biological questions through forms of "ambulatory animal microscopy," whereby optical imaging would be carried out on living animals without the need to bring them into a laboratory at all.

"Anytime we want to know about biological systems at the microscale, we have to take the tissue out of the animal, or else sedate the animal, surgically prepare it, and hold it still so we can use a conventional microscope to look at it," commented Dickensheets. "An ultra-miniature implantable microscope might allow us to see what cells are doing while an animal is going about its daily activities. This technology can play a role in such systems." ■

This article first appeared on optics.org.

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Eye screening at a school in Ghana.
Credit: Remo Nägeli/Swiss Red Cross

Wyant College Ophthalmology Tech Backed by Arizona Capital Fund

‘iCrx’ laser phoropter can automatically determine visual prescriptions in just 20 seconds

Laser technology that promises to eradicate the subjectivity of eyeglass prescription measurements has won investment from a venture fund set up by the University of Arizona (UA).

Under development at UA’s Wyant College of Optical Sciences—officially renamed after its founding dean and major donor Jim Wyant earlier this year—the “iCrx” technology is said to be capable of generating near-instant prescriptions.

It is expected to prove particularly useful in developing countries, where access to ophthalmic equipment and optometrists is limited.

BETTER OR WORSE?

As any wearer of glasses knows, determining an accurate prescription can be an interminable process, with tiny changes in vision clarity for each eye often requiring dozens of responses to an optometrist asking whether each lens switch provides “better” or “worse” sight.

In work led by Wyant College faculty members Nasser Peyghambarian and James Schweigerling, co-inventors of the new technology, a team including several students is working to design a prototype version of a compact automated phoropter.

Phoropter is the common name for the conventional ophthalmic testing device, also known as a refractor, that was invented in 1921.

And although that technology is nearly a century old, the phoropter is still commonly used by eyecare professionals during prescription eye examinations. It contains different lenses used for refraction of the eye during sight testing, to determine each individual’s refractive error and therefore his or her eyeglass prescription.

“The new iCrx invention is a handheld device that can produce an objective and accurate eyeglass prescription in approximately 20 seconds without any subjective input from the viewer,” claims the Arizona team.

PRESCRIPTIONS IN SECONDS

In October 2017, they published details of the automatic laser phoropter in the journal *Nature Scientific Reports*. The open-access paper describes a system based around a 785-nm laser from Thorlabs, three tunable-focus fluidic lenses, and thin-film holographic optical elements. That system was said to produce prescriptions within 15 seconds, without the need for supervision.

The three lenses are used to correct for defocus and astigmatism, while refractive error is measured using a Shack-Hartmann wavefront sensor that calculates the Zernike values of an infrared wavefront emerging from the eye.

“Holographic optical elements steer the emerging wavefront into the wavefront sensor, while simultaneously providing an unobstructed view for the subject,” note the researchers in their description of the system.

The work completed so far is sufficiently advanced to have attracted funding from the UA Venture Capital (UAVC) fund, whose unspecified investment will support further development and miniaturization efforts intended to turn the technology into a battery-powered commercial product that can be used in unmanned kiosks, or for rapid screening of large patient populations.

WYANT DONATIONS

Early work on the iCrx approach was completed by ophthalmologist and retinal surgeon Gholam Peyman, also a professor of both clinical ophthalmology and basic medical sciences at UA’s College of Medicine in Phoenix.

Peyman is also research director at the institution’s Department of Ophthalmology, but is perhaps best known for his invention of LASIK eye surgery, the laser technique that has been used to correct the vision of millions of people worldwide.

The investment represents the seventh overall by Tucson-based UAVC, which is dedicated to commercialization of UA innovation. ■

This article first appeared on optics.org.

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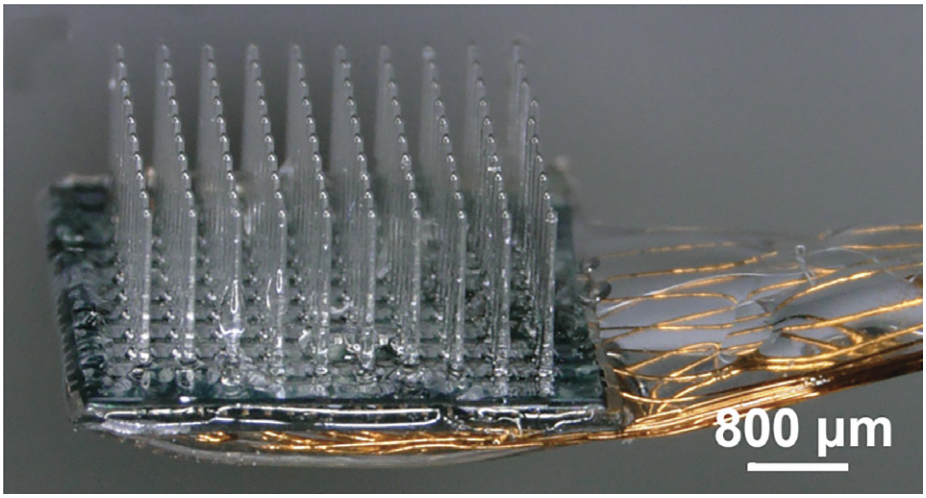
LED Array Implant Illuminates the Future for Optogenetics Studies



The integrated device with a glass optrode array bonded to a µLED array. ***Neurophotonics*** **doi: 10.1117.1.NPH.6.3.035010**

Using optogenetics, scientists can selectively activate or deactivate neurons by illuminating them with light, allowing researchers to perform fine-grained cause-and-effect studies between brain activity and behavior. Most studies are currently performed in mice and other small mammals, because their small brains can be accessed with just a few optic fibers.

However, if larger mammals are to be studied using this method, then new techniques to illuminate specific brain regions and even specific clusters of neurons need to be developed. The challenge is to overcome the problems of brain size, light scattering, and the undesirability of overheating brain tissue, while still allowing the subject the freedom to move around without being tethered to a light source or a computer.

The brain is a scattering medium: every vesicle, cell membrane, and fluid deflects the path of the light. The problem is further exacerbated by the fact that hemoglobin strongly absorbs blue light, which is the color most often used in optogenetics. Because of these obstacles, the light source must be quite close to the target to operate with any precision.

To address these challenges, a team of researchers from Universities of Strathclyde and Utah have developed an LED optical array that is capable of independently illuminating specific brain regions, while also being able to provide wide-area (4x4 mm) brain surface illumination [**spie.org/LED-implant**]. And if operated correctly, everything stays cool.

The device consists of a square 10 x 10 array of glass needles. An array of tiny light-emitting diodes (called µLEDs) are then aligned over the needles. This results in 100 glass needles that guide light from an individual LED to a depth of 1.5 mm in tissue. An additional 9 x 9 array (81 µLEDs) was placed in between the needles, allowing large-volume illumination as well.

However, even with careful placement, the team found that very little of the LED light makes it into the needles. This has two consequences: it means that the light exiting the needle is pretty weak and won't be able to control many neurons without using higher power, and also that the leaked light will activate neurons near the brain surface at undesired moments.

To overcome the first problem, the research team investigated the coupling between the light source and the waveguide. They discovered that the main problem is that the LEDs and the glass needles were too far apart (about 300 µm). In the current iteration of the array, the spacing was fixed due to the substrate on which the glass needles are produced and the substrate that holds the LEDs. Nevertheless, the researchers found that the current configuration delivered sufficient optical power to the end of the needle to impact up to 5500 neurons per needle.

The bigger problem of the poor coupling between the LEDs and the needles was the stray light emitted from the substrate into the brain surface. To solve this problem, the researchers simply placed a pinhole mask over the substrate so that light could only be emitted from the needles and the surface LEDs.

With all tweaks in place, the researchers showed that they had a good controllable light source that could, in principle, provide pinpoint control via the needles, as well as large-volume activation from the surface LEDs.

In the future, the group will modify the fabrication procedure. By replacing the glass substrate with a thinner silicon substrate, the coupling efficiency can be improved. And, because silicon naturally absorbs blue light, the substrate will also reduce stray light.

The team also modeled the thermal behavior of the array to estimate the temperature it would reach. To obtain sufficient light intensity to control a large number of neurons, the LEDs had to be operated at quite high power, and when they were all switched on continuously, the array heated up by some 60°C, which was unacceptable. To prevent heating brain tissue above 1°C under intense activation conditions, the LEDs must be operated with a duty cycle of one to two percent—a limitation that could be improved by using a silicon substrate with better coupling.

Even with a limited duty cycle, this device hints at an even brighter future for optogenetics. It delivers precisely controllable light via the needles, while also providing wide area illumination. The entire array can be battery powered and implanted using standard techniques. The authors state that, with only minor modification, the LED drivers can be controlled wirelessly, meaning that the subject could have full mobility. ■

*–**Chris Lee** is a physicist and writer living and working in Eindoven, the Netherlands.*

OCT Proves a Capable Partner in Radio Frequency Ablation Therapy

Credit: Christine Hendon, Columbia University

Somewhere between 2.7 and 6.1 million people in the US have atrial fibrillation, according to the Centers for Disease Control and Prevention. Atrial fibrillation—or AFib—causes uncomfortable symptoms for the sufferer, like chest pain, an irregular rapid heartbeat, and shortness of breath. As if those symptoms aren't worrisome enough, people with AFib are five times more likely to have a stroke, making cardiac arrhythmias a major source of morbidity.

In a normal heart, electrical impulses are conducted through myocardial tissue, and these involuntary impulses keep the heart beating regularly. The electrical impulse conducts best in homogeneous tissue. Irregularities, like fat within the muscle, thickened walls, deviations in myofiber orientation, and scar tissue, can all impact how the electrical signal propagates. Those abnormalities don't conduct the electrical signal, so it has to find another way to get around the fat or hardened part. That abnormal path produces the arrhythmia.

Since the 1990s, radio frequency ablation (RFA) has been the standard treatment for AFib. During RFA therapy, a guided catheter delivers RF energy to the area that's generating the bad signal, which creates a discrete area of necrosis that stops the abnormal electrical propagation.

Unfortunately, the procedure has just a 50 percent success rate for treating atrial fibrillation, and 20 to 30 percent of patients have to come back for another procedure. There are a few reasons for the low success rate. One is that physicians don't have very good imaging tools during the surgery. They rely on low-resolution two-dimensional fluoroscopic images that allow them to see the position of the catheter, but they can't actually see the heart muscle underneath. Even when the region is correctly identified, sometimes the lesion created by the RF beam isn't adequate—either because the catheter wasn't in good contact with the tissue, or was at the wrong angle for a successful ablation.

Being able to assess the ablation quality in real time could substantially increase the success rate of RFAs.

Fortunately, there's an imaging modality that is up to the task. Opti-

cal coherence tomography (OCT) uses time-delay information from light waves reflected from tissue to reconstruct a cross-sectional image of the tissue structure. OCT has been a popular imaging modality in ophthalmology for decades, but the past few years have seen an emergence of imaging applications ranging from breast cancer to dentistry to—yes, cardiovascular medicine.

SPIE Senior Member Christine Hendon began working on cardiac imaging using OCT when she was doing her PhD work with Dr. Andrew Rollins at Case Western Reserve University. Because myocardial tissue is highly scattering, an OCT imaging system can image up to one millimeter into the tissue, which is enough for physicians to determine good tissue contact during RFA. Rollins' group discovered that by attaching an optical fiber bundle directly to the tip of a standard therapeutic catheter, they could directly visualize the catheter–heart interface during the RFA procedure, *in vivo*, in real time.

Now an associate professor of electrical engineering at Columbia University, Dr. Hendon is continuing her work on OCT imaging for RFA. She has been able to characterize human cardiac tissue, including fat, infarction, fibrosis, and pulmonary veins, using OCT. Being able to distinguish these types of tissue is important, because they can affect cardiac function.

In the OCT images, tissue heterogeneities like fat slow down light penetration from the optical probe, causing birefringent artifacts to show up as black bands on the resulting image. To the trained eye, the presence of such an artifact can indicate an abnormality in the tissue architecture. The presence of these black band artifacts can also be useful during an RFA procedure to track the formation of the lesion; during the therapy, the dark bands will disappear in the OCT image, indicating that the tissue is becoming more scattering and homogenous as the ablation progresses.

Hendon has also expanded her work to explore the use of spectroscopy during RFA. Spectroscopy allows deeper imaging into tissue, and Hendon's group has demonstrated measuring lesions up to four millimeters in depth. Her group's work is far enough along to progress to live animal studies. "We've integrated our OCT and spectroscopy probes into therapeutic ablation catheters and showed that we can see all of these signals *in vivo* in pigs," she explains.

Moving these trials to human studies is the next hurdle, and one that raises some questions. Specifically, how is this tool going to be used by physicians in the operating theater? Should the physician see the optical data, or just the final parameters from the optical data? Hendon is aware that surgeons have a lot to pay attention to during one of these RFA procedures. She explains, "The physicians are looking at a lot of things. They may have an ultrasound, the fluoroscopy, electrical signals, they're navigating the catheter...we're not sure if we want to put another optical image up."

Although the probe can generate visual data, surgeons would have to be trained to interpret the OCT images, which are quite different than x-ray or MRI. That could be a barrier. A better approach might be to display the results of the optical data via a processing algorithm with straightforward results: the catheter is in contact, the catheter is not in contact; the lesion has formed, the lesion has not yet formed. Hendon's goal is to make things easier for the surgeon, not harder. "We want to provide automated unbiased confirmations to physicians."

In pursuit of these automated and unbiased confirmations, Hendon's group of electrical engineers are looking to machine and deep learning as a solution. "Anything you can see with your eye can be translated into an algorithm," she says. "First do this, then that, then finally this step. Then you just translate all those steps into math, and then you code them."

One of Hendon's graduate students, Xin Yu, presented the results of one such algorithm at Photonics West 2019 [**spie.org/OCT-RFA**].

This algorithm has one classifier with two subclassifiers, both developed using a convolutional neural network. First, the algorithm determines whether a catheter is in contact or not in contact with tissue. If the algorithm determines that yes, the catheter is in contact with the tissue, it proceeds to the next classifier, which looks at angle of contact: is it less than 30° or more than 30°? A small angle of contact may not deliver the RF energy adequately for a successful ablation, and should probably be repositioned.

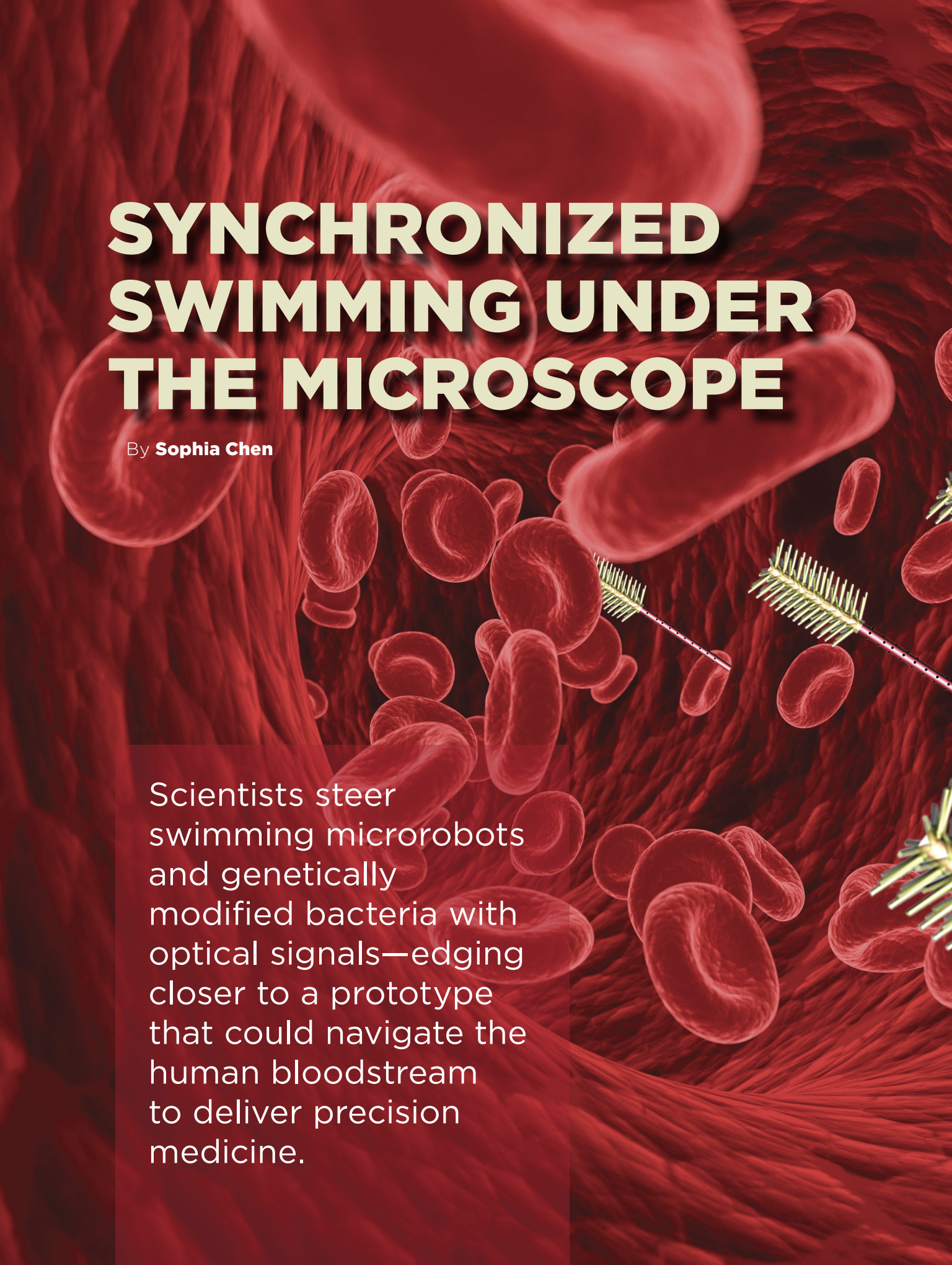
Their results showed that the contact classifier had an impressive accuracy of 99.96 percent—a pretty high degree of confidence that the catheter is in contact. The orientation classifier, on the other hand, was less accurate, at 91.58 percent. This variation is not surprising when you consider that the myocardial surface is not always a perfectly smooth plane. It can be lumpy, making it difficult to acquire a precise angle. Also, cardiac tissue is soft, so when the catheter is in contact with the surface, the angle can change at the point of contact, depending on how much force is being used.

Hendon's group is going to continue to pursue this deep learning approach to quickly and accurately interpret the OCT results, and she's relying on the clinicians who will ultimately use the tool to tell them what output will be most useful. "Our clinical collaborators ask very practical questions, and that really helps us in terms of optimizing our catheter design, our visualization techniques, what parameters should be shown, and where we should put our efforts," she says. "They're the ones doing these procedures every day, so they'll tell us which applications will have the biggest impact." ■

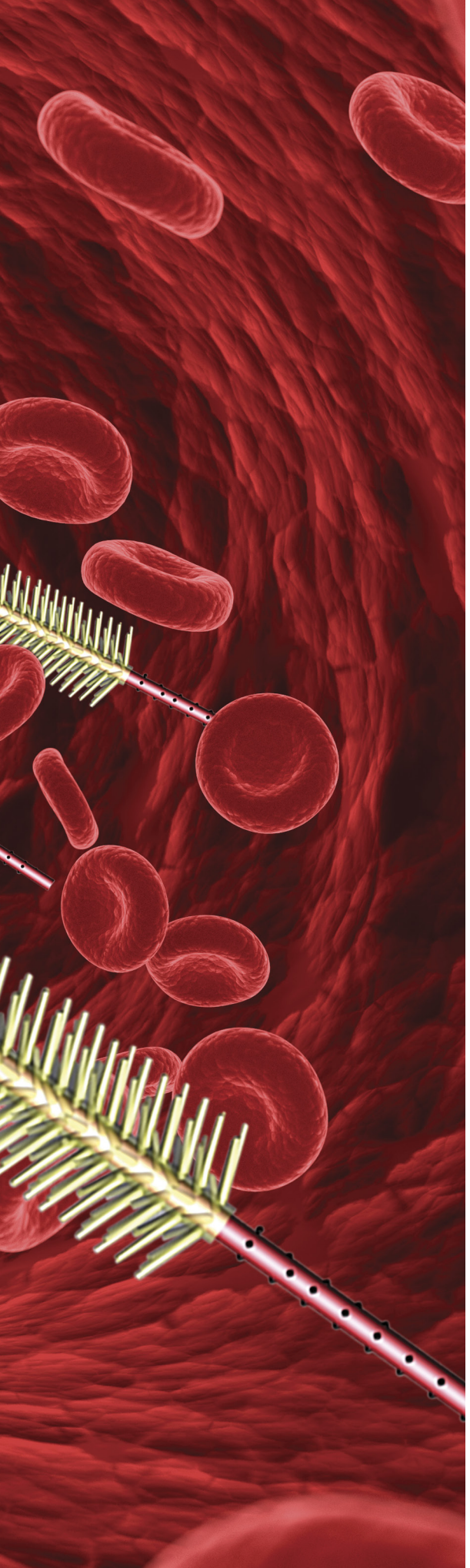
*–**Gwen Weerts** is the managing editor of* SPIE Professional.

SYNCHRONIZED SWIMMING UNDER THE MICROSCOPE

By **Sophia Chen**



Scientists steer swimming microrobots and genetically modified bacteria with optical signals—edging closer to a prototype that could navigate the human bloodstream to deliver precision medicine.



Jinyao Tang builds tiny swimming robots the size of dust specks. Magnified, they resemble miniature mascara applicators: each robot consists of a stem made of silicon and a brush tip made of titanium oxide bristles. He and his team engineered these machines to swim toward light. Under the microscope, they chase a blinking LED spot like a cat after a laser pointer.

Tang, a chemist at the University of Hong Kong, envisions a future in which doctors dispatch these robots into a patient's bloodstream, where the machines could deliver drugs directly to a tumor or perform intricate incisions in a small surgery. This science fiction isn't so far-fetched, he says. In 2015, for example, researchers at the University of British Columbia showed they could use self-propelling microscopic particles, attached to coagulants, to stop bleeding in live mice and pigs. When applied as a powder to the animals' wounds, the particles pushed against the flow to the source of the bleeding by fizzing like crushed seltzer tablets, boosted by their own bubbles.

Now, researchers like Tang are further developing such micron-scale motors to make them steerable. These machines, broadly known as microswimmers, range in size from a few hundred nanometers to a few microns, and their materials, geometries, and propulsion mechanisms vary. One potential steering control: light.

Light makes for a versatile control signal because it has a lot of properties, says Tang. An engineer can exploit different wavelengths and polarizations for multi-channel control, for example. "We can fit a lot of information in light to do very complicated maneuvers," he says.

Tang's team engineered their robots to respond to different colors of light by soaking them in three different dyes. Depending on its dye, the robot swims toward either red, blue, or green light, while mostly ignoring the other two colors of light. In other words, they can mix three colors of robots together and steer each type independently. Tang's team also recently completed a study in which they use light's polarization angle to orient the microswimmer.

But Tang doesn't use light just to steer. The light also activates the fuel that powers the robots. His team tested the robots in a toxic hydrogen peroxide solution, as well as a more biologically friendly solution of water mixed with hydroquinone, an organic compound. In both solutions, when the light hits a microswimmer, it triggers a chemical reaction in the liquid. The silicon stem absorbs light to produce negative hydroxide ions, while the titanium oxide bristles generate positive hydrogen ions. Because opposite charges attract, the ions move toward each other, pulling the liquid with them, which causes the robot to move toward the light. The robots can move at tens or hundreds of microns per second, depending on the intensity of the light source.

It's still unclear what material and shape make for the best microswimmers for any particular application, and effective designs must contend with the alien effects of microscopic fluid dynamics. "Swimming at the microscale doesn't work as it does at the macroscale," says chemist Juliane Simmchen of TU Dresden in Germany.

When tadpoles, fish, or humans swim, they create turbulent flow in the water that continues to carry them forward even if they stop moving. In other words, macroscopic objects can coast, even if just for a moment. But microscopic objects can't coast at all. They have to constantly propel themselves to move forward because water is an incredibly thick medium relative to their size. For them, it's like swimming through pudding. "If you want to move something continuously on the microscale, you have to put in energy continuously," says Simmchen.

To overcome these challenges, some researchers have opted to borrow chassis from nature, rather than making robots from scratch, like Tang. They outfit biological cells, such as *E. coli*, sperm, and varieties of algae, into microscopic cyborgs they can control.

These organisms have evolved efficient and intricate machinery over billions of years to navigate their environments. "I don't think, in our lifetime, that we can make something as complex as a bacterium artificially," says Simmchen. Some algae, for example, can move more than ten times their body length per second, which is more than a speeding car can do on the highway. Researchers can leapfrog technical challenges by hijacking these natural structures.

Researchers play with organisms that naturally respond to light, an ability known as phototaxis. So-called phototactic organisms include a variety of algae, which include the prokaryotic blue-green cyanobacteria, which produced much of Earth's oxygen during our planet's early years, along with other types of eukaryotic algae. You might find these microbes in a drop of your local pondwater.

Generally, phototactic organisms live and grow by undergoing photosynthesis: they make their own food via a set of chemical reactions that convert light, carbon dioxide, and water into usable energy. Thus, their sensitivity to light has allowed them to thrive over billions of years. "They're really ancient species, and they exist because they've been highly successful," says mathematical biologist Kirsty Wan of the University of Exeter (UK).

Genetically engineered *E. Coli* respond to light, forming images of Albert Einstein and Charles

For example, the single-celled alga *Chlamydomonas*, about ten microns in diameter, has a primitive light-sensitive structure known as its eyespot. "This is a localized region of the cell, which acts essentially as a single-pixel camera," says biophysicist Marco Polin of the University of Warwick in the UK. When photons hit the cell's eyespot, they cause ions in the cell to flow and generate an electrical current. In a cascade of chemical reactions, this current ultimately triggers the organism to alter the motion of its two whiplike flagella to steer the cell toward or away from light.

The mechanisms that govern such light-triggered motion vary among different species of organisms. The cyanobacterium *Synechocystis*, just two microns in diameter, does not have an eyespot. Instead, the microbe senses the direction of incoming light because its body acts as a tiny spherical lens, Annegret Wilde of the University of Freiburg and colleagues reported in 2016. This lensing focuses the incoming light at the opposite edge of the cell, indicating the direction of the light source.

Researchers have begun to adapt these organisms into controllable microswimmers. For example, Takayuki Shibata of Toyohashi University of Technology in Japan and colleagues used light to direct colonies of the multicellular algae *Volvox* to push a range of millimeter and submillimeter-scale blocks on a platform. They controlled the algae's motion by switching LEDs on and off around the platform, which exploited *Volvox's* natural phototaxis.

Researchers have also built biohybrids out of *Chlamydomonas* cells. Metin Sitti of the Max Planck Institute for Intelligent Systems and colleagues reported attaching drug-mimicking molecules to the cells and studying their swimming in various fluids such as human cell culture medium, bovine plasma,

Darwin in response to a projected image.

> "We can fit a lot of information in light to do very complicated maneuvers."

and mouse blood. However, they didn't take advantage of the algae's phototaxis to control the motion; instead, they stuck tiny magnetic spheres onto the algae and steered them with an externally applied magnetic field.

Researchers are also engineering light sensitivity in naturally light-insensitive bacteria. *E. coli,* for instance, doesn't exhibit much phototaxis. But some researchers have genetically modified the bacteria to produce proteorhodopsin, a light-responsive protein naturally found on the membranes of some marine organisms. This protein acts like a microscopic solar panel for the bacterium by helping it convert light into motion. Published in *eLife* in 2018, Roberto Di Leonardo of Sapienza University of Rome and colleagues showed that they could shepherd swarms of this modified bacteria using a light projector beamed into a microscope objective. By changing the projected light patterns, they directed millions of bacteria to arrange themselves into microscopic portraits of Mona Lisa, Albert Einstein, and Charles Darwin.

Still, basic design questions remain. Researchers don't understand which conditions make certain materials stick to bacteria, says Simmchen. For example, she and her colleagues have attached small spheres made of silicon dioxide, metal-capped on one side, onto *E. coli*. The bacteria like to stick to the metal side rather than the silicon dioxide, and they're not sure why. So she is conducting experiments to better understand the surface properties of these organisms, to optimize cargo design. "We want to tune materials to attach to the bacteria," she says.

In addition, researchers don't fully understand the organisms' biology. Sometimes they move toward light, and other times they move away from light. This makes sense from an evolutionary perspective: "Too much light becomes damaging," says Wan. Algae move toward or away from light given their needs, but scientists don't understand the response process in detail, she says.

This response is so complicated because light plays two roles that feed off each other: it orients the direction of the cell, and it's also a source of energy.

The orientation of the cell depends on whether the organism needs energy, and vice versa. Polin is currently studying the relationship between an organism's metabolism and its motion. "We want to understand this crosstalk," he says.

Tang prefers to work with fully synthetic robots, so that he can avoid these unknowns. "We understand the details of which part is which and what function does what," he says.

The simplicity of synthetic microswimmers also allows researchers to isolate and study the basic physics of fluid, robot, and light interactions. Celia Lozano of the University of Konstanz in Germany has taken this minimalist approach—her robots are simple microscopic spheres made of transparent silica that are half-coated in carbon.

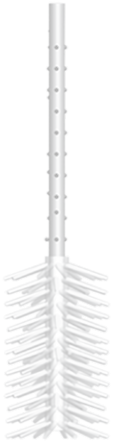
Placing the spheres in a mixture of water and lutidine, an organic compound, she and her colleagues found that the spheres could propel themselves when illuminated uniformly with a green laser. The laser heats the particle's carbon-coated hemisphere more, which causes the lutidine and water to separate. This creates a concentration gradient. To balance out the gradient, liquid moves along the sphere from its transparent face toward its carbon-coated face. This flow propels the sphere transparent-face first, like a rocket jettisoning fuel. "The particles were able to feel this gradient of light to move in a preferred direction, something that was unexpected," says Lozano. With these same spheres, Lozano has shown that she can use light pulses to make the particles gather like the cells that make up an amoeba.

The simplicity of Lozano's particles illustrates a fundamental aspect about phototactic organisms. To make a microscopic particle respond to light, it just needs to be asymmetrical in some way. For example, her spheres have two different faces. The asymmetry gives her particles a sense of direction: light interacts with one side of the particle differently than the other.

Biomedical applications will take some time, says Simmchen. Researchers haven't studied these microswimmers enough in conditions close enough to the interior of the human body. The bloodstream teems with salts, proteins, and other particles that would interact with the robots—a far more dynamic environment than researchers' idealized lab conditions, she says.

The microswimmers may prove useful in nonmedical applications, first. Simmchen's team has made small spherical particles that like to stick to tiny microplastic fragments. They can steer these particles through water using UV light, and they show that the particles accumulate microplastics as they move. They then deploy the particles on samples of cosmetic products and real seawater that contain microplastics. "I don't want to say we can clean the ocean, but at least we can clean the microscope slide," says Simmchen.

Chlamydomonas.

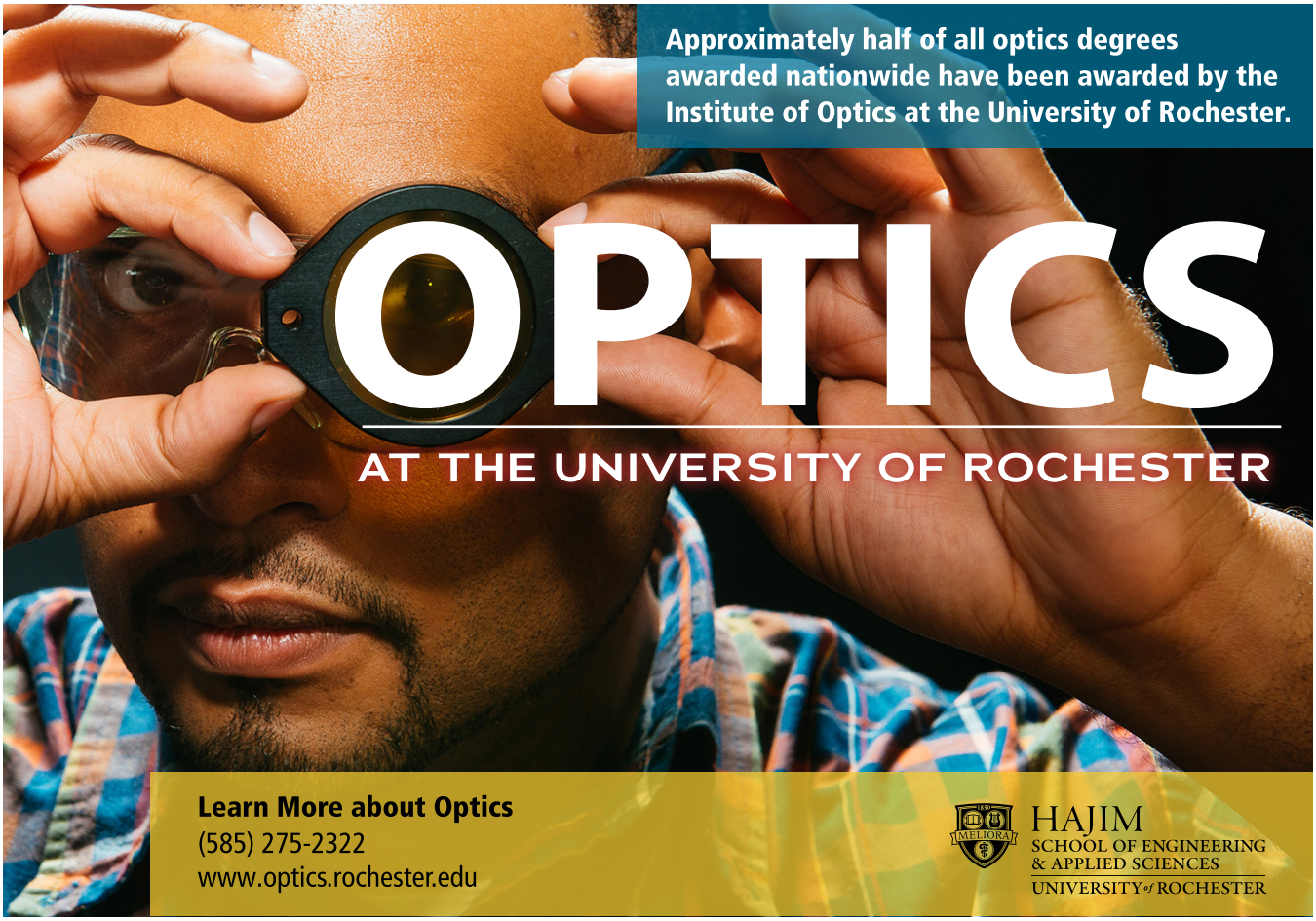


Researchers also need to study the human immune response to these objects, says Simmchen. To this end, over the next few years, Tang wants to improve the biocompatibility of his robots so that he can begin to test them in live animals. He anticipates being ready for these tests in five to ten years.

But the future of these robots doesn't just depend on technical success. "It's one thing for the technology to be ready," says Tang. "It's another thing for society to be ready." The question remains whether people will allow these tiny swimmers into their bodies. ■

*–**Sophia Chen** contributes to* WIRED, Science, *and* Physics Girl. *She is a freelance writer based in Tucson, Arizona.*

Read online for links to the research articles mentioned in this story: ***spie.org/microswimmers***



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MAPPING THE MIND

A Neuroscientist's Expedition into the Unknown

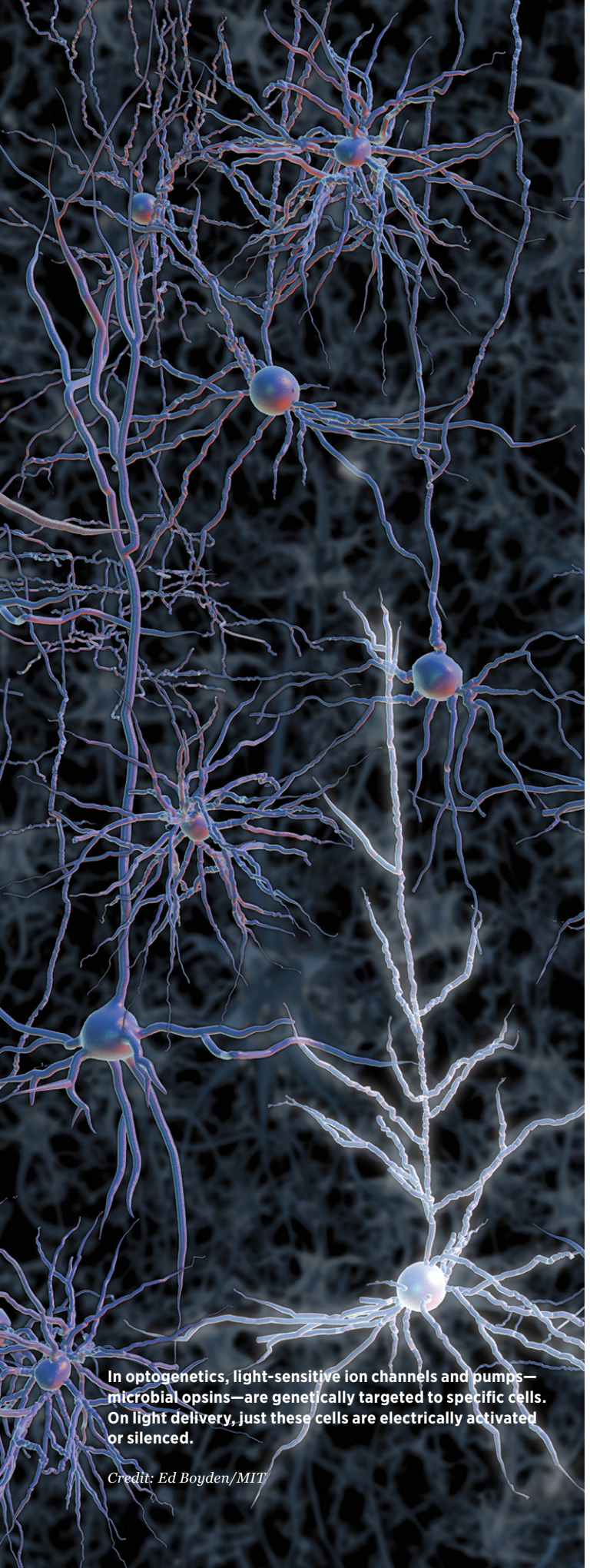
Ed Boyden has a plan to create a detailed map of one of the last uncharted terrains: the brain. Two out of three critical technologies are nearing completion, with the third well on its way.

By **Rebecca Pool**

When neuroscientist Ed Boyden first approached the National Institutes of Health for funds to develop expansion microscopy, he was rejected. So he applied again. Second time around he was also rejected, but undeterred, he applied again and again and again and again.

"Many NIH grant proposals were rejected one after the other as people just didn't believe this could work," says Boyden, from the MIT Media Lab and the McGovern Institute for Brain Research. "But I always knew expansion microscopy was going to be really useful."

"We've now taught hundreds of groups how to use it, and I really do think it's going to be applied across all of biology because you can use it to see very beautifully the building blocks of life," he adds.

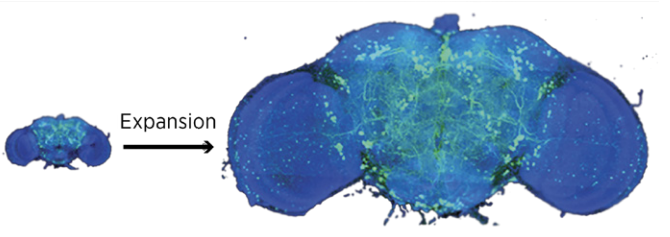


In optogenetics, light-sensitive ion channels and pumps—microbial opsins—are genetically targeted to specific cells. On light delivery, just these cells are electrically activated or silenced.

Credit: Ed Boyden/MIT

Expansion microscopy is like nothing else. Conceived during a research group brainstorming session, the method solves the problem of not being able to distinguish densely packed features in cells by making the tissue bigger, rather than improving microscope optics. The end result is that nanoscale structures can be scrutinized, even when using your everyday confocal microscope.

To swell tissue, sodium acrylate is infused into chemically fixed tissue, with polymerization agents then added to form a polymer network within the sample. The tissue-polymer sample is then chemically softened to homogenize mechanical properties, and finally rinsed in water to trigger linear expansion. Then, fluorescent labels are attached to specific targets, such as neurotransmitters, receptors, and ion channels, ready for imaging.



Credit: Gao et al./ Science 2019

After expanding the fruit fly brain to four times its usual size, lattice light-sheet microscopy is used to image all of the dopaminergic neurons (green).

Already, researchers worldwide have been using the method to expand tissues from rats, mice, zebrafish, fruit flies, even bacteria, from four to ten times, reaching up to 30-nm resolution. Boyden and colleagues have also optimized expansion microscopy for pathology to enable accurate computational discrimination between high- and low-risk lesions on cancer biopsies. And at the same time, they have reached twenty-fold expansion and 25-nm resolution by expanding mouse brain slices twice.

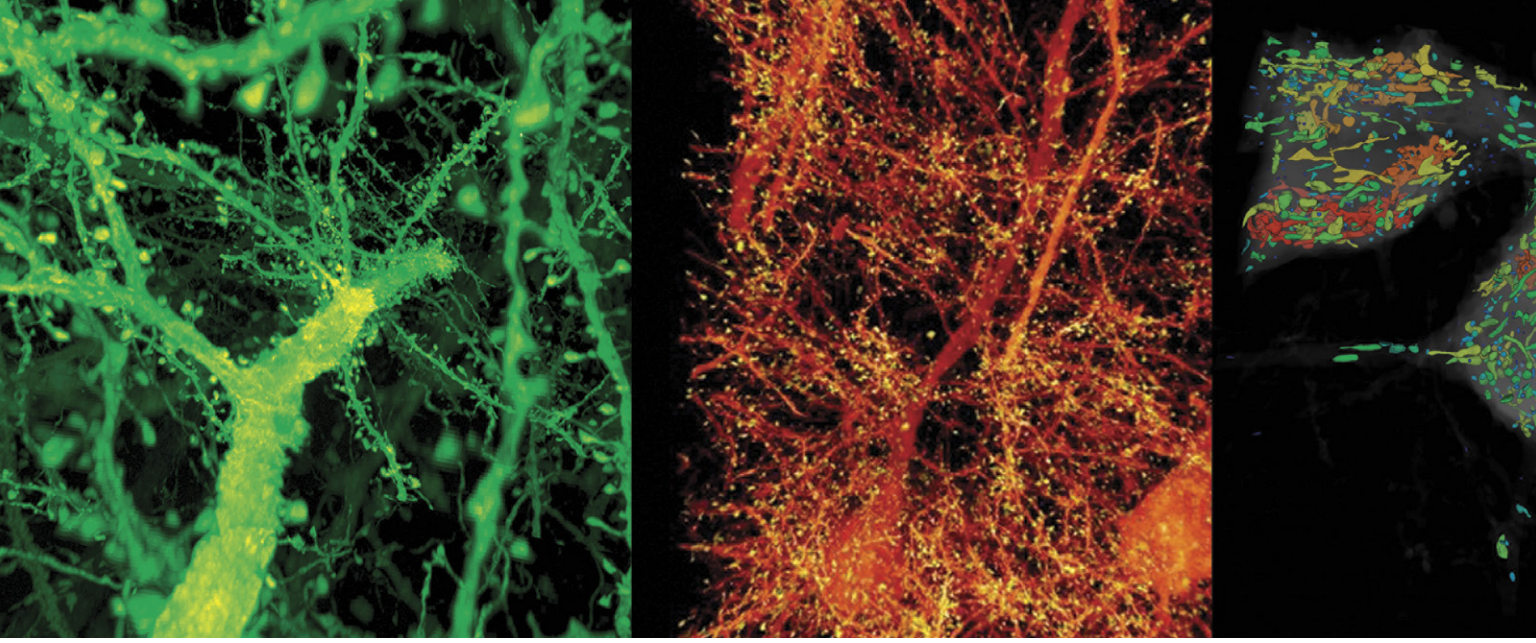
While these resolutions match those of superresolution imaging methods such as stimulated emission depletion (STED) microscopy, the story of expansion microscopy hardly stops here. Boyden is adamant there is no fundamental limit to his method, which he believes can be used to expand biological samples over and over again.

"What if one day we could map all of the biomolecules throughout an entire cell?" he asks. "That would mean getting resolution greater than any previous optical microscopy method and expanding the cell not just 100 or 1000 times in volume, but a million times in volume, or more."

Genuinely feasible? Boyden says yes. Anytime soon? Absolutely.

"This is just a matter of chemistry and we think we can improve this until we are able to expand individual biomolecules away from each other," says Boyden. "So this is one of our goals: to get down to single-molecule precision in the next couple of years."

Given the swift successes of expansion microscopy and his determination to understand the brain at a deeper level, Boyden



took his technology to Nobel Laureate, Eric Betzig, from the Howard Hughes Medical Institute's Janelia Research Campus, earlier this year.

By combining expansion microscopy with Betzig's incredibly fast high-resolution lattice lightsheet microscope, the pair imaged an entire fruit fly brain in a blisteringly fast 62.5 hours, showing some 40 million synapses in detail down to 60 nm.

This level of detail doesn't yet match that obtained with an electron microscope, but efforts to fully map the neurons and synapses of the fly brain with electron microscopy have taken decades with the efforts of dozens of researchers. Boyden reckons his method can be honed to scan an entire fly brain in just 12 minutes.

In addition to the fly brain, the researchers have also imaged large-scale circuits across a mouse cortex. At the time, Betzig said he "couldn't believe the quality of data" he was seeing.

"The imaging speeds we achieved are about one thousand times faster than the nearest best superresolution technology, and we think it's just a matter of, say, using more cameras and optics to go ten thousand times faster, and even more," says Boyden. "We're so excited about making scalable brain mapping a reality that this is now one of my group's main focuses."

The implications of swiftly imaging larger and larger volumes of the brain in 3D and with single-molecule precision are almost beyond imagination. If an incredibly detailed map of an entire brain can be made, this would provide a crucial step towards developing a brain simulation.

And since deeply understanding the brain has always been at the forefront of Boyden's mind, he has already developed additional technologies necessary to get him there. Long before expansion microscopy reached laboratories around the world, his first breakthrough brain analysis method, optogenetics, had already rocked the world of neuroscience.

Boyden conceived the idea of optogenetics with Karl Deisseroth, while each was at Stanford. The young students wanted to control neural circuits and decided that, thanks to its speed, light was the best means to deliver energy into the brain to then switch neurons on and off.

They went on to use blue light to control neurons in living brain tissue that had been genetically modified to express light-sensitive ion channels. The light modulates the membrane potential of the cells, switching transient electrical signals, which are the basis of neuronal computation, on and off.

Fast forward a decade-and-a-half, and thousands of research groups are using optogenetics while start-ups are pursuing optogenetics research in humans. For example, the method has been used to restore vision in mice, suppress Alzheimer's-related beta-amyloid plaque production in mice brains, and even trigger aggressive behavior in mice.

Meanwhile, Boyden has also developed fast-switching molecules that can be activated with red light for lower light scattering and minimal phototoxicity. Importantly, these molecules can be used to control neurons deeper within tissue.

"With our colleague Valentina Emiliani, we've reached single-cell submillisecond precision, so we're getting to the fundamental spatial and temporal limits of optogenetics," points out Boyden, "We will continue to refine the method, but it is nearing the endgame."

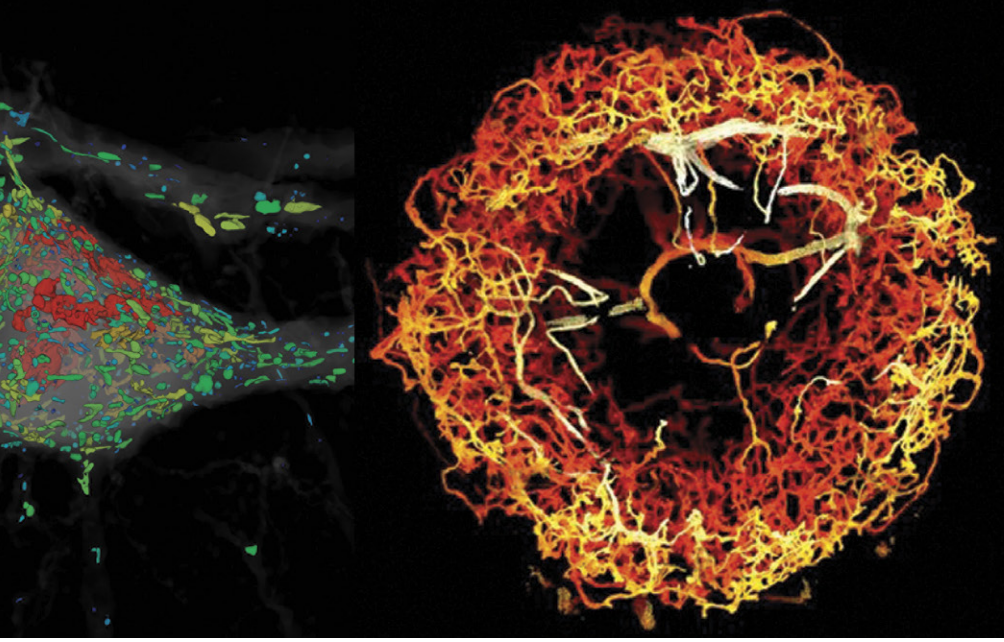
The rate of optogenetics development has been breathtaking, but in addition to controlling the neurons within a live brain, Boyden wants to watch neuronal processes in action, which requires a voltage indicator to image neural activity. It's nearly ready.

Last year, Boyden and colleagues developed a light-sensitive protein that can be embedded into neuron membranes to measure voltage in a cell. When exposed to red-orange light, the so-called Archon1 protein reporter emits longer wavelength red light with a brightness that corresponds to the cell voltage.

As Boyden points out, engineering the protein sensor wasn't easy. The fluorescent molecule has to respond rapidly to voltage changes while also being resistant to photo-bleaching.

To find the right molecule, the Boyden group adapted a microscope-guided cell-picking robot—originally developed by Professor Bálint Szabó from Eötvös Loránd University, Budapest—that can swiftly screen the millions of potentially suitable proteins. Made from commercially available parts, the cell picker can be installed onto any microscope equipped with a motorized stage, the necessary single-cell-picking software, and image-processing algorithms.

With robot in tow, Boyden and colleagues created 1.5 million mutated versions of an existing light-sensitive protein called QuasAr2 and placed each gene within a mammalian cell. Cells were



FROM LEFT:

1. A forest of dendritic spines protruding from the branches of neurons in the cortex. *Gao et al.* Science *2019*
2. A subset of pyramidal neurons (orange) in the mouse primary somatosensory cortex. The dendritic spines associated with the postsynaptic protein Homer1 are highlighted in yellow. *MIT*
3. Organelles of various shapes and sizes (colored areas) inside mouse neurons imaged by merging expansion microscopy with lattice light-sheet microscopy. *Gao et al.* Science *2019*
4. Dopaminergic neurons in the ellipsoid body of a fruit fly brain, color-coded by 3-D depth. *MIT*

grown and screened to assess each protein for membrane localization, fluorescence brightness, and voltage sensitivity.

The five best candidates were selected, and a further mutation round generated 8 million new proteins. After further cell growth and screening, 'Archon1' was selected as the best performer.

Using the new voltage indicator, Boyden and colleagues have already measured electrical activity in mouse brain tissue as well as in the brain cells of larval zebrafish and the *Caernorhabditis elegans* nematode, millisecond by millisecond, as the brains functioned.

And crucially, the researchers have clearly demonstrated that Archon1 can be used with optogenetically controlled cells, as long as these cells respond to colors other than red. *C. elegans* experiments have revealed that a neuron can be stimulated using blue light, with Archon1 then measuring the downstream postsynaptic response.

"Our voltage indicator has higher signal-to-noise than other molecules when used *in vivo* and is compatible with optogenetics, but we are still working on improving its properties," says Boyden. "We are continuing to screen indicators and will make them brighter than Archon1, which is a current limitation of our molecule."

As indicator developments continue, the researchers continue to measure brain activity in several species including living mice—as the creatures perform tasks—in a bid to map neural circuits and correlate data to behavior.

So where now? Clearly the next step for Boyden and colleagues is to combine optogenetics with an optimized voltage indicator so they can control a living brain while watching it in action.

And if the data from these experiments can be combined with the breathtakingly detailed brain maps that expansion microscopy is set to deliver, then Boyden can start trying to build his brain simulation.

"By sympathizing the three datasets from expansion microscopy, optogenetics, and voltage indicators into computational models, we hope to simulate those models into a computer," highlights Boyden. "If the maps of the brain are detailed enough, we may be able to do this."

The effects would be profound. For starters, brain disorders from Alzheimer's to schizophrenia could be tackled in ways that right now are simply not possible.

"Brain diseases affect more than a billion people around the world," says Boyden. "But with a detailed map of the brain, we might be able to figure out exactly where the diseases are in the brain, where they begin, and what are better targets for treating them."

Then there's artificial intelligence. Right now, AI is great at, say, playing chess and recognizing speech, but what about generalized learning?

While you or I can learn something new and apply it to many different problems, AI can only do that in science fiction films. However, Boyden reckons that his brain simulation may generate such intelligent behavior and could even create AI with ethical values.

"Right now, artificial intelligence requires zillions and zillions of trials to learn to perform a task," points out Boyden. "But if we can use detailed brain maps to create computer simulations, we maybe could design artificial intelligences that learn quickly."

Much remains to be done. While Boyden and colleagues have imaged an entire fruit fly brain and slices of a mouse brain, larger scale analysis will take time. A fly brain has around 100,000 neurons while a mouse brain has some 100 million cells.

Still, as the neuroscientist says, "We can see a path to the entire mouse brain—it's just going to take a lot of engineering."

What's more, combining data from expansion microscopy, optogenetics, and the voltage indicator will be challenging. From nanometers to centimeters, and fractions of a millisecond to minutes, the technologies cross vast spatial and temporal scales, which makes merging results no trivial matter.

"Everything is a challenge here, so right now we're really trying to figure out how to combine our technologies into a single pipeline," says Boyden. "But crossing spatial and temporal scales is at the core of what we do and that is why these technologies are taking off."

And despite the challenges, the world could see results sooner than you might think. Ask Boyden when we'll see his brain simulation, and in the face of mind-boggling complexity, his reply is surprisingly simple.

"It would be fun to see if we can model a small brain in a computer in the next five to ten years," he says. "You know, we could also try to make maps of larger brains over the same timescale as well." ■

*–**Rebecca Pool** is a science and technology writer based in Lincoln, United Kingdom.*

IN THE WAR ON OPIOIDS

525-NM LEDS OFFER HOPE

When it comes to managing chronic pain, a simple solution may be the best solution.

By **Ford Burkhart**

At age 15, Cindy Chillock was already battling chronic pain that would last a lifetime. Finally, at age 69, she has discovered a new weapon to use against that old enemy. It is simple, surprisingly effective, and almost free. Essentially, it's green LED light.

"It has improved my whole life," she says.

Now, keeping her string of green lights nearby has become her way to cope with crippling pain from interstitial cystitis. She plans to light them up on a cruise to Cabo San Lucas in Mexico.

Her personal success was part of the pioneering work by Dr. Mohab Ibrahim, director of the Chronic Pain Management Clinic at Banner-University Medical Center in Tucson, Arizona. His team, he says, was the first to fully characterize the effects of green light on pain in animals. And his work has shown solid benefits to humans with three top pain challenges—fibromyalgia, migraines, and interstitial cystitis.

Credit: Bob Deemers/UANews

Ibrahim convinced Chillock that his technology offered real hope when she thought she was out of options. She had to learn a new word for our body's opioid-like natural particles: enkephalins, derived from the Greek word "kephale" for "head." These painkilling proteins are found in everything from our earthworm cousins to us. Because the green light therapy triggers enkephalins without the harmful effects of opioids like morphine, oxycodone, or fentanyl, exposure to green lights, he told her, would release the body's own endogenous opioids.

"It was noninvasive, not your typical Western medicine," she recalls. "It was worth a try."

Chillock joined a ten-week-long pilot test, with daily periods of exposure to ambient green light at the 525-nm wavelength, the middle of the green band. The light was at a low intensity, just enough to let her read in an otherwise darkened room. The study recorded pain scores, medication use, and quality of life, and she showed improvement in all three areas.

Ibrahim says some of his early study participants began with migraines causing baseline pain scores of about 8/10, a score reflecting pain so severe it almost precludes any activity, even talking. Their scores fell to about 3/10—signifying mild, annoying pain—after green LED light treatment. "That's a reduction of more than 50 percent," Ibrahim notes.

Like the other participants, Chillock switched on her LED lights, rather like those on a Christmas tree, for about two hours a day. From the first week, she says her pain intensity was reduced enough that she could cut back on opioid painkillers usage by about 50 percent and fall asleep more quickly.

She says, "I felt a sense of hopefulness coming back into my life."

The NIH has reported that chronic pain affects more than 100 million Americans and takes a toll of upwards of $630 billion a year. Thus, some form of green LED therapy could mean huge savings in treating those with chronic pain, and it would be a lot safer.

Managing pain with a green LED light has no reported negative side effects, unlike sedatives—which can be fatal if respiratory arrest occurs—or a gradual buildup of tolerance to opioids, which leads to a need for a steadily higher dose to get the same effect.

And helping reduce use of pain killers, says Ibrahim, is the strongest factor motivating his work on green light as a complementary approach to prescription opioids.

For Ibrahim, who is also UA associate professor of anesthesiology and pharmacology, a family encounter got him thinking about phototherapy for the first time.

His brother suffered from headaches, and instead of taking pain medications, he simply went out to his backyard garden for a short time.

"Basically he gets better," says Ibrahim. "This was just his story until I got a headache one day, and I had no analgesics at home. While driving to the pharmacy, I remembered my brother. So I stopped at a park and sat among the trees there for 20 minutes, and my headache also started getting better. I thought of possible factors. The quiet environment. No stress. I was meditating in a way. Honestly, my headaches never get better during such a quiet time in my office."

That large park has acres of grass and trees. "Maybe the

trees were giving off something," Ibrahim guessed. "Or maybe it was just the green light reflected from leaves."

Green light, he thought, was the common element between his brother's garden and the city park. He decided to investigate.

Starting with animal models, he found that rats exposed to only green LED light—at about 4 lux, a very faint light from just one LED mounted on their cages—experienced less pain from, for example, contact with heat. The diminished pain was measured by how quickly they withdrew their paw from an irritant. Remarkably, the lab found that the lowest intensity light was sufficient to delay paw withdrawal, whereas the highest brightness was less effective.

In some of the rat experiments, the team employed special optical filters in the form of contact lenses—a step that resulted in researchers being bitten several times, Ibrahim recalls with a laugh—to allow the desired wavelength to pass through to the rats' eyes when they were exposed to white light. "This may be a future direction we will explore in human studies," Ibrahim said.

As a control group, rats equipped with tiny opaque contact lenses did not display any benefit. Thus, Ibrahim and his colleagues concluded that the analgesic effect of phototherapy took place through the visual system and not from being exposed through the skin.

The rats exposed to green light showed reduced pain in a day or two. Ibrahim says he was so stunned at the early rat results that he repeated those experiments five times. Yet while the results were impressive, the question remained why the green light caused such a drastic reduction in the pain response.

"From the eyes to the spinal cord, we don't know yet exactly the path taken by these signals," Ibrahim says. "We believe there is involvement of the endogenous opioid system, but this may not be the only mechanism of action. There may be a synergy with the inflammatory system and other pain mediators in the body. We are just scratching the surface."

One theory is that photons of green light reach the back of the patient's eye where they generate signals in the form of electrochemical telegrams. The signals travel in a neuronal network in the brain, through the optical nerve and other pain centers, until they eventually reach the spinal cord. At that point, the signals result in increased transcription of messenger RNA (mRNA) molecules. mRNA is necessary to create protein or peptide products such as enkephalins, which are pentapeptides that regulate the sensation of pain and act on opioid receptors to result in pain relief.

The research team was able to trace this path in rats, and they measured the resulting enkephalins from spinal cord tissue samples after the therapy. They also measured the increase in mRNA produced in blood samples.

Building on this encouraging data from the rat research, Ibrahim began human studies, in which 35 participants spanning three major categories of pain were exposed to LED light at levels as low as 4 lux and as high as 100 lux. The humans

Credit: Carolyn Niethammer

were asked to observe LED light for one or two hours a day. It was a big request, he admits, but he started at a level he knew really worked in the animal studies in order to establish a proof of concept with humans.

"Do they really need two hours?" he asked. "It could be less, and I would hope that we will need less time. The next step will be to test with 15 minutes and 30 minutes and more. But first, we needed the proof with one to two hours each night. Later we'll optimize that effect."

Overall, patients' pain was reduced by an average 60 percent, Ibrahim says. For those with migraines or fibromyalgia, opioid use dropped from a daily average of 280 morphine milligram equivalents, or MMEs, to about 150 MMEs during the pilot testing.

After Ibrahim reported his findings in April to the 2019 meeting of the American Pain Society in Milwaukee, several experts found the study promising.

At Duke University, Padma Gulur, professor of anesthesiology and specialist in pain management, says the Arizona project is an encouraging part of a small number of studies around green light therapy, including her own NIH-funded randomized green light trials. She believes the independent Duke and Arizona projects are on the leading edge of phototherapy with green light. "It's a new and exciting field," she says. "It is low cost and easy for patients to adopt and comply with." In her case, post-operative patients and chronic pain victims are also seeing benefits from being exposed to green light for a few hours a day. "It's still early, but green light holds a lot of promise to reduce the pain medicine requirements of patients," says Gulur.

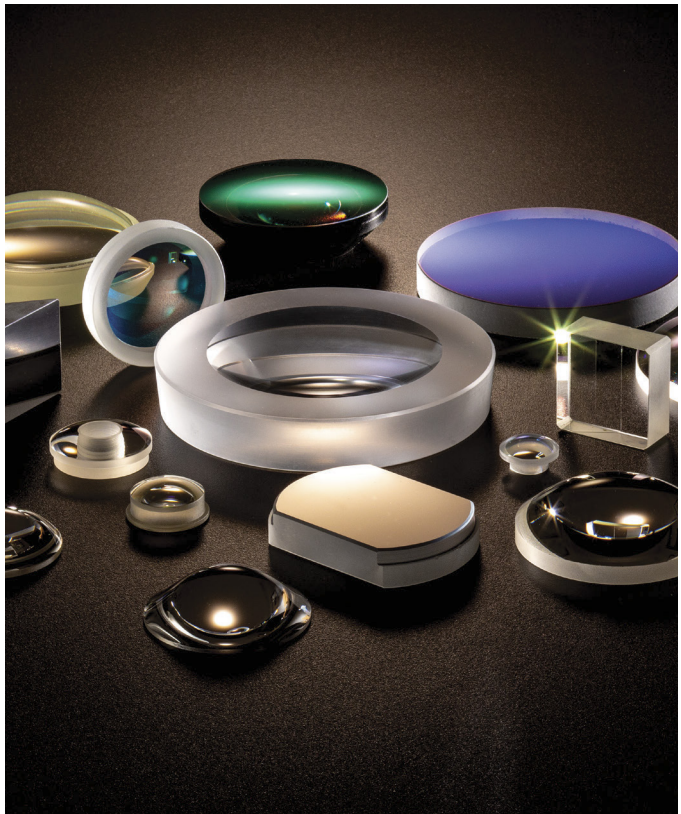
Ibrahim says his team is still in the early stages of what he predicts will be a long trajectory of research. Not all the patients responded to the green LED therapy, but he says he's proud that he helped "an overwhelming majority" of patients in early testing. Now, he says, "We are investigating how effective this will be in a bigger population."

Ibrahim's team is also expanding their work in several directions. For example, they plan to use phototherapy with HIV patients who have experienced persistent pain, a common side effect of HIV that is often treated with neuropathic pain medications and sometimes with opioids. The ground work for this project is being funded by a $1.7 million grant from the National Center for Complementary and Integrative Health, part of the National Institutes of Health, to advance his study of effects of green light on HIV positive rats before translating the therapy to humans.

Clinical applications, Ibrahim predicts, could include a range of new technologies including special contact lenses or sunglasses, or new LED devices to deliver the precise intensity and wavelength of green light.

"We are discovering something new every day. It is a wholly different way of thinking. What we are doing is somewhat unorthodox, but you can't argue with the data." ■

*–**Ford Burkhart** has covered science and medicine for* The New York Times *and writes about photonics for the* optics.org *newsroom.*



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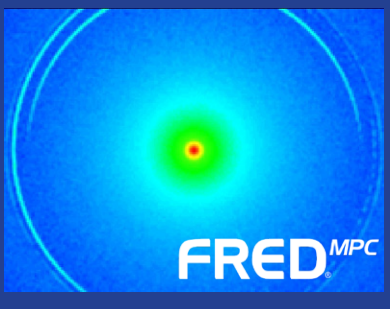

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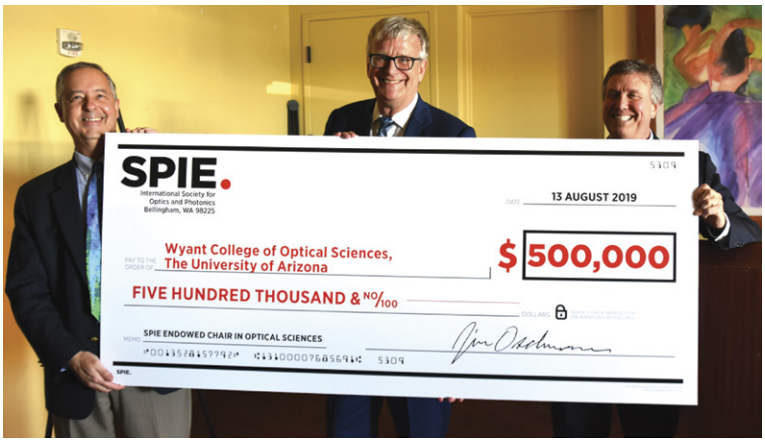
SPIE Announces $2.5 Million Educational Funding Initiative



On 13 August, SPIE announced a $2.5 million, five-year, educational-funding initiative. The SPIE Endowment Matching Program will enhance educational capacity in optics and photonics by supporting endowment funding at qualified institutions. The program adds to the more than $4 million that SPIE devotes annually to community support, including scholarships, travel grants, and student programs. The program's first grant of $500,000 creates the SPIE Chair in Optical Sciences at the University of Arizona.

With this new matching program, SPIE will support optics and photonics education and the future of the industry by contributing up to $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, matched by a factor of three with funds donated by James C. Wyant and his family, names a new, $2-million-endowed faculty chair. SPIE encourages qualified institutions to establish future endowments with the Society, structuring funds to ensure perpetual or long-term availability for teaching and research.

"SPIE's leadership and commitment is helping to scale-up the college with this new endowed faculty position, leading to more teaching, more research, and more students, enabling us to provide more expertise to the world," said Thomas Koch, dean of the Wyant College of Optical Sciences at the University of Arizona. "SPIE has long been a vigorous supporter of the College, but now we can generate even more talent to fuel innovations in robotics and autonomy, AR/VR, communications, biomedicine, astronomy, and all the other exciting fields enabled by optics and photonics. This is a critical and welcome investment in our faculty and students, and Jim Wyant's generosity and vision transforms the SPIE $500,000 contribution into a $2 million endowment."

SPIE CEO Kent Rochford emphasized the Society goal to partner with educators and universities to advance light-based research, technology, and applications for the betterment of the human condition. "As a not-for-profit educational charity, SPIE is uniquely positioned to devote resources that create a larger pipeline of scientists and engineers knowledgeable about optics," he said. "In partnership with the Wyant College of Optical Sciences, SPIE is helping to create the future."

SPIE President Jim Oschmann emphasized the support of the Society's Board of Directors for this initiative. "The proposal to fund an endowed chair, initiated by Jim Wyant's philanthropy, generated a terrific reaction from the SPIE Board. We were delighted to approve this exciting program and look forward to creating multiple new endowments in partnership with our colleagues at educational institutions across the optics and photonics community."

SPIE Election Results

On 13 August, the results of the 2019 election were announced. SPIE Fellow Anita Mahadevan-Jansen, professor of biomedical engineering at Vanderbilt University, has been elected to serve as the 2020 Vice President of SPIE. With her election, Mahadevan-Jansen joins the SPIE presidential chain and will serve as President Elect in 2021, and as the Society's President in 2022.

Mahadevan-Jansen is the founding director of the Biophotonics Center at Vanderbilt University. She has previously served on the SPIE Board of Directors and the following SPIE committees: Diversity and Inclusion Ad Hoc, Awards, Membership and Communities, and Fellows.

Jason Mulliner, Chief Financial Officer at Alluxa Inc., was elected to serve as the 2020 Secretary/Treasurer. He served in the same role in 2019.

The newly elected Society Directors, who will serve three-year terms for 2020-2022, are:

- Halina Rubinsztein-Dunlop, The University of Queensland (Australia)
- Katie Schwertz, Edmund Optics, Inc. (USA)
- Cristina Solano, Centro de Investigaciones en Óptica (Mexico)
- J. Scott Tyo, University of New South Wales Canberra (Australia)

The SPIE Nominating Committee accepts recommendations for the election slate on an ongoing basis. To make a recommendation, or for more information, email **governance@spie.org**.


Mahadevan-Jansen


Mulliner


Rubinsztein-Dunlop


Schwertz


Solano


Tyo

SPIE Awards

Since 1959 SPIE has honored the best in optics and photonics for their significant achievements and contributions in advancing the science of light.

GOLD MEDAL: Robert Alfano

"He is, and has long been, one of the most widely respected and influential figures in laser physics," says SPIE Vice President David Andrews, professor of physics at University of East Anglia. "Many young scientists regard him as almost legendary."

The legend Andrews refers to is SPIE Member Robert Alfano, professor of science and engineering at The City College of New York, New York, who is the 2019 recipient of the SPIE Gold Medal Award in recognition of outstanding seminal achievements and contributions to advancement of knowledge on fundamental properties of materials and their interaction with light in areas of biology, condensed matter, semiconductors, tunable lasers, and biomedical optics.

Among his most notable achievements, Alfano discovered and subsequently developed supercontinuum light produced with an ultrashort pulsed laser. Alfano also contributed to the burgeoning field of biophotonics in the 1980s and 1990s, work that resulted in development of techniques for optical biopsy. His work on time-gated diffusive light propagation in tissue during the same time period also helped develop the fields of near-infrared spectroscopy and imaging in random media. "The impact of these advances is clear to see," says Andrew Forbes, professor of physics at University of the Witwatesrand, Johannesburg. "There are entire conferences dedicated to these themes."

More recently, Alfano has applied his efforts to the study of structured light, where he has also made seminal contributions, including the theoretical construction of a new Poincaré sphere for the total angular momentum of light. According to Forbes, "It is no small feat to reinvent a concept so ubiquitous in optics."

The SPIE Gold Medal is the highest honor the Society bestows. Since 1977, it has been awarded in recognition of outstanding engineering or scientific accomplishments in optics, photonics, electro-optics, or imaging technologies or applications. Recipients have made an exceptional contribution to the advancement of relevant technology.

DIRECTOR'S AWARD: Carmiña Londoño

Dr. Carmiña Londoño is the Deputy Division Director of the National Science Foundation Division for Electrical, Communication and Cyber Systems. Over the last thirty years, Londoño has actively contributed to SPIE, supporting wholeheartedly its mission to advance light-based research, engineering, and technologies that address societal challenges at a global scale and result in the betterment of humanity.

Londoño was recognized with the SPIE Director's Award for her exceptional contributions to SPIE, her work on numerous conference and leadership committees, her advocacy for public policy that supports photonics, shaping the SPIE Student Chapter program, service as the SPIE representative to the International Commission for Optics, and co-founding the SPIE Women in Optics program.

The SPIE Directors' Award is presented to an individual who, in the opinion of the Board of Directors, has rendered a significant service of outstanding benefit to the Society.

SPIE SENIOR MEMBERS are Members of distinction honored for their professional experience, their active involvement with the optics community and SPIE, and/or significant performance that sets them apart from their peers.

See the list of 2019 Senior Members online:

spie.org/SeniorMembers

Many SPIE award recipients accepted their awards at the Awards Banquet at SPIE Optics + Photonics 2019. These notable individuals have all been highlighted in past issues of *SPIE Professional*.

PRESIDENT'S AWARD:

William H. Arnold

The SPIE President's Award is presented to an individual who, in the opinion of the President and the Board of Directors, has rendered a unique and meritorious service of outstanding benefit to the Society.

SPIE Fellow and former SPIE President William H. Arnold, ASML US, is the recipient of the 2019 SPIE President's Award. The SPIE President's Award recognizes his dedicated and generous commitment to SPIE through outstanding service, guidance, engagement, and leadership. He contributed decades of work to champion a range of activities that ensure SPIE continues to be relevant to industry, assuring not only the betterment of the Society, but the entire photonics community.

2019 SPIE President Jim Oschmann served on the SPIE Board of Directors when Arnold was President. He says, "I was fortunate to get to know Bill and witness his adept leadership in action as he achieved key accomplishments, including strengthening our industrial relationships and standing up the National Photonics Initiative. These represent but a small fraction of Bill's integrity and service to our community."

VISIONARY AWARD:

James C. Wyant

SPIE Fellow and former SPIE President James C. Wyant, University of Arizona (UA), has forged a highly successful life in optics, including his transformative work as the founding dean of the UA College of Optical Sciences, and his entrepreneurial leadership in such companies as WYKO and 4D Technology.

Under Wyant's future-facing direction and his deeply held belief in the importance of optics, that career-long success story has had a generous ripple effect. In 2013, his $10 million gift to UA's College of Optical Sciences helped to establish 30 first-year graduate student scholarships, and in late 2018, he and his family pledged $20 million for ten endowed faculty chair positions.

In acknowledgement and thanks for his role as founding dean of the College of Optical Sciences at the University of Arizona; for pioneering photonics at WYKO Corporation and 4D Technology; for deeply generous philanthropy to enable education in optics; and for thoughtful investment in the future of photonics, James C. Wyant is the 2019 recipient of the SPIE Visionary Award.

The SPIE Visionary Award is presented to individuals whose work demonstrates any or all qualities of exceptional foresight, creativity, advocacy, and vision, that furthers the research, development, and industries related to light-based technologies.

"The optics and photonics community has a number of luminaries who have made extraordinary impacts in education, invented new products and created new businesses, or generously given back to the community through outsized support of students or education," says SPIE CEO Kent Rochford. "But very few have done all three. Jim Wyant has. He met all of the qualifications of the SPIE Visionary Award, and then some. I, and the SPIE Board of Directors, am proud to honor Jim with this award."

HAROLD E. EDGERTON AWARD IN HIGH-SPEED OPTICS:

John Dudley

John Dudley, professor of physics at Université Bourgogne-Franché-Comte and the CNRS Institute FEMTO-ST, France, is a pioneer of applications of ultrashort-pulse measurement techniques in nonlinear fiber optics. Specifically, his studies of ultrafast self-similarity, supercontinuum generation, and novel classes of optical soliton and optical rogue waves have made a significant contribution toward understanding high-speed physical phenomena.

In honor of his achievements in ultrafast phenomena, SPIE Senior Member John Dudley is being recognized with the SPIE Harold E. Edgerton Award.

Professor Wilson Sibbett, Wardlaw Professor of Physics at University of St. Andrews, United Kingdom, worked in the field of high-speed photography and knew Harold Edgerton, the award's namesake. "Knowing something of Edgerton's originality and flair in research techniques, I can see many parallels with the approach taken by John Dudley in the ways that he chooses to convey his understanding and application of physics, and optics in particular," he says. "Both had an ability to translate rather complex concepts through complementary theoretical and practical routes in a manner that brings the concepts to life!"

The SPIE Harold E. Edgerton Award recognizes the application and understanding of high-speed physical phenomena, including the development of new technologies as well as new applications of existing technologies.

Photonics West BiOS 2020

A changing guard vows to continue the tradition of excellence

After 15 years as co-chairs of the SPIE Photonics West BiOS Symposium, Rox Anderson and James Fujimoto are passing the baton to Jennifer Barton, Director of the BIO5 Institute at University of Arizona, and Wolfgang Drexler, Head of the Center for Medical Physics and Biomedical Engineering at Medical University of Vienna.

Drexler brings his experience of managing a large research center that focuses on the development of cutting-edge technology for translational medical diagnosis and therapy, as well as nearly 30 years of experience in optical imaging.

Barton brings to this leadership role her experience as director of an interdisciplinary institute that tackles the big problems, such as how to detect cancer earlier, how to feed nine billion people, and how to have a health span that matches our lifespan. This type of big-picture thinking, combined with an emphasis on interdisciplinary collaboration, is well aligned with the BiOS Symposium.

Barton emphasizes the importance of interdisciplinary research, both at Photonics West and in academia. "There's still a need for disciplines—people need to be well-trained in a specific field—but the problems have become so complex that there's not a lot of headway being made by strictly staying within your own discipline," she says. "If we can put new people together, they may work together. For example, something like sensors for health involve optical sciences, health sciences, and engineering."

Drexler agrees that the cross-pollination of ideas that takes place at Photonics West is important to attendees, since the BiOS Symposium precedes the co-located LASE and OPTO Symposia. "On the weekend you have these more biomedical-oriented meetings that are a hybrid between technology and clinic, then the week transitions into the more engineering- and science-driven sessions," he says.

In addition to reinforcing the interdisciplinary nature of BiOS, the co-chairs believe it's important that BiOS maintains a balance between academic and industry, research and clinical. Drexler recalls that 20 years ago, the BiOS Expo had just 10 or 20 companies, but now there are more than 200 exhibitors. "It's good for students to see that there's industry for them to go to work in, not just academia," he says.

Likewise, Barton thinks the involvement of industry is important to the success of biophotonics research. Even with the most basic discoveries, she thinks it's important to have an eye toward how they are going to translate, either bench to bedside, or bench to marketplace. "I would absolutely love to have more industry participation in BiOS," she says. "I think it's good already, and can always be better."

Barton and Drexler are committed to ensuring that the BiOS Symposium remains technologically relevant in these rapidly changing times by looking for new trends and activities. In fact, they've gotten an early start by adding three new conferences to BiOS 2020.

A conference focused on biophotonics and exercise science will cover wearable technologies, which incorporates a broad range of sciences, including sensor technologies for gathering the data, transmission of that data to a server, data analysis, and finally implementing a feedback loop back to the person or environment.

Another new conference for 2020 focuses on optical and radiation source technologies, two central pillars for human medical imaging and therapy. Both radiative and optical techniques have their strengths and weaknesses in medical imaging, and this conference will explore their interaction.

The third new conference is multiscale imaging and spectroscopy, which is intended to address the development and applications of single and multimodality techniques that characterize biological systems over multiple temporal, spatial, or contrast scales. For example, if optical technologies provide a microscopic view, and modalities like MRI provide a macroscopic view, how do you combine those data in a clinically useful manner?

Drexler and Barton are both very busy people who run large centers while still conducting their own research. As for why they would want to take on such a large volunteer role as co-chairing BiOS, Barton doesn't hesitate. "It's *the conference* in biomedical optics, so who wouldn't want this job? SPIE has done an amazing job bringing this community together and growing this conference, and I feel like I've grown up with it. It's really very exciting to have an opportunity to help lead it."

Barton

Drexler

Drexler adds, "I feel very honored to be the first European co-chair of this prestigious conference, and being allowed to shape it to continue to be an exciting event for the entire scientific community. In this way I can give back for what I gratefully received over the last 20 years." ■

SPIE. PHOTONICS WEST BIOS

Review the program online

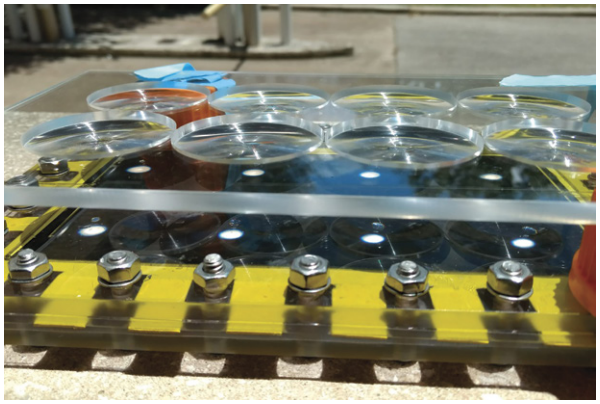
spie.org/pw

The Discoveries Are in the Details

Naomi Halas, plenary speaker at SPIE Photonics Asia 2019, discusses her research on nanoparticles and its broad-reaching applications

More than 15 years ago, Naomi Halas's team demonstrated that if they manipulated a noble metal nanoparticle's geometry, they could control the color of the light that it absorbed. "This is a fundamental concept," says Halas, who will be delivering a plenary at 2019 SPIE Photonics Asia in October. "But at the time the world of nanoscience revolved around quantum dots, not metallic nanoparticles with plasmon resonances. No one was thinking about nanoparticles as objects by which you could control light at the nanoscale and beyond."

Halas recalls, "At that time people were also just beginning to learn to exploit the light-penetrating properties of tissue, in particular the spectral regions of increased transparency, known as 'water windows'. We realized that we could design and create nanoparticles that could absorb light in those wavelength regions, which would induce a photothermal heating effect. That resulted in demonstrating—first in cells, then in mice—photothermal cancer therapy: the nanoparticles reside in the tumor, you shine light into it, and the nanoparticles heat up and destroy the cancer."



Credit: Pratiksha Dongare/Rice University

Concentrating the sunlight on tiny spots on the heat-generating membrane exploits an inherent and previously unrecognized nonlinear relationship between photothermal heating and vapor pressure.

A clinical trial on prostate cancer utilizing photothermal cancer therapy has been ongoing for the past year and a half, with a 94 percent success rate. "It's so promising," says Halas. "People have had this treatment without side effects. It has been a huge improvement for the better."

A more recent breakthrough for Halas' team has been enhancing the efficiency of their solar-powered desalination system by over 50 percent, simply by adding arrays of lenses that concentrate sunlight into "hot spots." Improving their nanophotonics-enabled solar membrane-distillation (NESMD) system also emerged from Halas' focus on understanding the fundamental science behind the vaporization process central to distillation. The NESMD technology, originally created five years ago to create a mobile, off-grid version of more conventional, much larger, energy-consuming facilities, utilizes light-absorbing nanoparticles to transform the membrane—a small, sheet-like-device that has hot, salty water flowing across one side while cool, filtered water flows across the other—into a solar-driven heating element.

The physical process of the system, says Halas, depends on the saturation vapor pressure of water which has a temperature dependence that is exponential. "Focusing light increases the temperature of the system in localized regions. Instead of trying to expand our equipment to capture more light, we just intensified the light we were already getting, and the efficiency jumped substantially."

Halas feels a strong sense of responsibility of science to society, and part of that means continuing to explore her own scientific discoveries. "The truth is that scientists are always curious. They're always going to stop and ask—even if they're doing something as mundane as building a membrane distillation apparatus to take outdoors—"Well, gee guys, do we really understand how this thing really works?" My business is nanoparticles and light, and the question always remains: how can we use that to develop innovative methods to solve our biggest challenges?" ■

*–**Daneet Steffens** is the PR Manager for SPIE.*

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Upcoming events and deadlines

OCTOBER

1-4: Seventh European Workshop on Optical Fibre Sensors, Limassol, Cyprus

9-10: SPIE Photonex, Coventry, United Kingdom

11: Deadline to apply for 2020 Prism Awards for Photonics Innovation

14-17: SPIE Optifab, Rochester, New York, USA

16: Abstracts due for SPIE Smart Structures + Nondestructive Evaluation 2020

16: Abstracts due for SPIE Defense + Commercial Sensing 2020

20-23: SPIE/COS Photonics Asia, Hangzhou, China

23: Applications due for Rising Researchers

NOVEMBER

2-4: 2019 International Conference on Optical Instruments and Technology, Beijing, China

13-14: SPIE Future Sensing Technologies, Tokyo, Japan

13: Abstracts due for SPIE Astronomical Telescopes + Instrumentation 2020

15: Applications due for Startup Challenge at Photonics West

DECEMBER

8-12: Australian and New Zealand Conferences on Optics and Photonics, Melbourne, Australia

15: Applications due for SPIE IDL Micro Grants

JANUARY

16: Abstracts due for SPIE Structured Light 2020

16: Abstracts due for SPIE/SIOM Pacific Rim Laser Damage 2020

17: SPIE Photonics West 2020 early registration deadline

FEBRUARY

1-6: SPIE Photonics West 2020, San Francisco, California, USA

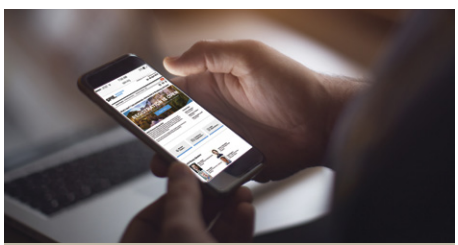
2-4: SPIE AR|VR|MR 2020, San Francisco, California, USA

12: Abstracts due for SPIE Optics + Photonics 2020

15: Applications due for SPIE Optics and Photonics Education Scholarships

15-20: SPIE Medical Imaging 2020, Houston, Texas, USA

23-27: SPIE Advanced Lithography 2020, San Jose, California, USA



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*Soft tolerancing units

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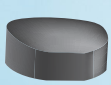
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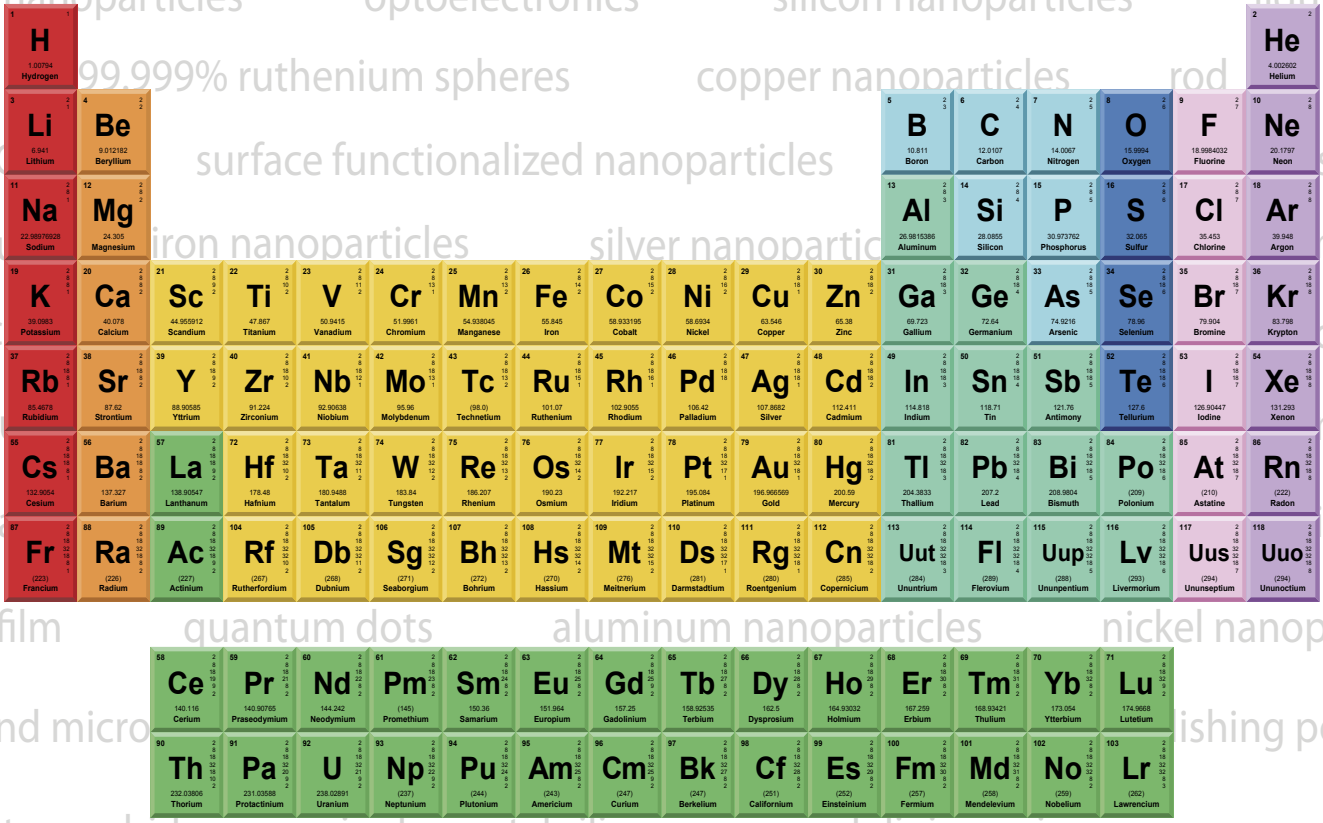

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