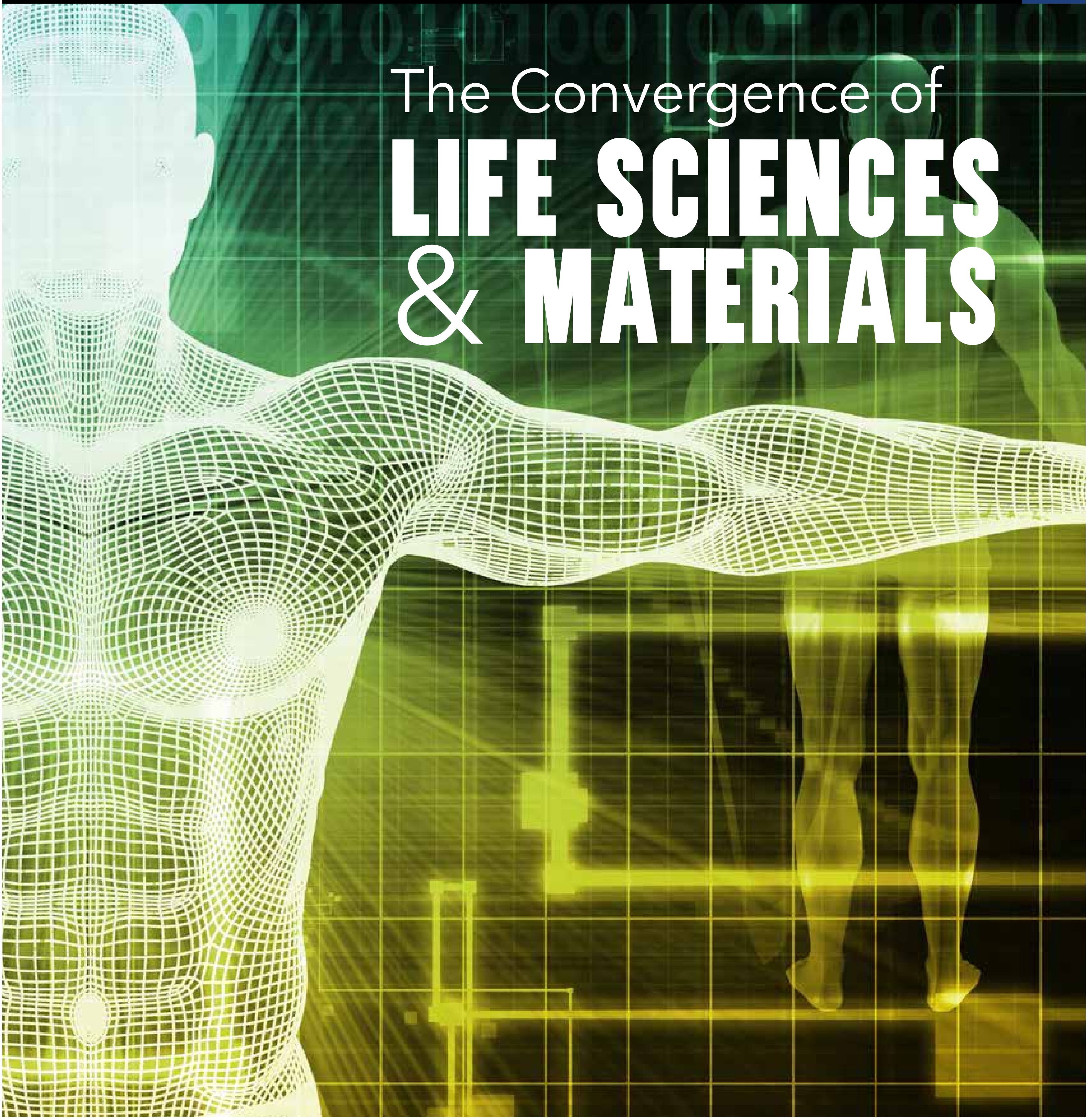
PennState
Materials Research
Institute

FOCUS on MATERIALS

MATERIALS RESEARCH INSTITUTE BULLETIN

SUMMER 2018



The Convergence of LIFE SCIENCES & MATERIALS

FOCUS on MATERIALS
MATERIALS RESEARCH INSTITUTE BULLETIN

Focus on Materials is a bulletin of the Materials Research Institute at Penn State University. Visit our web site at **www.mri.psu.edu**.

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U. Ed. RES 18-01

A message from the Director

The topic of this issue of Focus on Materials comes at a timely moment. We have just wrapped up our latest seed grant funding initiative on the convergence of materials and the life sciences.

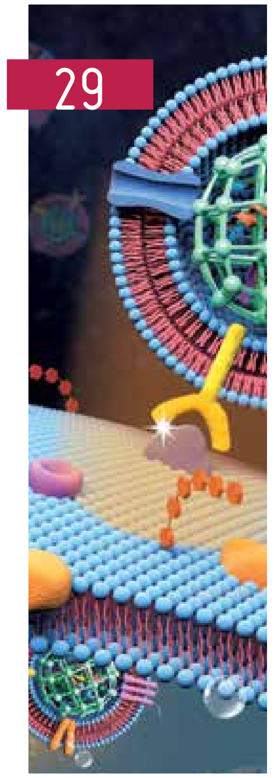
Led by MRI, in partnership with Penn State College of Medicine and the Huck Institutes of the Life Sciences, we received 38 strong proposals of which 10 will be funded. Our aim was to encourage faculty to propose high-risk research ideas that could have significant impacts on human health. Seed funding will allow researchers to gather preliminary data for future NIH grant proposals. We also encouraged forming collaborations across colleges and institutes. The funded proposals fall under three broad categories: regenerative medicine, bioimaging, and diagnostics. Our reviewers gave each of the 38 proposals high marks, but these 10 stood out in one aspect or another. Congratulations to all who participated.

Convergence, as described in this focus issue, is part of the institutes' and university's strategic plans. Over the past three years, Penn State has made a concerted effort to put the university in a leadership position in some of our strength areas at the nexus of materials, life sciences, and medicine, primarily through key faculty hires, but also through this and other seed grant initiatives. Research across the silos of departments and colleges is at the heart of the seven university-wide research institutes that include MRI and Huck, along with the Institutes for Energy and the Environment, the Institute for CyberScience, Clinical and Translational Science Institute, Social Science Research Institute, and Penn State Hershey Cancer Institute.

When you are in the neighborhood, we invite you to visit our Pioneers of Materials poster gallery, currently located on the 2nd floor of the materials wing of the Millennium Science Complex, to learn more about important figures in the rich history of materials at Penn State. More pioneers are to be added in due course, so that the culture and intellectual impact of those that came before will not be lost.

C A Randall

contents



Cover art: Shutterstock

4 HUMANITARIAN MATERIALS ENGINEERING

Six Penn State faculty attended the 9th International Conference of the African Materials Research Society in Gaborone, Botswana.

8 RESEARCH SNAPSHOTS

Short reports on atomic layer etching, sintering atomically thin materials with ceramics, water harvesting in air, and flexible ceramic foam that can harvest energy.

10 CONVERGENCE PENN STATE

AN OVERVIEW: An interview with two leaders of the Huck Institutes of the Life Sciences provides insights on the convergence of materials and life sciences on campus.

14 NANOCOMPOSITES IN THE BODY

Dan Hayes's "bone foam" fills voids in bone tissue and is almost ready for commercialization.

18 APPLYING PHYSICS TO BIOLOGY

Igor Aronson tells us that the rules of physics can be applied to biological systems.

22 A ONE-OF-A-KIND CRYOGENIC MICROSCOPE

In a quiet room in the basement of the Millennium Science Complex, a unique electron microscope is taking its scientific shake-down cruise under the leadership of Susan Hafenstein, an associate professor of biochemistry and molecular biology with experience in cryogenic microscopy for the life sciences.

26 MEET SLAVA ROTKIN

The development of synthetic DNA has opened up new territories of research at the forefront of biotechnology. Synthetic DNA could be used to create designer drugs and even new forms of life never seen in nature, for good or ill.

32 THE MECHANICS OF LIVING MATERIALS

A researcher brings his interest in the mechanics of materials deformation to the study of the consequences when cells, tissue, and organs undergo mechanical or other loading.

GABORONE, BOTSWANA

Penn Staters Attend the African MRS Conference in Botswana

Credit: Adobe Stock

SIX PENN STATE faculty attended the 9th International Conference of the African Materials Research Society in Gaborone, Botswana, over four days in December. Five of the six attendees are members of the Materials Research Institute, there to learn more about how they could help Africans solve challenges with the help of materials engineering.

Gaborone, the capital, is a modern city, and Botswana has a stable democratic government and one of the highest per capita incomes in Africa. But there are environmental problems, water shortage and spreading desertification – 70 percent of Botswana is in the Kalahari Desert. HIV-AIDS is also a significant health problem

“It was a typical research meeting in that you get to exchange ideas and research but in a context that is relevant to Africa,” said Ismaila Dabo, an assistant professor in Penn State’s Department of Materials Science and Engineering. “The themes of the meeting were materials for health, water, energy, agriculture and the environment, mining, construction, nanoscience and nanotechnology, plus computational materials science.”

Dabo, along with DK Osseo-Asare, Esther Obonyo, Kofi Adu, and Clive Randall, are all affiliates of the Materials Research Institute. Also attending was Michael Adewumi, vice provost for Global Programs, Penn State, who spoke at the meeting. Osseo-Asare also presented a talk on the topic of the mining of mineral resources in Ghana and finding new ways to extract resources without the environmental impact.

“There were a lot of young researchers there to present their Ph.D. research,” Dabo continued. “So, I got the perspective on what is going on in South Africa, Nigeria, and other African countries.

“I WOULD SAY that from my perspective, the research is the same quality as you would find anywhere, and I was very impressed by the students. There was a mixture of what you would find at a materials conference anywhere with research focused on African problems.”

There was a lot of interest in computational materials science, Dabo’s field, among students from Africa, because they could log in remotely to access computational resources that were not available locally. UNESCO has set up an exchange program between African countries and the International Center for Theoretical Physics, in Italy, and many of the students there were part of that program. Some of the African students were studying at universities in the U.S.

“There will be another edition of this conference somewhere in Africa in two years,” Dabo concluded.

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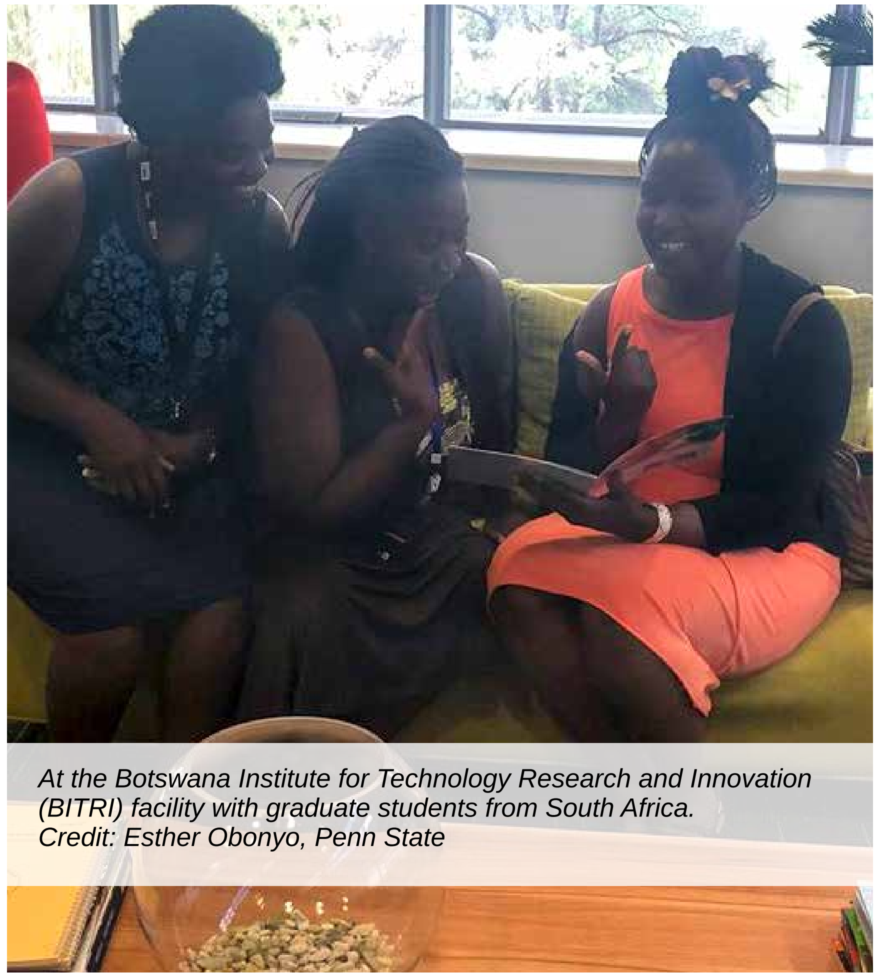
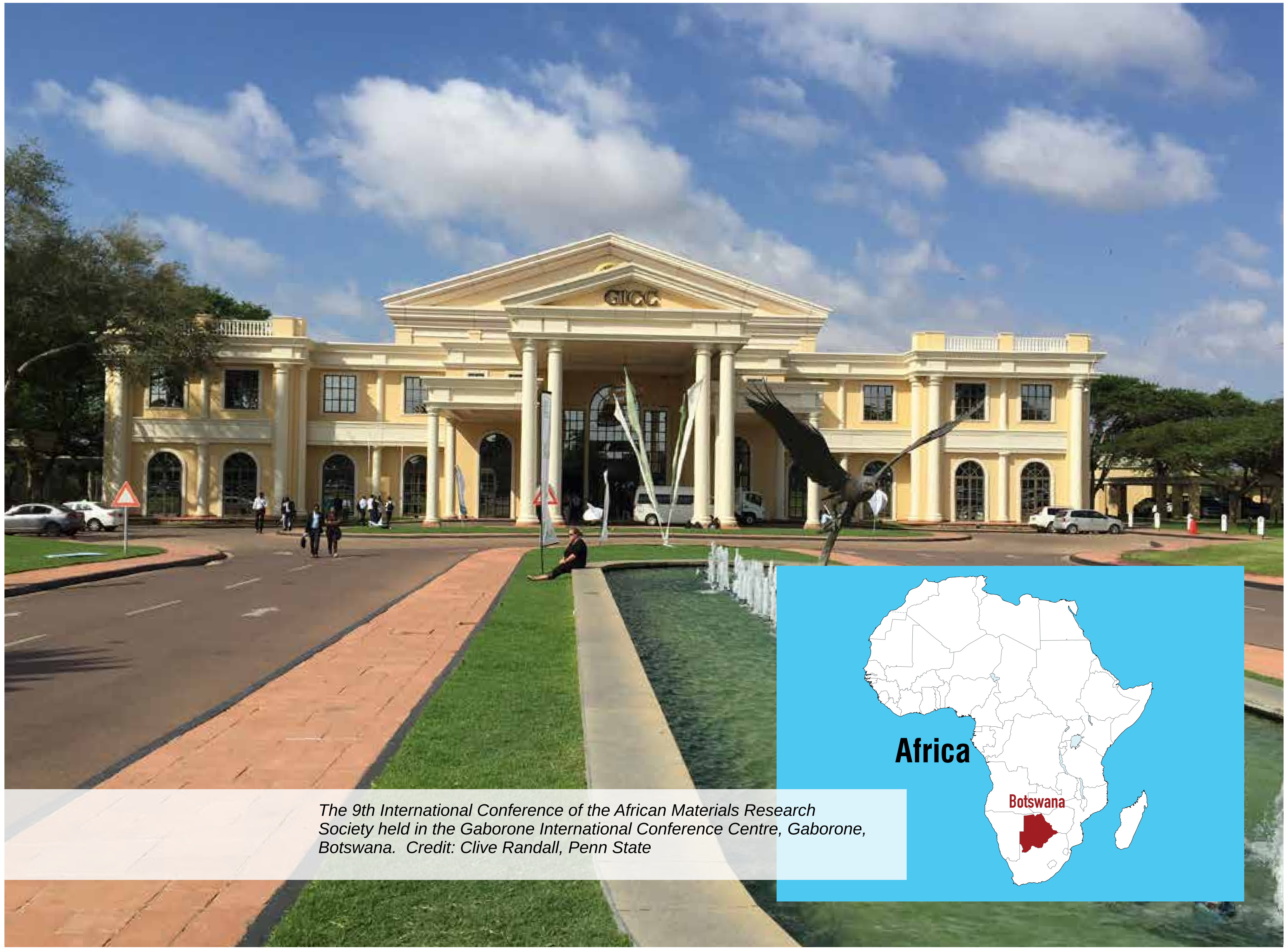


At the Botswana Institute for Technology Research and Innovation (BITRI) facility with graduate students from South Africa. Credit: Esther Obonyo, Penn State



The 9th International Conference of the African Materials Research Society held in the Gaborone International Conference Centre, Gaborone, Botswana. Credit: Clive Randall, Penn State

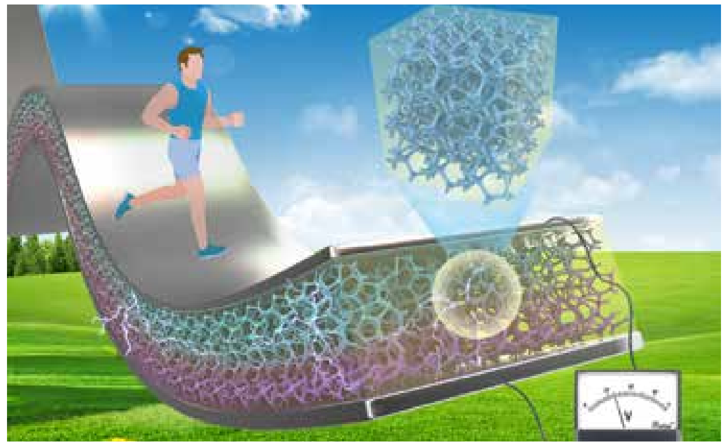
Materials Research Institute's Vision for Humanitarian Materials Engineering

The Materials Research Institute, which coordinates interdisciplinary materials-related research at Penn State, is actively expanding its humanitarian materials engineering initiative with strategic partners within the university and beyond.

Housing
Food Supply
Clean Water
Energy Resources
Global Health

research SNAPSHOTS

Research Snapshots are brief summaries of significant materials-related breakthroughs by MRI researchers.



A flexible ceramic foam for energy harvesting. Wang Lab/Penn State

Flexible, Highly Efficient Multimodal Energy Harvesting

A PIEZOELECTRIC CERAMIC FOAM supported by a flexible polymer support provides a 10-fold increase in the ability to harvest mechanical and thermal energy over standard piezo composites, according to Penn State researchers.

In the search for ways to harvest small amounts of energy to run mobile electronic devices or sensors for health monitoring, researchers typically add hard ceramic nanoparticles or nanowires to a soft, flexible polymer support. The polymer provides the flexibility, while the piezo nanoparticles convert the mechanical energy into electrical voltage. But these materials are relatively inefficient, because upon mechanical loading the mechanical energy is largely absorbed by the bulk of the polymer, with a very small fraction being transferred to the piezo nanoparticles. While adding more ceramic would increase the energy efficiency, it comes with the tradeoff of less flexibility.

“We see that this 3D composite has a much higher energy output under different modes,” said Qing Wang, professor of materials science and engineering, Penn State. “We can stretch it, bend it press it. And at the same time, it can be used as a pyroelectric energy harvester if there is a temperature gradient of at least a few degrees.”

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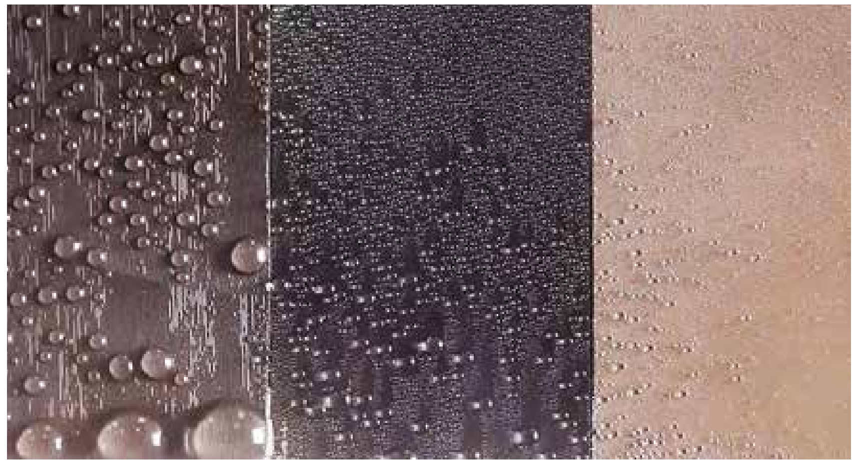
Microengineered Slippery Rough Surface for Water Harvesting in Air



The left panel is a directional slippery rough surface (SRS, this study), the middle panel is a slippery liquid-infused porous surface (SLIPS) and the right panel is a superhydrophobic surface. This image shows a comparison of water harvesting performance of SRS vs other state-of-the-art liquid repellent surfaces.
Credit: Xianming Dai/Nan Sun/Jing Wang/Tak-Sing Wong, Penn State

A SLIPPERY ROUGH SURFACE (SRS) inspired by both pitcher plants and rice leaves outperforms state-of-the-art liquid-repellent surfaces in water harvesting applications, according to a team of researchers at Penn State and University of Texas at Dallas.

“With an estimated 4 billion people living in a situation of water scarcity during at least some part of the year, an inexpensive method for harvesting water from water vapor or from fog droplets in air could have enormous practical applications, and will help alleviate the water scarcity issues in many regions of the world,” said the project’s leader, Tak-Sing Wong, who is the Wormley Family Early Career Professor in Engineering and assistant professor of mechanical engineering, Penn State.

“With SRS, we combined the slippery interface of pitcher plant with the surface architecture of rice leaf, which has micro/nanoscale directional grooves on its surface that allows water to be removed very easily in one direction but not the other,” said Simon Dai, Wong’s former post-doctoral scholar, now an assistant professor at UT Dallas.

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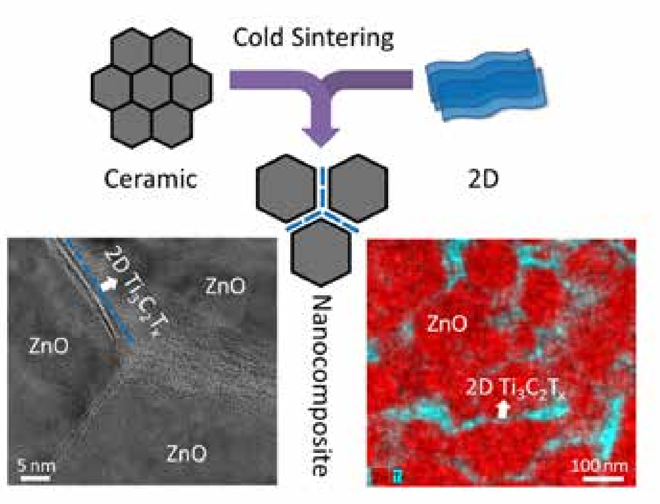
Sintering Atomically Thin Materials with Ceramics Now Possible



The schematic illustration showing the co-sintering of ceramics and 2D materials using cold sintering processing, and TEM image and energy dispersive spectroscopy (EDS) map of cold sintered 99ZnO-1Ti3C2Tx nanocomposite. The MXene nanosheets are distributed homogeneously along the ZnO grain boundaries, as seen in the TEM image and EDS map. Credit: MRI/Penn State

FOR THE FIRST time, researchers have created a nanocomposite of ceramics with a two-dimensional material, MXene, that opens the door to new designs of nanocomposites with a variety of applications, such as solid-state batteries, thermoelectrics, varistors, catalysts, chemical sensors and much more.

“We have industry people who are already very interested in this work,” said Jing Guo, a post-doctoral scholar working in the group of Clive Randall, professor of materials science and engineering, Penn State.

“This opens a whole new world incorporating 2D materials into ceramics,” said Randall.

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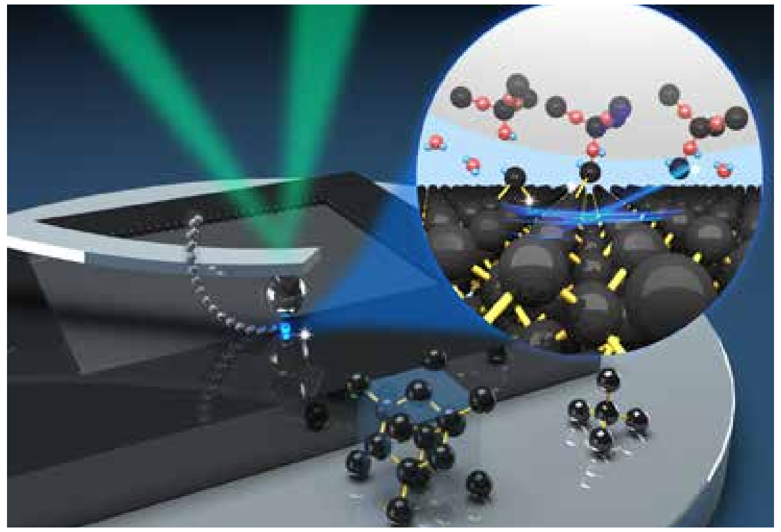
A Simple Method Etches Patterns at the Atomic Scale

A PRECISE CHEMICAL-FREE METHOD for etching nanoscale features on silicon wafers has been developed by a team from Penn State and Southwest Jiaotong University and Tsinghua University in China.

In standard lithography, a photosensitive film is deposited on a silicon wafer and a pattern called a mask is used to expose the film. Then, chemicals, such as KOH solutions, etch patterns into the silicon. Further steps are required to smooth out the roughened surface.

The researchers at Penn State and Southwest Jiaotong University developed an entirely different, chemical- and mask-free one-step process. They lightly rub a rounded silica tip of an instrument called a scanning probe microscope across a silicon substrate – the material typically used to make electronic devices. When exposed to the water vapor in air, the top layer of silicon forms bonds with the tip of the scanning probe and a single layer of atoms slides off as the probe moves across the silicon. Because the atoms below do not take part in the chemical reaction, they are completely undamaged.

“Atomic layer etching can provide the depth resolution that people would like to get without the use of sacrificial layers and harsh chemicals,” said Seong Kim, professor of chemical engineering, Penn State.



A single layer of silicon atoms (black) bind to the moving silica tip of a scanning probe microscope.
Credit: Lei Chen/Southwest Jiaotong University

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research SNAPSHOTS

Full articles on all snapshots can be read at **mri.psu.edu/news**

Credit: Adobe Stock

CONVERGENCE PENN STATE:

AN OVERVIEW

“Convergence is a deeper, more intentional approach to the integration of knowledge, techniques, and expertise from multiple disciplines in order to address the most compelling scientific and societal challenges.”

NSF Director France Córdova

FOCUS ON MATERIALS asked Peter Hudson and Jim Marden of the Huck Institutes of the Life Sciences for their thoughts on convergence of materials and life sciences at Penn State.

“Without question, the Millennium Science Complex is central to the idea of convergence at Penn State,” said Peter Hudson, director of the Huck Institutes of the Life Sciences. “I think the construction and vision that went into that building have been really important.

> “I CAN’T THINK of another university that has done it to the scale we have. To construct a building where life sciences meet materials sciences is, I think, unique.”
>
> PETER HUDSON

Hudson, who is an epidemiologist and Willaman Professor of Biology at Penn State, believed early on that some of the significant issues in the life sciences, ranging from blood disorders to genomic problems, infectious diseases to problems with the brain and nervous system, could be addressed by materials scientists with the knowledge and skills to build devices to interact with the human body.

“I thought that this was something special we could do, and I’m gratified to say that it has really worked better than I had expected,” he said. “And the first and ▶

most important reason for this is the appointment of new faculty who bridge the gap between materials and life sciences."

Hudson points to the recent hire of Igor Aronson, Huck Chair Professor of Biomedical Engineering, Chemistry, and Mathematics, as an example of someone who brings a materials approach to look at life science questions. (See pp. 18-21.)

"All by himself, he is an interdisciplinary team," Hudson said. "Igor is special because he really is a mathematician. He really is a physicist. He is doing both mathematical modeling and lab studies at the same time. So, he is somebody who can be a node for bringing these areas together."

One of the most significant moves toward convergence is the recent acquisition of a cryogenic electron microscope (Cryo-EM) to look at soft materials, primarily biological materials but also with materials science applications. A joint venture between the Huck Institutes and the Materials Research Institute, the Krios Cryo-EM is uniquely configured, with full life-science capabilities plus a number of standard materials science components that will allow for cross-disciplinary approaches.

"The really important thing we've done is to appoint exceptional faculty to work in that area, including Susan Hafenstein," Hudson said. (See pp. 22-25.)

JIM MARDEN

Jim Marden is director of operations for the Huck Institutes and a professor of biology.

"Much of our impact on convergence comes in the form of co-hires, mostly between Huck and engineering departments," he said. "We've made a number of co-hires with Biomedical Engineering. Or if not co-hires, we provide space for them or sweeten the pot for the faculty."

> "One way to measure success is when you brought this discipline and that discipline together and made something novel that neither could have done alone."

Marden sees another big part of Huck's contribution is connecting new faculty with others on campus who complement their research. "We do a lot of personal introductions. We try to accelerate the curve of their collaborations and research."

Huck faculty also frequently present their research at the Millennium Café, where speakers often describe issues that could call for collaborations across disciplines. The Millennium Café takes place in the Millennium Science Complex (MSC) Commons most Tuesdays throughout the year and features two 15-minute technical talks fueled by excellent coffees and pastries.

The co-location of instrumentation in the basement of the MSC also allows for an exchange of knowledge between life sciences and materials. "We've encouraged breaking down the culture walls between materials and life science. We have a lot of materials scientists working on our equipment and lots of our scientists use the Materials Characterization Lab, their TOF-SIMS, Cryo-FIB, and atomic force microscopy, for example."

Instruments such as these are common in materials science but have made little penetration into the life sciences, he said. But the kind of data that can be attained with these instruments would add value when writing a grant proposal or publishing a research article. To encourage crossing over these disciplinary boundaries, Huck and the Materials Research Institute (MRI) created a program, called Common Vision, to fund crossover instrument use and joint projects.

"ONE WAY TO measure success is when you brought this discipline and that discipline together and made something novel that neither could have done alone."

Marden spoke of new projects and opportunities involving orthopedic surgeons from the Hershey Medical Center and faculty in Kinesiology and Engineering, to try to predict when an elderly person might take a fall. It turns out that 50 percent of the total lifetime cost of medical treatment comes in the last six months of life, and that cost is often driven by a fall event. The project will require sensors, which MRI has expertise in, and will call on the expertise of social scientists to roll the project out to a larger community.

"There is a lot of knowledge across Penn State that is at the convergence of biology, mechanics, and engineering. Materials is also part of this, because you are putting materials in the body," Marden said.

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James H. Marden
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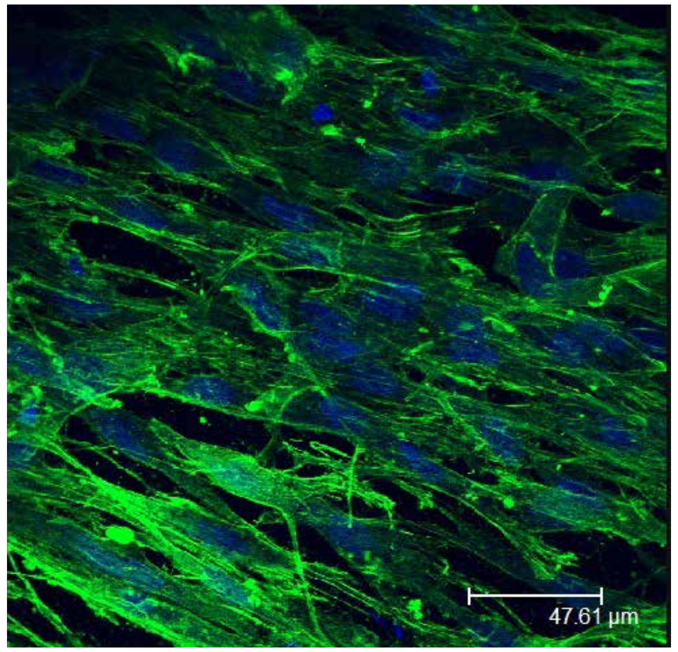
NANOCOMPOSITES in the BODY

After eight years at LSU, Dan Hayes brings his research program in biomaterials engineering back to Penn State.



Immunofluorescence image of cell sheet using F-Actin staining
Credit: Hayes Group

OPPOSITE:
Dan Hayes in his lab in the Millennium Science Complex

THE HAYES RESEARCH group focuses on two main topics: bone and tissue grafts, and nanoparticles for targeted delivery of therapeutics. Hayes is associate professor of biomedical engineering.

For the tissue grafts, his team develops injectable nanocomposites that polymerize at the desired location. Hayes calls this invention bone foam, and he says it is moving toward commercialization.

“The magic behind these in situ polymerizing materials is something called ‘click chemistry,’” Hayes said. Click chemistry reactions are powerful tools used in both materials and life sciences to couple small molecular units such as biomolecules together in a very specific and biocompatible manner.

Bone foam is an improvement on similar synthetic graft technologies, which are either more toxic than bone foam or cannot polymerize in the defect site. Most current grafts are made either from a patient’s own bone taken from another site in the body, or by bone taken from cadavers, neither of which is ideal.

“Our synthetic material is not rejected by the body. It’s akin to polyethylene glycol, which is a commonly used biomaterial,” Hayes said.

They increase the cross-linkage of the polymer chains and add a nanoceramic component to change the mechanical properties into a much more bonelike material. With their start-up company, OsteoSynth, they intend to first target the dental market, which is on the order of $800 million globally. Once they have cracked that segment, the market for all bone void filler products is closer to $2 billion annually.

“If the FDA regulates bone foam as a medical device, it is a short step to getting our product commercialized. We are targeting a 2020 launch date,” Hayes said.

NANODELIVERY

In a new project sponsored by the Department of Defense, Hayes and company will use nanoparticles to deliver small interfering RNA as a therapeutic to bone tissue. siRNA mimics a potent regulator of bone formation and needs to be carefully targeted to the bone-defect region to avoid ectopic bone growth, which is bone growth where it is not wanted.

To deliver the siRNA, Hayes’s team will use a nanoparticle that has two different metals – one side will be gold and the other side a magnetic material. On one side they attach a payload, and on the other side they attach the targeting molecule. The targeting molecule carries the nanoparticle to the progenitor cells in the bone defect site. When the magnetic side is stimulated by a radio frequency signal, the nanoparticle begins to wobble and heat up. The siRNA gets released in a controllable manner that is dependent on the linking chemistry and the amount of heat.

▶

“WE USE RADIO frequency because, unlike light, it penetrates the body,” Hayes said. “Gold is well tolerated in the body and iron is common in the body. For the most part the nanoparticles just get cleared out.”

This same technology can be used to deliver potent anticancer drugs. In fact, Hayes has a project started with Adam Glick, professor of molecular toxicology and carcinogenesis in Penn State's Huck Institutes of the Life Sciences, to improve cancer therapeutics while reducing side effects.

Because the nanoparticles will likely be considered a pharmaceutical by the FDA, Hayes thinks that project has a 10-year timeline.

3D BIOPRINTING FOR TISSUE ENGINEERING

Associate professor of engineering science and mechanics Ibrahim Ozbolat is an expert at 3D bioprinting of tissue. In his laboratory in the Millennium Science Complex, Ozbolat is developing a number of 3D printing techniques and materials for tissue reconstruction and regeneration. He is also building organ-on-a-chip devices to study diseases of the pancreas and heart, as well as cancer.

Hayes's interactions with Ozbolat is in trying to drive the progenitor cells or stem cells to induce the differentiation pathways that they want, particularly for bone and cartilage formation.

> “Our synthetic material is not rejected by the body. It's akin to polyethylene glycol, which is a commonly used biomaterial.”

“When you print these cells, they have both environmental clues from the material you are printing around them, and molecular clues for the nearby tissue,” said Hayes.

THOUGHTS ON CONVERGENCE

“The convergence of materials research and biology or the health sciences is a very ripe area,” Hayes remarked. “A lot of the solutions that we are going to see in the future to disease prevention and treatment are going to leverage both materials and traditional molecular biology. Those are two very valuable toolsets, and we are beginning to understand them well enough to leverage them both.”

The work that Ozbolat is doing is a classic example of a convergence problem, Hayes said. Molecular clues are driving the cell biology and materials are also driving cell biology and providing structural support and the form factor required by physicians to put the bone or cartilage to use.

“WE RECOGNIZE IN the field of regenerative medicine that we have to bring both fields together. If you have one without the other, you are left where we are today,” he said.

The Millennium Science Complex drives convergence. Unlike a traditional building that houses researchers from the same department, the MSC is filled with electrical and mechanical engineers, materials and computational scientists, in one wing, biologists and epidemiologists, neuroscientists, and plant scientists in the other wing.

“Having that fertile environment is important. Along with all those different investigators come all of these different suites of techniques. And then having the core facilities all in one building, these all accelerate the processes tremendously.”

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Hayes is also working with Dino Ravnic, a Penn State surgeon and assistant professor in the College of Medicine and Aman Dhawan an associate professor and orthopedic surgeon, who is a co-PI on the DoD-funded nanodelivery project.

HOW DID YOU GET INTERESTED IN THIS FIELD?

“I was working in the field of neuroscience, cell biology for neural development, at New York University in the lab of Ed Ziff and Tom Horniak. Because I am originally from State College and was family friends with Steve Fonash, who was then running the Penn State Nanofabrication facility, he reached out to me and invited me to come back and do some research over a summer,” Hayes said. “One thing led to another and he invited me to stay for graduate school.”

Fonash, who has since retired, became Hayes's adviser in the Department of Engineering Science and Mechanics. His vision of the possibilities at the intersection of nanotechnology and biology captured Hayes and led to his own career.

“He had a vision of leveraging nanofabrication to control protein function, cellular function, and tissue function,” said Hayes. “A lot of the work we have done has grown evolutionarily from Steve's work years ago.” ■

convergence SNAPSHOT

A Safe Optical Fiber for Delivering Light and Drugs into the Body

A view of light delivery through a citrate-based optical fiber Credit: D. Shan/C. Zhang / Penn State

IN PENN STATE'S Materials Research Institute, an electrical engineer and a biomaterials engineer have joined their expertise to develop a flexible, biodegradable optical fiber to deliver light into the body for medical applications.

The ability to deliver light into the body is important for laser surgery, drug activation, optical imaging, diagnosis of disease and in the experimental field of optogenetics, in which light is used to manipulate the function of neurons in the brain. Yet, delivering light into the body is difficult and typically requires the implantation of an optical fiber made of glass.

“THE PROBLEM IS that visible light can only penetrate to a certain depth, maybe hundreds of microns. Near infrared light might be able to penetrate a few millimeters to a centimeter, but that is not enough to see what is going on,” said Jian Yang, professor of biomedical engineering, Penn State.

Yang is collaborating with Zhiwen Liu, Penn State professor of electrical engineering, on using Yang's citrate-based polymer to create a step-index optical fiber for light delivery inside the body.

“This new type of fiber creates a transparent window for peeking into a turbid tissue, and can enable new opportunities for imaging,” Liu said.

This work was supported by the National Institutes of Health.

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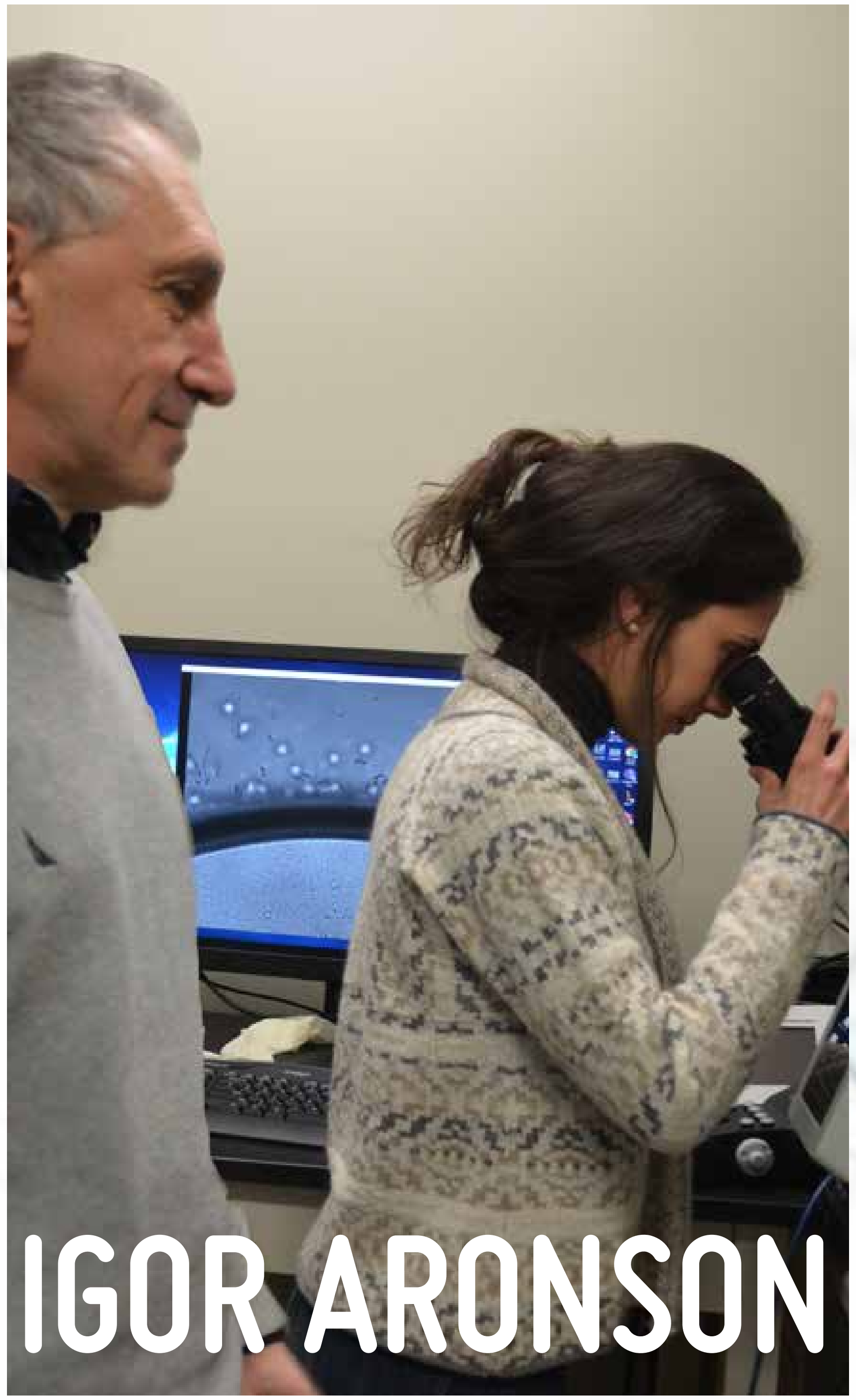
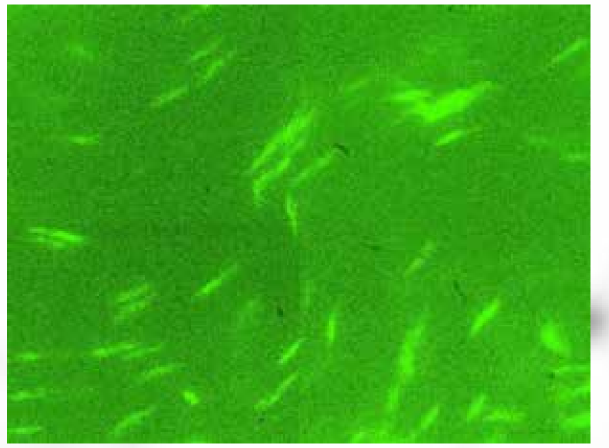


IGOR ARONSON APPLIES PHYSICS TO BIOLOGY



IGOR ARONSON LANDED at Penn State in January 2017 after a long stint as a staff scientist and group leader at Argonne National Lab. A theoretical and experimental physicist, he also has a strong interest in biology and biomedical engineering. The Huck Chair Professor of Biomedical Engineering, Chemistry and Mathematics, Aronson has his fingers in multiple research areas.

His physics background led him to study physical systems that are out of equilibrium, that is, subject to changes in their state. There is a similarity to out of equilibrium systems in physics and biological systems, Aronson said. He decided to merge his long-term studies on the physics of granular matter, such as magnetic microparticles, with biological materials, like bacteria or cells, looking for new interactions and similarities between living and nonliving systems. Granular materials have interesting properties that can sometimes mimic living materials, such as self-assembly and collective motion. They are of interest in many industrial applications, including the chemical, pharmaceutical, food, metallurgical, agricultural, and construction industries.

“IT TURNS OUT you can capture emergent collective behaviors of biological materials and describe them in terms of conservation laws, like we do in physics,” he said. “My vision is to conceive of materials that have a small amount of active component, be it bacteria or nanomotors, such as those made by Tom Mallouk and Auysman Sen, to change the properties of the material and implement something new, for instance, self-healing in a plastic material. You can see from my vision that my research lies at the convergence between biology and materials.”

Penn State chemists Mallouk and Sen are known for their work with nanobots, small bimetallic swimmers that rely on chemical reactions for propulsion. His research gives insight into Mallouk and Sen’s artificial systems, but his own systems using bacteria are easier to work with, he said.

He calls one of his swimmer designs “living liquid crystals,” because they incorporate rod-shaped bacteria into a water-based nontoxic liquid crystal. The orientation of the crystals determines the direction in which the crystals move, and the bacteria flagella are the propellers. Aronson speculates that living

▶

> “My philosophy is to teach students to be interdisciplinary and open-minded. I teach from first principles and am very rigorous. It is not about memorization; I show them the connections between disciplines.”

OPPOSITE:
LEFT
Prof. Aronson with postdoctoral researcher Nuris Figueroa-Morales in the Active Biomaterials Lab

TOP RIGHT
Observation of fluorescent bacterial flagella in liquid crystal. Credit: Aronson Group

> "I think fundamental science is tremendously important and often overlooked. My research is curiosity driven."

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liquid crystals could be useful for biosensing and other biomedical applications.

Aronson is co-director, along with mathematician Leonid Berlyand, of the Center for Mathematics of Living and Mimetic Matter. The Center's mission is to form a better understanding of the dynamics of living and mimetic matter (nonliving materials that mimic biological processes) under out-of-equilibrium conditions. The Center draws on expertise from mathematicians, biologists, chemists, materials scientists, and engineers from across campus.

"For me it is easy to talk to people from all departments. I speak their language," he said. "And my students are also from different disciplines."

He has a grant from the National Science Foundation to use active materials to change the properties of 3D printed materials. The work is underway now, and it is a challenge.

"Nanorobots are still fundamental research. People talk about drug delivery and cleaning debris out of arteries, but there is still a long way to go. But it is important research, and there is a bright future for it."

THOUSANDS OF SYNTHETIC SWIMMERS

In the MRI Nanofabrication Laboratory cleanroom in the Millennium Science Complex, a new machine is churning out thousands of artificial swimmers for Aronson's research. The Nanoscribe 3D laser photolithography system takes 3D printing to a whole new (small) scale.

Using a CAD file to control a laser, the Nanoscribe prints submicron features in polymer. The tiny devices are torus-shaped propellers that spin across a microscope's video camera in a straight line.

Aronson worked with MRI and Huck to get the Nanoscribe. The machine can do thousands of copies in one pass over 2 to 10 hours, all within a droplet of polymer. The Nanofab can also coat or metalize the polymer pieces.

Aronson's graduate student, Remmi Baker, is making the micropropellers that are 7 microns across and use hydrogen peroxide as their fuel source. She is co-advised by Auysmen Sen.

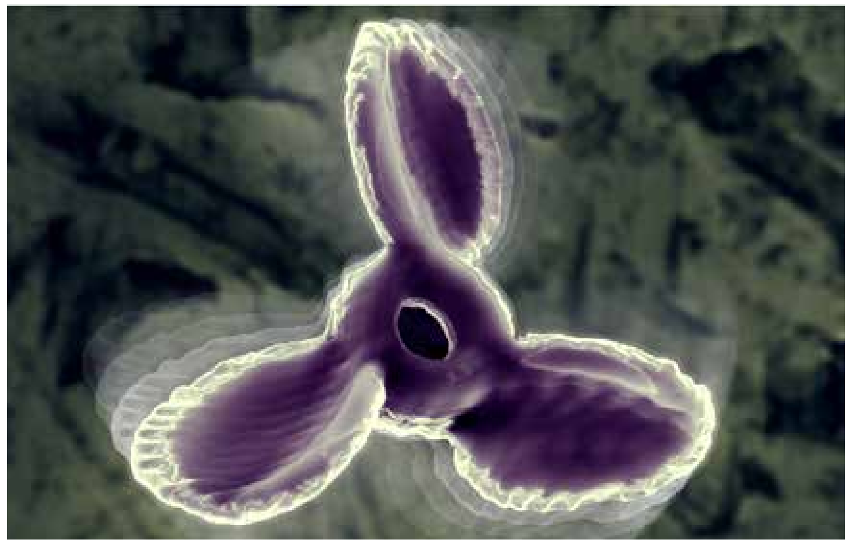
"Traditional lithography can only make 2D parts," Baker explained in a talk at the Millennium Café recently. "The Nanoscribe allows us to print three-dimensional shapes."

TEACHING PHILOSOPHY

For a staff scientist at a national laboratory, Aronson had an uncommon opportunity to mentor students. While at Argonne, Aronson had joint appointments with the University of Chicago and Northwestern University.

"Argonne was a great place to work," he said. "I had interactions with students, although it was a little unusual. At Northwestern, I was a member of the graduate faculty, and I was able to bring my students to Argonne. Most of the students you would see there were my students.

"My philosophy is to teach students to be interdisciplinary and open-minded. I teach from first principles and am very rigorous. It is not about memorization; I show them the connections between disciplines. I think fundamental science is tremendously important and often overlooked. My research is curiosity driven."



ABOVE:
Self-propelled particles (micromotors) are being investigated as future autonomous agents for fluid mixing in Lab-on-Chip Device (LOCs) and cargo delivery applications, such as pollution cleanup or drug delivery. Credit: Remmi Baker, Graduate Student MatSE.

LEFT:
Remmi Baker pitches her research on micromotors.

ONE-OF-A-KIND CRYOGENIC MICROSCOPE

IN A QUIET room in the basement of the Millennium Science Complex, a unique electron microscope is taking its scientific shake-down cruise under the leadership of Susan Hafenstein, an associate professor of biochemistry and molecular biology with expertise in cryogenic microscopy for the life sciences.

About three years ago, there was a transformative advance in the hardware for cryogenic (ultra-low temperature) electron microscopy, Hafenstein explains. Called the direct electron detector, this camera provides dramatically higher resolution and quality in each image.

“INTRODUCTION OF THIS detector really propelled us forward,” she says. “In the life sciences, it took us from being able to reconstruct maps of fully hydrated particles from moderate resolution to atomic resolution. For people who were studying biological samples that have no symmetry, it was a tremendous opportunity.”

In Hafenstein’s field – viruses and their interaction with their host – the camera has made it possible to look at protein-protein interactions at the atomic level. Instead of having to interpret poorly resolved information, the detector makes it possible to see the interactions of a drug with a virus directly.

As a result of the advance in microscopy, institutions all over the world began acquiring the Titan Krios. In the U.S., around 50 institutions installed the instrument in order to take advantage of the breakthrough, despite the insanely high cost. But Penn State’s Titan Krios is different from all of the others.

“We worked with engineers for almost a year to configure our Krios to be unique,”

▶

Susan Hafenstein’s office is located in the west wing of the Millennium Science Complex. She can be reached at suh21@psu.edu.

she says. “We configured it so we could do materials science applications on both biological samples and inorganic samples.”

An example of a materials science application with biological implications is called elemental mapping. A common tool in materials science, it is a novel approach for biological samples. In Hafenstein’s case, she intends to show how a virus uses calcium during entry into a cell. No one has ever seen that happening under a microscope, she says.

Calcium is also of interest to food scientist Federico Hart, who studies calcium contained in micelles, small complex structures in milk. With the Krios, he is able to see the micelles directly as they incorporate calcium.

A number of Penn State research teams are developing nanoparticles for drug delivery. Being able to directly watch as the cell incorporates the particles and the drug is released could be of help in designing more effective particle uptake strategies.

“A lot of people on campus are curious about how inorganic elements are used in biology,” Hafenstein remarks.

A UNIVERSITY-WIDE COLLABORATION

Hafenstein is the faculty director for the Krios microscope. This puts her in contact with people across the university working to make the instrument operational. Among the major tasks is handling the huge amounts of data the Krios can acquire, datasets that can reach as much as ten terabytes (10 trillion bytes) over a couple of days.

“The Krios network has reached out across campus,” she said. “We had to meet with people in cyberscience, people in the Huck (Institutes), to create the foundation of computer support just so we could get the data flowing off the Krios at the same rate it is being generated. And then we have this whole network of interactions with materials science to further develop the unique capabilities of this microscope.”

They call this stage of learning the capabilities of the Krios “developmental time.” It involves biweekly meetings with a team of microscopists from the life science and materials science wings of the Millennium Science Complex to determine and write standard operating procedures. The five-person team includes three materials staff scientists, herself, and a life sciences microscopist.

“We get together to talk about which experiments have succeeded, what we want to do next, how to book time on the microscope, whose samples can we use? It is useful to try to generate some useful information at the same time we are developing a technique and not just configure the instrument,” she said. “There are also a number of PIs involved in the developmental stage scientific discussion to take advantage of Penn State expertise.”

THOUGHTS ON CONVERGENCE

“I think the idea of the convergence of materials with life sciences is groundbreaking. I think it is an awesome idea, and I moved here for this convergence approach. Arizona State has tried to do it, and Cornell has tried to do it, but we are really doing it, with a machine that is beautifully configured to perform without sacrificing any life science imaging,” she says.

Hafenstein has worked with MRI faculty such as polymer scientists Enrique Gomez and Manish Kumar, and nanoparticle drug delivery expert Jim Adair. All of them will find the Krios extremely useful in their research, she believes.

> “TO ME IT’S a fantastic opportunity to sit in a room with someone who is talking about things that make me stretch. It may have been these kinds of interactions that made me feel that this was a way to grow innovative science, not just for me in my research, but for everybody.”

The FEI Titan Krios is a joint venture between the Huck Institutes of the Life Sciences and the Materials Research Institute.

convergence SNAPSHOTS

Building a Better Bandage

A COLLABORATION BETWEEN PENN STATE’S College of Agricultural Sciences and Penn State’s College of Medicine is changing the way trauma wounds are treated.

As anyone who has tried to pull traditional bandages made of cotton gauze off of a healing wound will attest, they stick, and when they finally separate, the wound often is torn open. A team of Penn State researchers from the College of Agricultural Sciences and the College of Medicine has developed a biofoam pad that could replace these cotton bandages and revolutionize wound treatment. This biofoam could be useful in treating wounds in surgical, military, veterinary and countless other settings.

Jeffrey Catchmark, professor of agricultural and biological engineering at Penn State’s College of Agricultural Sciences and collaborator, Dr. Scott Armen, chief of the Division of Trauma, Acute Care and Critical Care Surgery at the Penn State Milton S. Hershey Medical Center are working to commercialize their patent-pending biofoam pad, made from a combination of starch from potatoes and chitosan from shellfish, for wound and trauma care.

> “BECAUSE PENN STATE has an outstanding culture of interdisciplinary research, engineers, scientists and medical doctors can work together here effortlessly,” said Catchmark. “Penn State understands and supports interdisciplinary collaboration. It is simply the most effective path toward discovery.”

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A biopolymer liquid bandage for wound care.
Credit: Aleo BME

An Elastic Skin-Like Liquid Bandage Wins FDA Approval

STATE COLLEGE, PA--BIOMATERIALS and medical device company Aleo BME has received notification from the U.S. Federal Drug Administration that it has been approved for the sale and licensing of ElaSkin™ as a liquid bandage for the protection and treatment of a broad set of skin conditions and injuries.

The compelling features of ElaSkin™ include: transparency, elasticity, clean and easy removal, water resistance, rapid drying, bacterial impermeability and the sensation of true protection.

Aleo BME is a start-up developing nature-inspired biomaterials. Aleo BME’s foundational technology is comprised of novel biomaterials and devices developed by its medical R&D program in addition to technology licensed from the lab of company co-founder Jian Yang, professor of biomedical engineering at Penn State.

Learn more about Aleo BME at Penn State’s Innovation Park: www.aleobme.com

MEET SLAVA ROTKIN

A Physicist Studies Nanotubes Wrapped With DNA

Slava Rotkin and his graduate student, Michael Blades, in Rotkin's lab. Credit: MRI

THE DEVELOPMENT OF synthetic DNA has opened up new territories of research at the forefront of biotechnology. Synthetic DNA can now be ordered online at a cost of $0.07 a base pair, and in the future, synthetic DNA could be used to create designer drugs and even new forms of life never seen in nature, for good or ill.

Slava V. Rotkin is a professor of engineering science and mechanics who has recently moved to Penn State but already is forming multiple strong connections across campus. Trained as a theoretical physicist, he has turned one focus of his research on the connection between nanoscience and biology, using synthetic DNA-wrapped nanotubes to study their effect on cells.

“BY TRAINING, I am a hardcore physicist/materials scientist,” said Rotkin. “Until five years ago, I had never even done anthing with soft matter; all of my research was nanoscience of hard materials.”

The barriers between life sciences researchers and physics and engineering researchers seemed too high to cross. “Not just the different tools and methods we use, but also the different language.”

He got an inkling of how to approach the barrier while at the University of Illinois in a group of Karl Hess in the Beckman Institute that was doing semiconductor device modeling and expanded into theoretical biophysics. The Beckman Institute was designed to house faculty from multiple disciplines to do interdisciplinary research.

“I DIDN’T DO much in biophysics, but we started crossing over, cross-fertilizing,” he said. “They just happily worked together, a graduate student of mine and her husband from Klaus Schulten’s group – one of the world leaders in theory of nucleic acids and proteins.”

When he moved to Lehigh University, he wanted to expand his nanotechnology research into the biology sphere. He began wrapping his nanotubes in synthetic DNA as an easy way to suspend the nanotubes in solution. Then, two new graduate students began working with the optical properties of DNA- wrapped nanotube systems.

They wanted to see how cells would react to the nanotubes. Would they live or die? The cell line his colleague was working with were neural stem cells. They fed the DNA/nanotube systems to the stem cells and the cells “drank” them. They found that the cells did indeed survive, if they were not fed too many nanotubes.

But the cells started to behave differently. “We saw that stem cell differentiation rates, which is how many neurons and how many non-neurons you get after a division, changed significantly after we introduced the nanotubes.”

They ended up learning a lot about the effects of nanotubes in neural stem cells: That they stay in the cells for weeks; that introducing the nanotubes at different points in the cell’s life cycle gave different outcomes; and that if the nanotubes are functionalized with DNA, RNA, or other polymers, they can go inside the cell without killing it. They traced individual nanotubes through the cell, which required learning Raman confocal microscopy techniques. Most researchers use large quantities of nanotubes for research on cells because it is very difficult to see a single nanotube.

“This study is still ongoing,” Rotkin said. “We are trying to get a deeper understanding of how the cells are influenced by the nanotubes. We have good instrumentation to study that and what is more important, faculty interested in this field.” At Penn State Rotkin found new colleagues to continue this research: Dr. Krasilnikov in Biochemistry and Molecular Biology (BMB) is a specialist on DNA biochemistry; Dr. Daniel Hayes in Biomedical Engineering (BME) studies nanomaterials for drug delivery; Dr. Makova in Biology specializes in genetics aspects.

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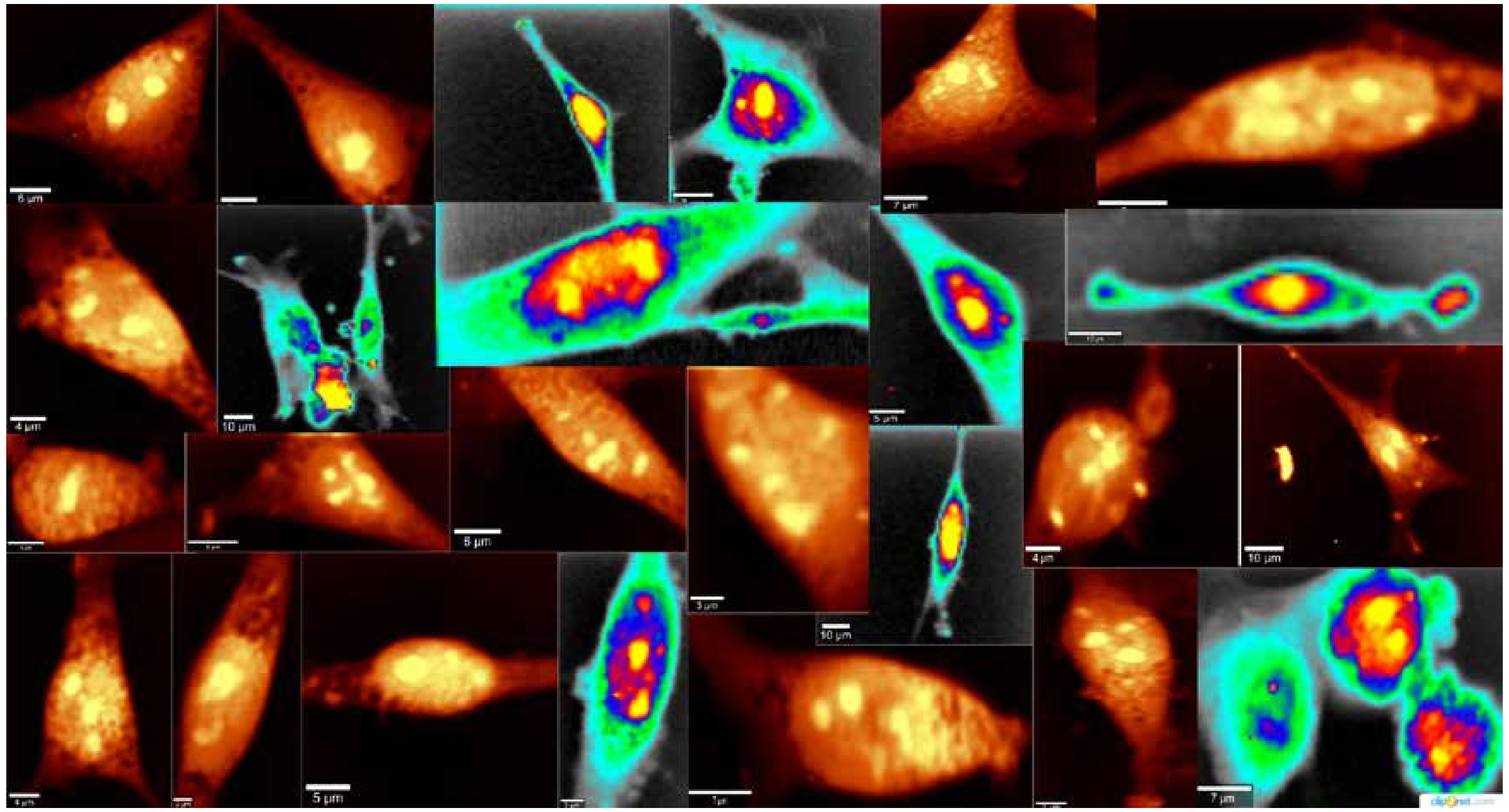
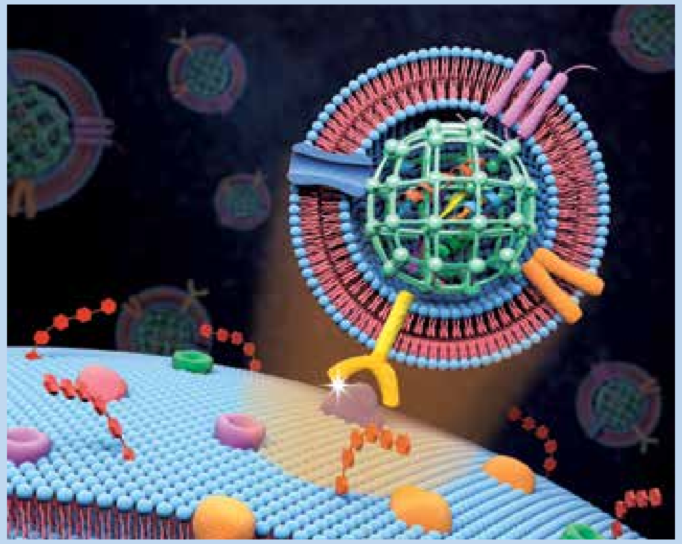


LEFT:

Confocal Raman microscopy images of mice neural stem cell, some containing individual DNA-wrapped single-wall carbon nanotubes: advancing micro-Raman characterization to the level of single particle detection has made possible a detailed investigation of the distribution of nanotubes inside stem cells, resulting in increased differentiation rates into “adult” neurons. Credit: Rotkin Lab

convergence SNAPSHOT

Camouflaged Nanoparticles Used to Deliver Killer Protein to Cancer



Extracellular vesicle-like metal-organic framework nanoparticles are developed for the intracellular delivery of biofunctional proteins. The biomimetic nanoplatform can protect the protein cargo and overcome various biological barriers to achieve systemic delivery and autonomous release. Credit: Zheng Lab

A TEAM OF PENN State researchers has developed a biomimetic nanosystem to deliver therapeutic proteins to selectively target cancerous tumors. Using a protein toxin from a plant found in the Himalayan mountains, called gelonin, the researchers caged the proteins in self-assembled metal-organic framework (MOF) nanoparticles to protect them from the body’s immune system. To enhance the longevity of the drug in the bloodstream and to selectively target the tumor, the team cloaked the MOF in a coating made from cells from the tumor itself.

Blood is a hostile environment for drug delivery. The body’s immune system attacks alien molecules or else flushes them out of the body through the spleen or liver. But cells, including cancer cells, release small particles called extracellular vesicles which communicate with other cells in the body and send a “don’t eat me” signal to the immune system.

“We designed a strategy to take advantage of the extracellular vesicles derived from tumor cells,” said Siyang Zheng, associate professor of biomedical and electrical engineering. “We remove 99 percent of the contents of these extracellular vesicles and then use the membrane to wrap our metal-organic framework nanoparticles.”

Their work was supported by Penn State’s Materials Research Institute and Huck Institutes of the Life Sciences, and the National Institutes of Health.

Read the full story at: *mri.psu.edu/mri/news/camouflaged-nanoparticles-used-deliver-killer-protein-cancer*

Contact *Prof. Zheng at sxz10@psu.edu.*

2D MATERIALS

The early days of nanoscale research brought on concerns about the toxicity of nanotubes and nanoparticles entering the body though air or water. Comparisons were made to asbestos, because in early studies, researchers used huge amounts of nanotubes in testing, and found them damaging to cells.

The issue of the safety of nanoscale materials has not been resolved, especially with the advent of a new type of nanomaterials called two-dimensional materials, such as the widely studied supermaterial graphene. A 2D material is like a postage stamp, but its surface is only a single atom high and the entire stamp is typically invisible to the eye. 2D materials are being studied for a variety of electronic and optoelectronic applications. Penn State has an active center to study 2D and layered materials, which are three-dimensional materials made by stacking 2D layers of various kinds one on top of the other to create new materials not seen in nature.

"If we properly engineer our system, we can have a huge enhancement of the density of the photonic state (of light)."

"TWO-DIMENSIONAL MATERIALS ARE important to us, because of their large versatility. Penn State is recognized nationally for its strength in 2D materials," Rotkin said. "The field is huge. But the biological importance and safety of 2D materials is an open question. From my experience, I am seeing that these materials are not as terrible as people expected in the beginning, but to be honest, we have not explored all the palette of potential materials or cell lines to make a comprehensive safety list."

NANOTUBES FOR SENSING INSIDE THE CELL

Rotkin has a National Science Foundation program based on using nanotubes as antennas inside the cell. Because nanotubes are very tiny, they can be near whatever is going on inside a cell, and potentially transmit that information to an observer. In this sense, an antenna is something that is capable of taking distributed radiation of any kind and focusing it at a certain point to enhance the radiation.

In both experimental and theoretical studies, Rotkin's group has shown that the nanotubes can interact with a specially designed dye molecule and an external light source to transmit energy between the tube and the dye molecule.

"If we properly engineer our system, we can have a huge enhancement of the density of the photonic state (of light)," Rotkin said. "It is somewhat similar to a tsunami: The wave is going through the ocean at a low height, and then when it approaches the shore the wave energy is concentrated and the wave grows huge."

DNA ORIGAMI

These days, it is almost routine to make DNA origami, where you use complementary DNA to make 2D shapes, Rotkin said. Now researchers are starting to make 3D DNA origami shapes that incorporate nanoparticles.

Rotkin and Krasilnikov would like to utilize DNA chemistry to make more complex objects out of nanoparticles and potentially DNA chemistry and nanotubes for smart sensing. "This is something we will definitely try, given all the life science and biomedical people here at University Park and Hershey (Penn State College of Medicine.)"

Rotkin is still building his lab, which will include a new state-of-the-art optical system as well as a number of other instruments for optics and plasmonics research. Rotkin also has several undergraduate students who have volunteered to work in his lab.

"I LOVE TO interact with undergraduates. I started to do real scientific research early, in fact in high school. That is why I don't believe there is a minimum age for doing research."

Rotkin has already formed a number of collaborations at University Park, but he is actively seeking new collaborators, particularly from life sciences.

"Penn State has met or exceeded my expectations," he said. "The life here is very energetic. I meet good people." ▣

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convergence SNAPSHOT

Study Finds How Salmonella Bacteria Die at Low Temperature

HEAT IS THE most economical way to kill the bacteria responsible for the common food-borne illness Salmonella enterica. But until now, the mechanism that killed the bacteria at lower temperatures was not known. Because bacteria in the wild can develop ways to cope with heat shock, it is important to develop a complete understanding of how heat kills bacteria.

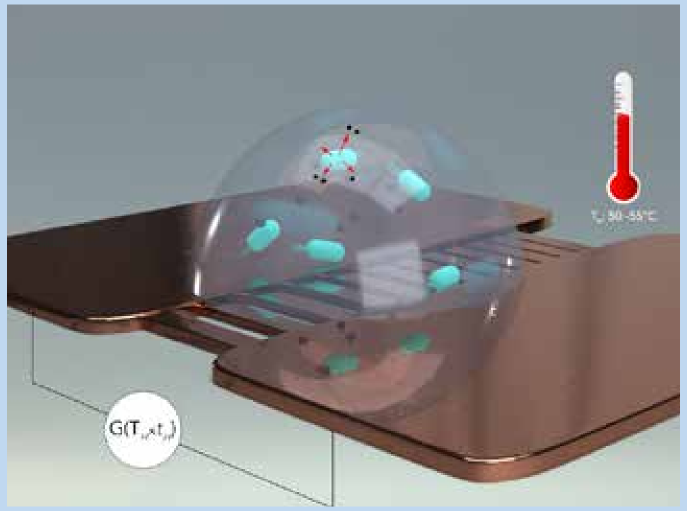
Using a technique called droplet-based electrical sensing in a device she developed as a Ph.D. student at Purdue University, Aida Ebrahimi, assistant professor of electrical engineering, Penn State, has determined that mild heat stress at temperatures around 120° F. damages the bacteria's cell wall.

"WE HAD A hypothesis that the Salmonella bacterium might die due to leakage of the cell wall," Ebrahimi said. "If you heat them, the lipids that make up the cell wall vibrate. As the cell wall weakens, it allows small molecules to leak out."

In order to prove their hypothesis, the team developed a sensor that was sensitive to the changes in electrical conductance of the growth medium. As the bacteria's cell walls lost integrity, charged molecules were ejected from the cells into the solution containing the bacteria, changing the electrical conductivity of the solution.

By better understanding the mechanisms of bacterial death at elevated temperatures, the team hopes to improve food safety strategies and provide more efficient ways to deactivate bacteria using shorter duration heating at lower temperatures.

For the complete news release visit: www.mri.psu.edu/news



ABOVE:
Under mild heat shock, Salmonella dies mainly due to leakage of small cytoplasmic molecules.

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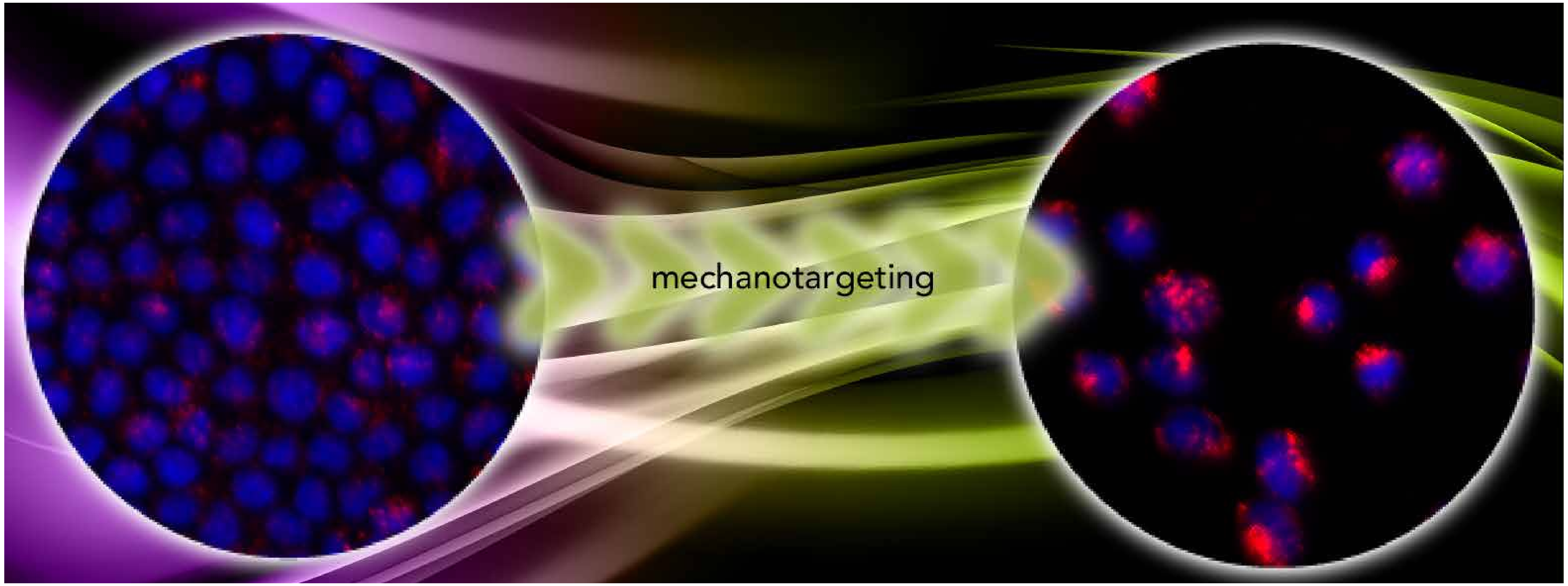
THE MECHANICS OF LIVING MATERIAL



LEFT
In the transition from benign to malignant, cancer cells transition from stiff to soft. Mechanotargeting harnesses mechanics to improve targeting efficiency of nanparticle-based therapeutic agents. Credit: Zhang lab/vecteezy.com

> "We don't currently have the rules to predict the properties of living matter, but we have a lot of pictures and videos from our experiments showing cells moving."

SULIN ZHANG'S RESEARCH is at the interface of life sciences, materials, and mechanics. Early in his career, he was interested in how materials deform and fail under different loading conditions, such as thermal or mechanical loading, or when an electrical current runs through a material.

His new research direction brings his interest in the mechanics of materials deformation to the study of the consequences when cells, tissue, and organs undergo mechanical or other loading.

"PEOPLE NORMALLY SAY that cancer metastasis is the real fatal problem," he said using an example to illustrate his work. "If you don't have metastasis the tumor is benign. And people also said that this benign-to-metastasis change is genetically programmed."

But some researchers started to question this understanding. They asked, What stimulus can cause cancer to metastasize? It turns out that if you put cells in a different mechanical environment, they can undergo a malignant transformation. Meaning, mechanical forces on their own can drive the progression to malignancy.

"WE HAVE OBSERVED that, and another group in Europe has as well," Zhang said. "There are many other examples as well."

Such as the recent call for proposals from the National Science Foundation to fund research on controlling epigenetics, changes in gene expression unrelated to changes to the genetic code. NSF in an unusual move has called for materials scientists and engineers to get involved in what is intrinsically biological research.

Another NSF call for proposal at the boundary of materials and life sciences is called LEAP-HI – Leading Engineering for America's Prosperity, Health, and Infrastructure. This is a large-scale program that involves 10 big ideas that NSF is supporting. One of the ideas is to understand the rules of life involving phenotype. Phenotype is the way genes interact with the environment resulting in differences in observable characteristics, such as height. Genotype is our genes, whereas phenotype is our appearance. Predicting ▶

phenotype is an incredibly difficult proposition that will require multiple approaches from across disciplines.

“WITH THE CONVERGENCE of materials and life science we are trying to do the following,” Zhang enumerated. “First, we are trying to understand cells and tissues as active materials. As materials scientists we have tools to predict the properties of the materials we study. We have quantum mechanical calculations on the electron level; we have molecular dynamics simulations on the atomic level; we also have calculations on the continuum level. But we don’t have a lot of tools to predict the behavior or response of cells, tissues, and organs.

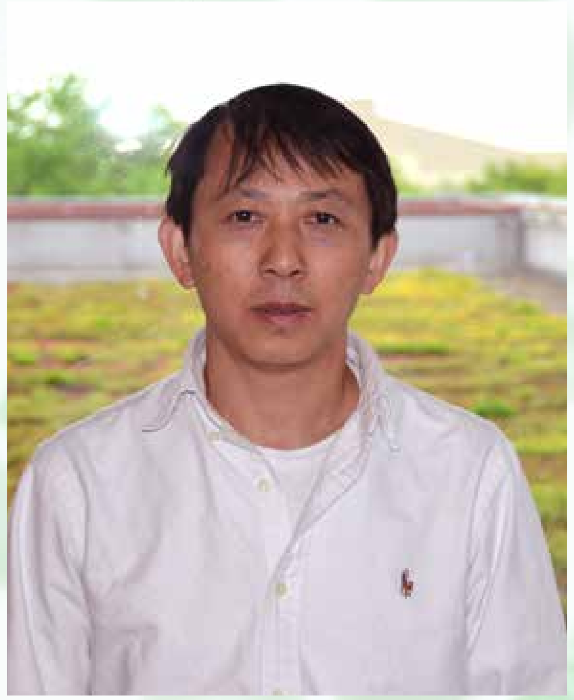
“Second, materials scientists can synthesize materials that can interface with cells and elicit tissue functions. These are two major areas where materials scientists and life scientists can work together to make something happen.”

UNDERSTANDING MALARIA

Zhang uses mechanics as a tool to understand how malaria works. When red blood cells are infected, they undergo what materials scientist would call a phase transition. Life scientists wouldn’t use that concept. They might refer to it as protein remodeling. But once the cell is remodeled by the malaria parasite, its mechanical properties are changed.

Normal red blood cells are deformable and flexible so they can slip through tiny blood vessels. When infected, however, they become much stiffer and stickier and end up getting jammed up in small blood vessels, avoiding being cleared through the spleen. Zhang created a computer model of how this transformation takes place. His model was detailed enough to understand how the red blood cell is deformed in a multistep process but not so detailed as to make the model computationally expensive to solve.

> “With this model, researchers may be able to find a therapy to reverse the stiffness of the cells.”



Sulin Zhang is professor of engineering science and mechanics and bioengineering.

“Experimental techniques could not have picked the key factors underlying the change, but modeling can point to the underlying mechanism, With this model, researchers may be able to find a therapy to reverse the stiffness of the cells,” Zhang said.

TARGETING CANCER CELLS

Using nanotechnology to target cancer cells with drugs is called chemotargeting, and is an active research area. It involves manipulating the surface chemistry of the nanoparticles so they can recognize and only attach to cancer cells, leaving healthy cells unharmed. It is like a molecular lock and key system, Zhang explained.

“FROM A MATERIALS perspective, this nanoparticle’s ability to get into the cell also depends on the mechanical properties of the cell. We came up with a strategy called mechanotargeting in contrast to chemotargeting.”

By combining the two approaches, Zhang believes they can increase the efficiency of the drug therapy. In a new paper in the journal *Advanced Materials*, Zhang and his coauthors describe laboratory experiments with two different cancer cell lines intended to show how the mechanical state of the cells affects the uptake of the nanoparticle. They discovered that metastasized cancer cells that have dispersed from the tumor are softer and have around 5 times more nanoparticle uptake as the predispersed cells. Zhang believes this could provide a potential target for using mechanics to design improved nanomedicine.

THE MECHANICS OF WOUND HEALING

When tissue is wounded, a mechanical process determines whether or not the wound can heal on its own. If there is an open gap, the repair cells will sense how strong the wound rim is. If it is strong enough, the cells will attach to it and form a new rim in a process that will eventually close the wound. If the rim is not strong enough, the gap won’t close.

“Biologists wouldn’t think this way,” Zhang said. “But if we give them the facts, then they will have to believe.”

THE BUILDING BLOCKS OF LIFE

If materials scientists consider atoms to be the basic building blocks of matter, then what are the building blocks of life? Zhang says that it’s cells. If physical scientists can use the movement of atoms to predict the properties of materials, can life scientists with the help of materials techniques, such as molecular dynamics simulations, develop a similar capacity to predict tissue properties? Zhang believes that within the next decade a program to predict how cells in aggregate become tissue will be developed.

“We don’t currently have the rules to predict the properties of living matter, but we have a lot of pictures and videos from our experiments showing cells moving. I’m thinking that using data analysis and machine learning, we can generate new rules for life.”

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convergence SNAPSHOT

Mechanotargeting of Cancer Cells

Diseased cells such as metastatic cancer cells have markedly different mechanical properties that can be used to improve targeted drug uptake, according to a team of researchers at Penn State.

Nanoparticle-based drug delivery systems selectively target tumors. They rely on a key-and-lock system in which protein keys on the surface of the nanoparticle click into the locks of a highly expressed protein on the surface of the cancer cell. The cell membrane then wraps around the nanoparticle and ingests it. If enough of the nanoparticles and their drug cargo is ingested, the cancer cell will die.

The adhesive force of the lock and key is what drives the nanoparticle into the cell, says Sulin Zhang, professor of engineering science and mechanics. “It is almost universal that whenever there is a driving force for a process, there always is a resistive force. Here, the driving force is biochemical – the protein-protein interaction.”

Until now, bioengineers only considered the driving force and designed nanoparticles to optimize the chemical interactions, a targeting strategy called “chemotargeting.” Zhang believes they should also take into account the mechanics of the cells to design nanoparticles to achieve enhanced targeting, which forms a new targeting strategy called “mechanotargeting.”

Support for this work in Advanced Materials was provided by the National Science Foundation and a National Institutes of Health grant to Butler and Zhang.

For the full story go to mri.psu.edu/mri/news/mechanotargeting-cancer-cells

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PennState

Credit: Shutterstock