IN MOVIES, IT ALWAYS SEEMS THAT SEQUELS ARE NOT AS COMPELLING OR AS INTERESTING AS THE ORIGINAL. However, what’s true for Hollywood isn’t true for engineering at Duke University. As in the first issue of “Leading Research,” which came out last autumn, we are highlighting in these pages avenues of research and exploration in which Duke engineers are providing significant national leadership.

This publication focuses on three main areas—big data, disease detection and treatment using light, and materials genomics. These research thrusts set Pratt apart, just like the others described in the first publication—metamaterials, computational optics and quantum computing, aeroelasticity, biomaterials and environmental nanotechnology/chemistry.

Taken together, both of these publications should give you an insight into the metamorphosis of Duke Engineering over the past decade and why we are so enthusiastic about the future. We now have 123 full-time faculty members, nearly 75 percent more than in 2000. External research funding has more than tripled in that time, making Duke the fastest-growing among the top-tier engineering schools—and after reading the following stories, I’m certain you’ll understand why.

One thing I am sure you’ll notice is the exceptionally high level of collaboration not only among our engineering faculty, but with researchers from across the campus and around the world. As you’ll see, those teams extend to our undergraduates, like Kevin Shia (page 22), who not only learn at the elbows of faculty but contribute to the amazing advances we experience every day. And, best of all, these advances are helping to solve some of the global grand challenges of our time—making their way from Duke labs to start-up companies to applications that improve the lives of people around the world.

I hope you enjoy reading about Duke engineering research, and invite you to stay connected through our website, pratt.duke.edu. I also welcome your comments on this brochure and Duke Engineering in general (e-mail me at tom.katsouleas@duke.edu).

Sincerely,

Tom Katsouleas
Vinik Dean of the Pratt School of Engineering
Duke University
“Engaging in leading-edge research that involves fundamental discoveries applied to the grand challenges of our time.”

—PRATT RESEARCH MISSION
Big data, big insights

The new Information Initiative at Duke (iiD) brings together a supergroup of experts to translate massive data into major breakthroughs—in arenas from homeland security to human health.

We’re at a moment in which we seem to have become better at collecting data than understanding it. Sensors, cameras, computers and smartphones capture and store an unending torrent of data about human activity via ubiquitous wireless signals, making nearly everything measurable and identifiable.

Billions of fingers perform trillions of keystrokes and clicks, all of them leaving traces somewhere.

Every two days now, wired humanity creates 5 exabytes of new data (10^18 bytes). That’s about how much was recorded from the dawn of civilization until 2003. YouTube’s collection of video grows by 72 hours each minute of the day, double the growth rate from the previous year.

Thousands of people have had their 3-billion-bit genomes sequenced, and millions more will follow.

Google chairman Eric Schmidt has said we’re fast approaching an age in which “everything is available, knowable, and recorded by everyone all the time.” But for now, it’s a tower of Babel.

There are surely some profound and useful insights buried in this mismatched mountain of information that could improve public services, homeland security, environmental stewardship and global health if we could only see the patterns. But parsing through a boundless sea of incompatible, wildly diverse data sets will take some extraordinary effort.

Duke is assembling a supergroup of talents to begin making sense of this “Big Data.”

“We are going to bring the engineering discipline of control into things you never thought it could be applied to,” said Robert Calderbank, the Phillip Griffiths professor of computer science, mathematics and electrical and computer engineering at Duke University. With support from Pratt School of Engineering Dean Thomas Katsouleas, Provost Peter Lange and many other campus leaders, Calderbank is leading the launch of the Information Initiative at Duke (iiD).

The effort is bringing together nearly a hundred faculty and student researchers from diverse fields and backgrounds into a shared space on the third floor of Duke’s newly remodeled Gross Hall. They will join forces to turn “Big Data” into big insights, and start creating the next generation of thinkers who can carry the data revolution forward.

The initiative draws on Duke’s expertise in Bayesian statistics, image processing, genomics, remote sensing, wireless devices, social science, health care, signal processing, finance, machine learning, computer science and a host of other fields.

“There are a group of people here—math, stats, engineering-type people—who work together already on a wide variety of projects related to big data,” said Lawrence Carin, the William H. Younger distinguished professor and chair of electrical and computer engineering (ECE), who helped to launch the new initiative. The group has already won major grant competitions such as a $3 million Mathematics of Sensing, Exploitation and Execution program through DARPA, and is also involved in large research programs for the Department of Homeland Security.

“‘It’s not something where we said ‘We wish we had a center, let’s make one.’ This initiative formalizes something that already exists,’” Carin said.

“There are people who just decided they wanted to get together,” said Calderbank. “We are really good at this.”

Once assembled, the experts at the iiD will be ready to reach out to people from across campus who have big data problems. One of those researchers is neuroscientist Ahmad Hariri, who has fMRI brain scans, genetics and questionnaire data on hundreds of volunteer study subjects. It’s a massive and complicated collection that requires equally complicated analyses to reveal important clues about varying responses to life’s challenges that can distinguish risk and resiliency to mental illness. Working with Carin, statistics professor David Dunson and others, the big data team is jointly studying the MRI scans, questionnaire data and associated genetic data as a package to identify specific patterns connecting genes, brain and behavior to mental illness.
The social scientists, one floor below, are also moving in for a year or so to work intensively with the team on a problem and then return to their home unit with new skills and collaborations. "What this initiative hopes to be is the hub of a world where information science meets the social sciences," Calderbank said.

For their study to scale up, Egger would like to see how much of the coding could be automated requiring several hours to code two hours of tape per patient. "A company with a big data problem wants to be able to talk to somebody who can listen to their challenges and then build something quantifiable," Duke students engaged with real-world problems of big data will be equipped with the quantitative and communication skills to help them thrive in the data-driven world, he said.

"The student experience will start with some new gateway courses dealing with big data in modules to get students excited about the intersections of information, society and culture," Calderbank said. "We're going to have them navigate our curriculum in a more intentional, purposeful way," to assemble the tools they need.

David Dunson said the new initiative is also interested in partnerships with outside companies. "These companies and researchers have needs; we have methods. You have a problem, you can come to us and we'll help you solve it," he said. Corporate partnerships may also supply some funding to the iiD and could create real-world opportunities for Duke students. "The idea is to make Duke a leader in this field," through both research and teaching, he said.

"If you want to engage with the world, you're going to engage around data," Calderbank said.
“The collaboration at Duke is very attractive—this is the fun of research, working with people who have different knowledge than we do, right? The new space in Gross Hall is only going to enhance that, with engineering and social sciences and other faculty working literally side-by-side. Proximity does matter. We’re bringing together disciplines that don’t normally interact, and I think it gives us unmatched potential.”

—GUILLERMO SAPIRO

Making room for big data

In summer 2013, the Information Initiative at Duke moves into its new home—part of a $29-million, 96,000-square-foot renovation of the university’s Gross Hall to support interdisciplinary academic activities. The space features labs, team rooms, classrooms, offices, and a two-story “Winter Garden” (above) designed to foster cross-disciplinary interaction.
Data-based detective work

Precisely planting electrodes in the most delicate regions of a patient’s brain to still the tremors of Parkinson’s, Compressing images taken by rovers on Mars to speed them down to earth, Tracking the outer contours of the flu virus to find new footholds for vaccines, Changing the background in a home video or translating black-and-white film to color with speed and ease.

It’s hard to believe that such a variety of advances could come from one researcher, but for Guillermo Sapiro that’s just the start. The maestro of image processing develops algorithms that interpret vast numbers of pixels from photos or video and translate the findings into breathtaking array of practical solutions—from medical breakthroughs to new crowd-surveillance methods to improvements in consumer products such as Adobe’s After Effects software.

Recently arrived at Duke from the University of Minnesota, Sapiro is particularly excited by the new directions his work is taking in this highly interdisciplinary environment. “At Duke it’s hard to understand which departments people are in—and that’s a positive thing,” he said. “Most of us have multiple appointments, so there are no boundaries.”

Among his new collaborators is Duke child psychiatrist and epidemiologist Helen Egger, with whom he’s starting a project to improve early diagnosis of childhood anxiety and other disorders. The effort builds on Sapiro’s earlier work using techniques that automatically pick up on abnormal activity on videos to detect early signs of autism. While a clinician or daycare provider might not always recognize a brief but significant delay in a toddler’s eye movement, say, or a lack of eye contact, video analysis could potentially raise the red flag automatically—enabling earlier diagnosis and intervention.

Now Egger and Sapiro will mine information from thousands of hours’ worth of video, parent interviews, and clinical data to see if they can automate recognition of anxiety symptoms. “If we can find patterns in the data that point to just a few simple tests or questions that truly indicate a problem, that would be a tremendous tool for clinicians,” he said.

Through a new Duke program called Bass Connections, undergraduates will join the interdisciplinary research team, taking the study into local schools and gaining valuable hands-on experience. “It’s an exciting project because the contribution to society could be huge,” Sapiro said.

Geometries of data, from molecules to threat detection

We’re used to objects having a certain length, width and depth. They usually exist in time as well, giving them four dimensions.

But to Mauro Maggioni, a professor of mathematics, computer science and electrical and computer engineering (ECE), four dimensions aren’t enough to understand how enzymes and proteins work, or to distinguish tanks from trees in military images. Maggioni works with the geometry of high-dimensional data—millions of points graphed in hundreds or thousands of dimensions. For example, to understand the motion of biomolecules, researchers simulate countless possible molecule configurations. Even on powerful computers, these simulations take a very long time to run.

Collaborating with chemists, Maggioni analyzes all the coordinates of atoms in a molecule and identifies geometric and dynamical properties that let him build low-dimensional representations of the molecule’s dynamics. The simplified representations can then speed up simulation time, and understand and map out the complex landscapes accessed by the molecule, he says.

Another of Maggioni’s “big data” projects is studying the hundreds of colors in what is known as hyperspectral imaging. Right now, images from smartphones and hand-held cameras have three basic colors, all in visible light. Hyperspectral images, on the other hand, combine colors from across the electromagnetic spectrum—everything from radio to ultraviolet radiation—and provide clues to the chemical properties of photographed materials.

“With such multi-dimensional data coordinates, you can tell the perfect time to harvest a crop, see if a gas leak is really chemical warfare, or monitor concentration of key chemicals in blood,” Maggioni said. He is also working with ECE professors David Brady and Larry Carin to design faster and more accurate X-ray scanners, which use new algorithms and imaging designs to screen airport baggage for weapons and explosives.

One feature of many of these data sets is that they change with time and have different levels of granularity, or bits of data, at various stages. Maggioni’s algorithms allow him to detect and measure these changes in molecular configuration space, hyperspectral movies or networks and network traffic.

“The algorithms often enjoy a sort of universality dear to mathematicians, in that they are easily adapted to different types of data, as they attempt to capture crucial properties of data by learning from the data itself,” Maggioni said.
The art of analysis

You wouldn’t think that art from the 14th century could be a subject for big data. But Duke professor of mathematics and of electrical and computer engineering Ingrid Daubechies has been collecting information about artworks, trying to understand the differences between originals and copies and how cracks and other degradations resulting from the aging process are distributed over the artwork.

In her earlier work, she developed mathematical constructs called wavelets, which have informed image compression standards now widely used in image compression as .jpg2000s, and other digital formats. Now, she is working with the North Carolina Museum of Art and Dutch artist and art historian Charlotte Caspers to reconstruct a missing panel of an altarpiece by Francescuccio di Cecco Gissi, an Italian painter from the 14th century. The museum has three panels of the series of panels in its collection. Other panels are on display at the Metropolitan Museum of Art and other museums. But one panel is missing, so Caspers has researched and created a substitute in Gissi’s style so that the full altarpiece can be put on display in 2015.

The math comes in as Caspers and Daubechies prepare the art for display, “aging” it with very precise placement of cracks and other dating details. They can study crack patterns and other processes on the older paintings, “learn” digitally how they affect the piece and then transpose that to the recreated piece, so the new art closely resembles its historic counterparts.

Daubechies can also use her mathematical tools to combine data from different imaging technologies and show hidden information. Many artists reuse canvases. Taking different kinds of images of a Van Gogh painting, Daubechies and her collaborators uncovered details in a woman’s portrait over which the artist later painted blooming grasses.

In another study, they analyzed under-drawings, used by many of the best artists to begin their works. Comparing the style of the under-drawings with the finished surface of the painting, Daubechies says, can reveal more about an artist and what he or she was working on before producing a masterpiece, as she and her collaborators showed recently in their examination of paintings by 16th-century artist Goossen van der Weyden.

Duke professor Ingrid Daubechies is internationally recognized for discovering a data compression technique using compact wavelets—an innovation that allows electronic images to be stored on computers and phones. Among other honors, she was awarded the Franklin Institute’s 2011 Benjamin Franklin Medal in Electrical Engineering and in 2000 became the first woman ever to receive the National Academy of Sciences (NAS) Award in Mathematics.
David Dunson is a statistician who helps neuroscientists and physicians to better diagnose illnesses. “Right now, if you combine data from different brain imaging modes—fMRI, structural MRI and other variants of the scan—there are billions of data points on that one patient. Making sense of all of that is a problem,” said Dunson, a professor in statistics and electrical and computer engineering at Duke.

Working with others in the new Information Initiative at Duke and in the medical center, he is developing a project where multiple physicians diagnose a patient’s mental illness clinically and then use data from multiple imaging modes to come up with a method to predict mental health conditions computationally based on brain scan images.

This is a ‘big data’ problem because patients don’t have just one type of information. Their record is a collection of different kinds of data—images, recordings, writing, and genetic profiles—that are all mismatched. Dunson tries to pull all of that information together, using Bayesian statistics—a method for understanding uncertainty based on mathematical probabilities—to search for patterns that could identify a patient’s condition from all of the individual’s entire medical record rather than a short doctor visit and a few diagnostic tests.

Dunson’s expertise in Bayesian statistics adds a diverse perspective to the big data group. A recent winner of the prestigious COPSS Award, given annually by the Committee of Presidents of Statistical Societies to a person under the age of 40 in recognition of outstanding contributions to the profession of statistics, Dunson says he thinks about problems “quite a bit” differently than traditional mathematicians, computer scientists and engineers.

“A distinct characteristic of a statistician who works on big data is that we care about uncertainty and doing inferences on that uncertainty,” said Dunson. He said he doesn’t want to come up with one estimate, or best guess, that describes what he calls the low-dimensional structures, or patterns in the data. “Instead, I like to come up with a probability distribution of low-dimensional structures that are consistent with the data and information I have, which is how I do analyses differently than most people in a big data project.”

Making data pop

Much of the 21st century will surely be taken up with making an avalanche of data useful. But what to do when useful data are sparse? Enter Rebecca Willett, who specializes in making sparse datasets pop with meaning.

As a non-parametric statistical specialist, Willett has developed algorithms that take datasets with limited information—such as those created by night vision goggles, where available light is very low—and fill the data gaps. Her algorithms could eventually make images from night vision goggles considerably sharper, while enabling the goggles to be smaller and lighter.

But making night vision clearer is only one of many applications for Willett’s methods. In modern astronomy, advanced filters screen out extraneous energy waves to create stunning images of distant galaxies. These coded apertures will soon be creating “pictures” of nearly imperceptible black holes. Willett’s work is helping astronomers ensure that the reconstructed data collected from these compressive coded apertures accurately represents the underlying structure.

The challenge is to use extremely small numbers of random events to perform inference on the underlying high-dimensional, nonparametric and intrinsically complex phenomenon. In this case, standard models of sensing and noise do not apply, requiring development of new computational methods for high-dimensional point processes.

“When you are working with point processes [such as an individual photon of light hitting a detector] the statistics you use are different, and you can’t use ordinary techniques when you are writing an algorithm,” said Willett. “You have to take the physical constraints of your system into account. That’s what we do.”

Going forward, Willett and her students in Duke’s electrical and computer engineering department are working on applications for modeling the firing pattern of neurons in the brain and for analyzing patterns created by online social network interactions.

“There are a lot of problems where these point processes show up,” she said. “The question is: can we find and exploit the structure underlying this data to solve real problems?”

Probability, not certainty

Rebecca Willett, associate professor of electrical and computer engineering, serves as associate director of the Information Initiative at Duke.
Watching TV is one of the things that computers cannot do better than humans. They're terrible at it, in fact. But Leslie Collins' signal processing group in ECE is working to change that.

The "big data" potential is vast: Turning a moving picture into data that could be analyzed statistically in something approaching real time opens up all sorts of questions to ask of security cameras, Google Street View, environmental sensing images, just about anything visual.

Their interest in video analytics grew out of the Collins group's work on landmine detection. Looking at a long-running stream of 3-D ground-penetrating radar scans as a military vehicle drove a bouncing and potentially mine-laden road in Iraq, assistant research professor Peter Torrione got to thinking "It's kind of a movie. We could probably get into video processing."

Unfortunately, the best algorithms developed so far take a couple of seconds per frame to make a statistical determination of whether there's anything unusual in the visual data. Smooth video shot at 30 or 40 frames per second would quickly overwhelm such a system.

A big part of the problem for video analytics is that computers haven't learned their shapes yet. The state of the art in detecting a human is developing, but can be thrown off by lighting, objects in the way, or the camera angle, Torrione said. Show the computer a car in any orientation, and it doesn't have a clue.

With support from an industry partner, the group is now working to solve that in a step-wise fashion. Their proof of concept so far is a rather spectacular demonstration of a webcam and five PCs driving a red sports car at 130 miles per hour on a winding mountain road in the video game Need for Speed. With no more input than the video camera, the computers are interpreting what they see on the screen and sending controls to the PS3 game console to operate the virtual car's steering, acceleration and brakes. It's a remarkable advance for natural vision recognition.

The system makes these interpretations and decisions rapidly enough that the car doesn't just go sailing off into oblivion, and it wins races against the gaming console most of the time.

"We want to take data from real-world scenarios and use it to make decisions that solve real-world problems."

—LESLE COLLINS, PROFESSOR OF ELECTRICAL AND COMPUTER ENGINEERING

Assistant Research Professor Kenneth Morton and Professor Leslie Collins are programming computers to analyze video data fast enough to drive a virtual car at 130 miles per hour.
Detecting and treating disease with light

Duke engineers are lighting the way to a new era in medicine—literally.

As one of the world’s leading biophotonics research teams, these specialists focus on harnessing the unique properties of light to detect and manipulate biological materials. With colleagues from across Duke’s medical center and university, they are developing a spectrum of solutions to pressing problems in health care, from diagnosing and treating cancer, to guiding and improving surgery, to designing new tests to identify telltale biomarkers of disease.

Joseph Izatt, program director for biophotonics at Pratt’s Fitzpatrick Institute for Photonics, and collaborators are using optical coherence tomography (OCT) to improve treatment of serious eye diseases. Early in his career Izatt helped develop the first clinically viable OCT, an optical imaging method that uses near-infrared light to capture diagnostic images from inside the eye. Today, it’s a $1 billion-per-year industry and standard technology for diagnosing retinal problems—but its potential is hardly exhausted.

In 2007, Izatt and his company, Bioptigen Inc., made the technology portable, designing a handheld device 40 times faster than existing OCT equipment. Suddenly, ophthalmologists could obtain previously elusive diagnostic images, such as retinal views in infants to detect neonatal vision loss.

Recently, his team created a way for OCT to profile individual cell membranes with nanosecond spatial and millisecond temporal resolution. They used this technology to monitor the “heartbeat” of individual heart muscle cells growing in culture.

Their next goal, he said, is to extend OCT for image guidance of retinal microsurgery. While OCT doesn’t yet guide operations in real time, it is impactful, said one of Izatt’s collaborators, Duke retinal surgeon Cynthia Toth.

“OCT images give you more information about the retina before you begin surgery,” she said. “So, you operate smarter, and it translates into better patient outcomes.”

In particular, she said, OCT assists surgeons in repairing macular holes that form at the retina’s center and impair vision. The enhanced, imaging-provided detail helps surgeons select the most appropriate method to treat each hole and offers insight into why and how it formed in the first place.

The team is also working to help OCT fill a critical and growing need in cataract surgery, one of the most often-performed of all surgeries worldwide, Izatt said.

“In cataract surgery, the surgeon replaces an older patient’s cloudy lens with a plastic one, but in order to choose the new lens correctly he or she first needs to know the power of the patient’s cornea,” he said.

“The current instruments for measuring corneal power were not designed for people who have had vision correction surgery such as LASIK. Adapting the three-dimensional imaging power of OCT in the front of the eye will help surgeons pick the right replacement lens in this growing population.”

Since its invention just over 20 years ago, the imaging speed and resolution capabilities of OCT have increased manifold. But each new generation of these improvements causes a sharp increase in the size of imaging datasets, said Sina Farsiu, director of Duke’s Vision and Image Processing (VIP) Laboratory. The hardware produces an extraordinary amount of micron-level information that cannot be analyzed or searched without computer assistance.

“Ophthalmologists get minutes to spend with patients, and they don’t have the time to analyze all the images from a scan,” he said. “They want data to be compressed into a meaningful quantitative measurement – that’s what I do.”

Farsiu’s computer-automated algorithms mine the diagnostic images Izatt’s tools capture, searching for and quantifying disease biomarkers. His latest improvements could be particularly effective for diabetes-related blindness, he said. Currently, treatment is trial-and-error. Physicians try therapies until one...
Undergrad engineer makes scans speedier

Duke senior Kevin Shia is part of the team working in Joseph Izatt’s lab to improve the efficiency and clarity of optical coherence tomography (OCT). His efforts are focused on reducing the artifacts in diagnostic images caused by eye movements.

To do this, Shia has already doubled the OCT imaging speed from 100 nearly 200 images per second. Increasing the scan speed reduces the likelihood that eye movements will create any blurs in an image, he said. Now, he is working with a graduate student on a novel technique to double the speed yet again by splitting the laser beam used in OCT into two beams to image different parts of the retina simultaneously.

“Effectively, what we’re doing there is making the image depth twice as long, so we can fit two images into a single scan,” Shia said. “Then, potentially, we’ll take the dual-site imaging technique, incorporate it with the previous project that speeds up the imaging, and, hopefully, we’ll have 400 images per second.”

Shia is one of 60-plus Duke engineering undergrads gaining hands-on research experience as a Pratt Research Fellow. The competitive fellowship program pairs students with faculty advisors for intensive research experience in their majors, including summer research and course credit opportunities.

works. Using Izatt’s hardware and Farsiu’s algorithm, the team aspires to image patients to help physicians immediately identify the best biomarker-based treatments.

Very soon, Farsiu’s algorithms may need to process even more data. With a new multi-center grant headquartered at Duke from the National Institutes of Health, the team is hard at work on the latest hardware improvements to improve OCT imaging speed from 100 nearly 200 images per second. Increasing the scan speed reduces the likelihood that eye movements will create any blurs in an image, he said. Now, he is working with a graduate student on a novel technique to double the speed yet again by splitting the laser beam used in OCT into two beams to image different parts of the retina simultaneously.

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Solving health problems across the spectrum

Tuan Vo-Dinh and collaborators at Duke’s Fitzpatrick Institute for Photonics are moving the field of photonics forward fast, developing an array of optical technologies that make detecting and treating disease faster, cheaper, more accurate and less invasive.

For instance, Vo-Dinh developed a nanoprobe with a 50-nanometer tip, small enough to “see” inside a living cell without harming it. The nanoprobe also can be used to detect at a single-cell level the effectiveness of photodynamic therapy drugs to treat cancer. Tumors absorb the drugs, which absorb light to trigger the signal for producing toxic singlet oxygen, leading to cell death. Vo-Dinh and his postdoctoral associate Hsin-Neng Wang are also working with Duke medical researchers to develop tools that can detect disease based on the unique ways various biomarkers interact with plasmonic metal nanoparticles to reflect light. For example, by using an inexpensive, miniaturized optical reader to examine biopsied patient tissue extracts, the Vo-Dinh group and gastroenterologists Dr. Katherine Garman and Dr. Anna Mae Diehl can detect a quick color change that can indicate gastrointestinal cancer.

Vo-Dinh has also been working with Drs. Geoffrey Ginsburg, Christopher Woods and Aimee Zaas at Duke’s Institute for Genome Sciences & Policy to develop a sensor chip for rapidly detecting biomarkers of infectious diseases.

“The convergence of new technologies will enable us to produce low-cost, sensitive tools to detect multiple diseases at once, right at the point of care,” Vo-Dinh said. “This will be a great advance, especially in developing countries or remote areas with a lack of resources or trained personnel.”

Biophotonics also promises to help caregivers monitor health in real time. In his latest endeavor, Vo-Dinh, with Duke collaborators Bruce Klitzman and Thies Schroeder and an industry partner, PROFUSA, received a grant from the Defense Advanced Research Projects Agency (DARPA) to develop in-body nanosensors.

The goal is to develop a nanosensor that can recognize disease biomarkers and trigger a signal recognized by an optical detector. “This is a very exciting and also very challenging project,” Vo-Dinh said.

His team must strengthen the signal to ensure detection through tissue, as well as keep the nanosensor biocompatible and sturdy in the long term.

As director of the Fitzpatrick Institute for Photonics, Vo-Dinh is often called on to explain the Institute faculty’s work to people who don’t know much about photonics.

“It’s an exciting area with profound societal impact!” Vo-Dinh said. “This will be a great advance, especially in developing countries or remote areas with a lack of resources or trained personnel.”
Cancer treatment is notoriously brutal—which is why Jennifer West’s work is creating such a buzz. The Duke engineer has developed a way to kill tumors without the kinds of negative side effects associated with chemotherapy and radiation.

West and her team discovered that they could destroy soft-tissue tumors by injecting gold-covered nanoshells about 100 nanometers (nm) in size into the body, then heating them up with light. The method is currently being tested in three human clinical trials focused on prostate, lung, and head and neck cancers.

“From our animal trials, we saw a complete regression of tumors and no regrowth or adverse effects,” West said. “This is different from using drugs because it’s really a mechanical effect. You’re not binding something to a biochemical—you’re cooking something.”

This method works, she said, because blood vessels that form quickly to support tumors are leaky, and they readily absorb the gold-covered nanoshells. The gold covering is 15 nm thick—laid on an inert silica core at the exact thickness and curvature needed to absorb infrared light. (One nanometer is approximately 1/75,000th the thickness of a human hair, or 1/8,000th the size of a red blood cell).

Roughly 24 hours after injecting the nanoshells, researchers shine a 800 nm wavelength infrared light over the cancerous tissue for four minutes. The gold, the most biocompatible inert metal, heats up and burns away the tumor.

The novel treatment is breaking new ground with the Food and Drug Administration, West said. It’s one of the first nanotechnologies to seek agency approval, so they’re navigating new regulatory waters. Her company, Nanospectra Biosciences, Inc., hopes to bring a product to market within two years.

### Turning genes on with light

Shining light on plants usually promotes photosynthesis, but Charles Gersbach merges plant genes with human cells and exposes them to blue light to make them produce proteins.

This system, involving two light-sensitive plant proteins that have been genetically introduced into human cells, could give researchers greater control over human gene expression, the process by which genes give instructions for critical protein production.

“Currently, we take stem cells and, by turning on genes, make muscle, bone, cartilage, but we must tell all cells simultaneously,” he said. “We want to use light to control this so eventually we can make more complicated structures—ones prompted to grow more naturally when lights are turned on and off.”

This process, called Light Induced Transcription using Engineered Zinc finger proteins (LITEZ), combines two proteins from the common flowering plant Arabidopsis thaliana, gigantea and Efl. Zinc finger proteins are used to control how these plant proteins interact with human genes.

Essentially, Gersbach said, his team hijacked the plants’ ability to sense the length of day and imported it into human cells to control genes.

To test their gene expression control, Lauren Polstein, a graduate student in Gersbach’s laboratory, fused the plant proteins to the zinc finger proteins and introduced them into human cells in a Petri dish. Next, they placed the dish on a blue LED display and turned on the lights. That exposure prompted gene-activating proteins to gravitate toward genes with newly-added zinc finger proteins, causing those genes to turn on.

The team exposed the dishes to blue light for a pulse of three seconds at three minute intervals. Within 24 hours, maximum gene expression was achieved, and the team could precisely control gene expression by covering up certain cells.

According to Gersbach, this technology could be applied broadly.

“I envision a Star Trek-type scenario where we expose tissue to a therapy, and then use fiberoptics to light up where we want it to turn on,” he said. “But, more immediately, it can be used for more precise genetic engineering that will advance basic research.”

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**Left:** Jennifer West, the Fitzpatrick Family University Professor of Engineering at Duke, is internationally recognized for pioneering advances in nanotechnology and tissue engineering. **Above:** Nanoshells, appearing as tiny points of light, accumulate in tumor vessels.
Detecting colon cancer—earlier and easier

More than a million Americans suffer from inflammatory bowel disease—a chronic condition that increases the risk of colon cancer. But the usual surveillance method to spot precancerous tissue—colonoscopy with biopsy—is cancerous tissue. But the usual surveillance method to spot cancerous tissue—colonoscopy with biopsy—is

Colon polyps are removed or burned off,” he said. “With this improvement, it will be easier to discern malignant potential, and you can change therapies immediately if you need to.”

A better malaria test

Worldwide, malaria infections are dropping, and infected patients have fewer parasites in their bodies. This is good news on the global health front, but it presents a challenge to caregivers—who need a better, more sensitive way to diagnose the disease.

Duke biomedical engineer Kam Leong and collaborators met this need with a new, non-invasive malaria test that pinpoints the parasite using a single drop of bodily fluid, usually saliva or blood. They’re now working to commercialize the test.

This technique, known as rolling-circle enhanced enzyme activity detection (REEAD) and developed by Birgitta Knudsen at Aarhus University in Denmark, identifies the enzyme topoisomerase I (pTOpl) present in the malaria-causing Plasmodium parasites by using a lab-on-a-chip (LOC) technology developed by Sissel Juul and Megan Ho in the labs of Leong and Knudsen.

LOC devices combine several laboratory functions in a small chip designed to analyze small-volume fluid samples with high sensitivity.

The technology offers advantages over a common laboratory tool used to detect malaria—polymerase chain reaction (PCR), which replicates DNA to create a sample size large enough to detect the DNA of the Plasmodium parasite. This technique presents two problems: it requires extensive sample preparation and a heat source that alternates between low to high temperatures.

“The many temperature cycles needed means the process is often expensive and bulky,” said Leong. “REEAD is much simpler, so it has a real advantage over PCR in remote, resource-poor areas.”

REEAD is isothermal, he said. At room temperature it’s sensitive enough to detect the pTOpl enzyme in cells. Its detection limit is potentially less than one parasite per microliter of unprocessed body fluid, and it costs less because it doesn’t need electricity or a clean water supply.

To test whether REEAD could identify pTOpl in a small sample, Leong in collaboration with Knudsen’s team encapsulated blood samples from 31 infected and uninfected individuals in water-in-oil droplets and, then, killed the cells with a low-salt solution. Next, they transferred the samples to a primer-coated slide and exposed them to light for optical detection of the pTOpl signals.

The technique correctly identified all 20 malaria-infected blood samples, and it accurately pinpointed the four infected saliva samples from a group of 12.

Leong and his collaborators at Duke, as well as in France, Denmark, and Africa, are now adapting the technology for portability and functionality in visible, rather than ultraviolet, light.
Can photons tell good tissue from bad?

Nimmi Ramanujam is showing that light can be a powerful tool for making cancer diagnosis faster and treatments more effective. To identify cancerous tissue in the breast, for example, Ramanujam’s team shines non-ionizing white light between the visible and ultraviolet wavelengths into breast tissue after it has been removed from the body. Photons from the light either scatter throughout the tumor or are absorbed as they come into contact with optically-detectable cancer biomarkers, such as blood oxygenation levels, beta-carotene concentration, and collagen content.

The team collects data based on the diffuse reflectance spectrum—the range at which light reflect at different angles. Ramanujam’s Monte Carlo feature extraction algorithm separates the diffuse reflectance spectrum into the absorption or scattering levels of the tissue, which in turn can help distinguish whether tissue is benign or malignant.

While white light can’t penetrate deeply into tissue, it’s a useful diagnostic tool, especially for areas that can be penetrated non-invasively, such as the breast, mouth, nasal cavity, or cervix, said Marlee Junker, a research analyst in Ramanujam’s lab. “It’s non-destructive, simple to use, and it doesn’t require us to use any large and expensive instrumentation.”

To translate the technology into clinical practice, Ramanujam founded the company Zenalux in 2006 with funding from one of the first Duke-Coulter Translational Partnership grants. With their flagship product, Zenalux reduced the large instruments from Ramanujam’s lab to a 4-by-5-by-9 inch formfactor. The Zenascope is a small spectroscopy system packaged into a convenient console and equipped with a single-channel, pen-like probe designed to be held in the fingertips and the Monte Carlo feature extraction algorithm. Future generations of the device will be able to self-calibrate to adjust for lamp fluctuations and have pressure-sensing capabilities that capture measurements the moment a specified pressure is achieved.

Once in place, the probe shines light on the tissue and collects the reflectance spectrum. The algorithm converts the reflectance into the intrinsic absorption and scattering of the sampled tissue. The algorithm is employed in real-time, so the team is able to view the quantified endpoints during an experiment. The process takes milliseconds to complete, allowing for real-time data analysis—for example, enabling surgeons performing breast-conserving surgery to check whether they’ve removed all the cancerous tissue during surgery.

Ultimately, Ramanujam anticipates that this technology will allow physicians to give patients a bedside, real-time diagnosis, while increasing accuracy and reducing unneeded surgeries. The team is currently testing whether the probe can accurately diagnose cervical cancer in Haitian women.

From the lab to Haiti

First-year PhD student Chris Lam (pictured at right in blue) is working to adapt the white-light spectroscopy system from Nimmi Ramanujam’s lab for effective use with cervical cancer screening in Haiti. A master’s graduate of the Duke Global Health Institute, Lam is also a biomedical engineer who builds the various system components. It takes a full day, he said, to print a housing for the sensors with a 3D printer. To make the system widely useful in the field, Lam is working to miniaturize it and reduce the amount of power it needs.

“Eventually, we want something totally battery-powered or run off a tablet or cell phone,” Lam said. “Our power sources right now are limited because the area is resource-poor.”

Lam, a John T. Chambers Fellow, is one of five Duke graduates to receive a 2012-2013 fellowship at the Fitzpatrick Institute for Photonics. Each fellow is funded by the sponsor’s support and recognized as a Chambers Fellow or Fitzpatrick Fellow.

With a world-class medical center steps away from a leading engineering school, Duke is fertile ground for biomedical innovation—and the Duke-Coulter Translational Partnership is providing the seed money for a bumper crop of breakthroughs.

The partnership began in 2005, when the Wallace H. Coulter Foundation selected Duke as one of nine universities to accelerate the translation of university biomedical engineering projects into commercial products and clinical practices. The partners in 2011 invested an additional $20 million to foster collaborations between biomedical engineers and clinicians—with an ultimate goal of developing new technologies to improve patient care.

So far, the partnership has reaped big results:

26 projects funded, from drugs for stroke, to diagnostics for hemophilia, to imaging to improve regional anesthesia in surgery

Six startups with Duke-Coulter intellectual property

Three additional licenses to existing companies

Over $105 million in follow-on support from private equity and federal, state and foundation grants

Learn more: bme.duke.edu/coulter
A Highway Without Speed Limits

Duke engineers are creating a computational autobahn to accelerate the discovery and creation of innovative materials.

Stefano Curtarolo jumped for joy when he heard President Barack Obama’s call for a national Materials Genome Initiative. As he saw it, the work he had started more than ten years earlier would now grab the attention, and the support, of the public and politicians in Washington. That support in turn would help stimulate the creation of the vast computational infrastructure necessary to create the next generation of materials out of which to build the latest technologies.

Curtarolo, professor of mechanical engineering and materials science and of physics at Duke, believed that just as the biological scientists made stunning discoveries after the Human Genome Project began, the new national initiative would do the same in advancing the abilities of materials scientists to come up with novel materials and alloys with unique characteristics. Additionally, he felt, since he had already been laying the fundamental groundwork for several years, he had a head-start on the newcomers to this new field.

“To help businesses discover, develop and deploy new materials twice as fast, we’re launching what we call the Materials Genome Initiative. The invention of silicon circuits and lithium-ion batteries made computers and iPods and iPads possible—but it took years to get those technologies from the drawing board to the marketplace. We can do it faster.”

—PRESIDENT BARACK OBAMA, JUNE 2011

To take advantage of this potential, Duke Engineering created the Center for Materials Genomics, which was founded by Curtarolo with associate director Omar Knio, professor of mechanical engineering and materials science and director of uncertainty and risk assessment. “Modern technology is demanding new materials at an increasing pace,” Knio said. “In order to tackle some of the most pressing energy and defense problems, we must develop new materials. And these new materials must be smarter, cheaper, environmentally friendly and compatible with existing manufacturing processes.”

“The task might seem at first glance to be insurmountable,” Knio said, “but a new highway has opened in the materials discovery world—the high throughput computational method, which not only allows computers to churn through all the characteristics desired in a new material, but to produce the recipe quickly.”

The Duke center recently received more than $300,000 from the Department of Defense to obtain the necessary computing power to beef up current capabilities and $1 million from the Department of Energy to develop materials discovery algorithms—with more federal grants, as well as...
Theory Guides Experimentation

In his work with Duke’s Center for Materials Genomics, Stefano Curtarolo provides the theoretical underpinning for creating novel materials with distinctive properties. While these insights will certainly help further the development of new materials, one of his Duke collaborators used the theories to improve materials already in production for use in everyday products—in this case carbon nanotubes.

These nanotubes are man-made, microscopic, “mesh-like” tubular structures that are used in hundreds of products, such as textiles, solar cells, transistors, pollution filters and body armor. Curtarolo saw his theories of optimizing the properties of nanotubes confirmed by a series of intricate experiments conducted by Jie Liu, Duke professor of chemistry. Liu developed a novel method for measuring not only the lengths of growing carbon nanotubes, but also their diameters.

“Normally, nanotubes grow from a flat surface in an unorganized manner and look like a plate of spaghetti, so it is impossible to measure any individual tube,” Liu said. “We were able to grow them in individual parallel strands, which permitted us to measure the rate of growth as well as the length of growth.”

By growing these nanotubes using different catalyst particle sizes and at different temperatures, Liu was able to determine the “sweet spot” at which the nanotubes grew the fastest and longest. As it turned out, this occurred when the particle was in its viscous state—between a solid and liquid—and that smaller was better than larger, exactly as predicted by Curtarolo.

These measurements provided the experimental underpinning of Curtarolo’s hypothesis that given a particular temperature, smaller nanoparticles are more effective and efficient per unit area than larger catalysts of the same type when they reside in that dimension between solid and liquid.

By reliably controlling the growth and size of these carbon nanotubes, manufacturers will be able to take full advantage of their properties. These findings will also help manufacturers grow the nanotubes faster and more efficiently, Liu said.

“Typically, in this field the experimental results come first, and the explanation comes later,” Liu said. “In this case, which is unusual, we took the hypothesis and were able to develop a method to prove it correct in the laboratory.”

An Elemental Cookbook

In the simplest of terms, Curtarolo and his colleagues have created a Joy of Cooking for scientists wishing to develop materials for ultra-specialized uses, such as highly efficient electrical components to cool down electronics like laptops (replacing the bulkier fans now in use).

However, in the past, finding the right com-
any specific combination of elements under investigation. On one end of the spectrum, Curtarolo explained, is “fragile.” “We can rule those combinations out because, what good is a new type of crystal if it would be too difficult to grow, or if grown, would not likely survive?” Curtarolo said. A second group of combinations would be a middle group termed “feasible.” But what excites Curtarolo most are those combinations found to be “robust.” These crystals are stable and can be easily and efficiently produced. Just as importantly, these crystals can be tailored to provide unique electrical properties.

**Thermodynamic Applications**

Thermoelectric devices take advantage of temperature differences on opposite sides of a material—the greater the temperature difference, the greater energy potential. On Earth, such devices power campsite coolers. In space, they provide power for deep-space satellites, where the side of the device facing the sun absorbs heat, while the underside of the device remains extremely cold. The satellite uses this temperature difference to produce electricity to power the craft.

In the past, scientists have not had a rational basis for combining different elements to produce these energy-producing materials. Different material combinations may be a more efficient method of turning these temperature differences into power, according to Shidong Wang, a post-doctoral fellow in Curtarolo’s laboratory. Thermoelectric materials can be created by combining powdered forms of different elements under high temperatures. Not only does the new system provide the recipes, but it does so for the extremely small versions of the particular elements, known as nanoparticles. Because of their minuscule size and higher surface areas, nanoparticles have properties unlike their bulk counterparts.

“Having this repository could change the way we produce thermoelectric materials,” Wang said. “With the current trial-and-error method, we may not be obtaining the most efficient combinations of materials. Now we have a theoretical background, or set of rules, for many of the combinations we currently have. The approach can be used to tackle many other clean-energy related problems.”

Curtarolo pointed out that as steel made possible the steam engine and industrial revolution, and silicon made the information age a reality, developing new materials are crucial to revolutionize future advances.

As President Obama said in his speech, “It’s worth remembering, there was a time when steel was about as advanced as manufacturing got. But when Andrew Carnegie discovered new ways to mass-produce steel cheaply, everything changed. Just 20 years after founding his company, not only was it the largest, most profitable in the world, America had become the number one steelmaker in the world.”

The Duke engineers believe they can lead the same type of revolution in materials science—though a lot faster.
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10% Underrepresented minorities
92% Graduate in four years
90% Have an intensive research experience or an industry internship
32% Study abroad

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Total graduate enrollment has increased from 594 to 867 since 2008

Launched new Master of Engineering programs in 2010

Ph.D. Plus Enhancement program launched in 2012 is one of the first in the country to offer entrepreneurship and professional training for Ph.D. students

FACULTY GROWTH

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PRATT PRIDE

3 Rhodes Scholars (since 2000)
3 Marshall Scholars (since 2000)
8 Goldwater Scholars (since 2000)
7 Fulbright Scholars (since 2000)
2 Churchill Scholars (since 2000)
11 Whitaker International Scholars (since 2006)
12 NSF Graduate Fellows (2012)
6 research papers published in Science and Nature in 2012
24 alumni and faculty elected to National Academy of Engineering
17 companies started by Pratt faculty
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GROWTH IN RESEARCH EXPENDITURES*

*Does not include Computer Science or joint faculty with primary appointments outside Pratt

Cover Illustrations: Details of renovated space in Duke’s Gross Hall, home to the new Information Initiative at Duke (see page 6)