Interdisciplinary approaches to improving public health began with the School’s first dean, Charles F. Chandler, a chemist, who, in 1866 began to improve standards in New York City for milk and water purity. Then, in 1896, electrical engineering professor Michael I. Pupin created a fast-exposure X-ray that was first used by a surgeon to locate buckshot in a patient’s hand. The following pages present a sample of the work of current faculty from many of our departments, all making discoveries that improve human health at a local and global scale.
minimally invasive, or laparoscopic, surgery has many advantages. By using several small incisions rather than one large cut, it reduces patient trauma and pain while speeding recovery and lowering costs. Yet it remains a niche procedure. Peter Allen, who likens it to pushing long sticks through small holes, sees several reasons why.

First, laparoscopic tools move counter-intuitively. Surgeons must move left to go right, or up to go down, for example. That means extensive training to learn to make precision cuts or tie sutures. The use of long, rigid sticks also limits the complexity of potential procedures. Finally, laparoscopy demands a high level of teamwork by surgeons inserting tools through several incisions.

Allen's solution is much simpler: small, intuitive robotic tools that provide a single surgeon with everything he or she needs to conduct a procedure through a single incision. He has already taken the first step, licensing a small robotic imaging system co-developed with Columbia physician Dennis Fowler. The device pans, tilts, and zooms to generate 2-D or 3-D images, and tracks surgical instruments automatically. The system has been tested in vivo on animals.

Building the device presented many engineering challenges. The package's high-resolution camera, bright lights, powerful motors, and control system had to fit through a single half-inch incision. "We want to create a robotic surgical platform that is so small, it can perform surgeries through natural orifices without an incision," said Allen. "That's the way surgery is moving. We could move it through the esophagus to the stomach, perform the operation, stitch it up, and take it out again."

To control costs, Allen opted for common off-the-shelf parts that he could buy through catalogs. He assembled the device from five-millimeter watch motors, small surveillance cameras, and LED lights. "The idea was to keep costs down," Allen said. "Ultimately, we want to drive component costs under a few hundred dollars so we can make it disposable."

Automated tracking is one of the device's most innovative features. Physicians manually box an image of whatever they want to track. The software keeps the camera aligned. "It's a challenging environment, with blood spills and occlusions. If the camera loses the target when it moves behind an organ, it does an intelligent search to reestablish its position," Allen said.

“What we have now is a robotic platform inside the body that can move a camera,” he continued. “We want to extend that by adding more tools and creating a small, affordable platform for robotic surgery.”
Little is known about the biological causes for psychiatric disorders like schizophrenia and bipolar, which combined afflict an estimated 10 million people nationwide. Columbia researchers are working hard to change that by exploring the role of genetics from a multidisciplinary approach.

Dimitris Anastassiou’s aim is to discover novel biological mechanisms responsible for psychiatric disorders. Given the limited success of identifying significant individual risk-conferring genetic variants, such as single mutations in DNA, Anastassiou says discovery of responsible interactions among multiple genetic variants may reveal new disease mechanisms.

Anastassiou and Maria Karayiorgou, professor of psychiatry and medical genetics at the Columbia University Medical Center, are principal investigators on a project that will identify single nucleotide polymorphisms (SNPs, pronounced “snips”) that are jointly, rather than individually, associated with disease.

A SNP is a small genetic change that can occur within a person’s DNA sequence. The genetic code is specified by the four nucleotide “letters” A (adenine), C (cytosine), T (thymine), and G (guanine). SNP variation occurs when a single nucleotide, such as an A, replaces one of the other three nucleotide letters—in this case C, T, or G.

An example of a SNP is the alteration of the DNA segment AAGGTTA to AAGTTTA, where the fourth letter in the first snippet, G, is replaced with a T. On average, SNPs occur in the human population more than one percent of the time, but because neighboring SNPs are statistically linked, researchers only need about one million of them to analyze our genomes.

The traditional approach looked only at individual SNPs. Anastassiou’s research investigates the possibility that a person may be predisposed to a disease if two SNPs at different locations in the genome have the unusual letter combinations, rather than each one of them alone, a phenomenon called “synergy.” There is a huge number (about a million squared) of “synergy” pairs of SNPs, resulting in significant computational and statistical challenges for this project. To perform this research, Anastassiou has a high-performance computer cluster containing 800 processors at his disposal.

“The aim is to discover the biological mechanisms responsible for psychiatric disorders,” said Anastassiou. “Once such mechanisms are discovered, the ultimate vision is to develop drugs that would interfere with these mechanisms.”

Anastassiou is a prominent leader in digital technology. His research has resulted in Columbia being the only university in a consortium that licenses MPEG-2, the technology used in all forms of digital television transmission, including DVDs, direct satellite TV, HDTV, digital cable systems, personal computer video, and interactive media.

Dipl., National Technical University of Athens (Greece), 1974; M.S., University of California-Berkeley, 1975; Ph.D., U.C. Berkeley, 1979

Finding the Mechanisms of Psychiatric Disorders

DIMITRIS ANASTASSIOU

Charles Batchelor Professor of Electrical Engineering
About 25 million U.S. adults suffer from osteoarthritis, a debilitating degeneration of the joints that can cause extreme pain and limit mobility. Cartilage, the thin, white connective tissue lining the ends of the bones, normally works as a cushion that redistributes stresses and reduces friction. But with osteoarthritis, it wears away. As a result, bones rub directly against each other. The problem is getting worse as the U.S. population gets older and heavier. (Extra weight puts more pressure on joints.)

Gerard Ateshian and his team are trying to understand how normal cartilage provides lubrication. That way, they can slow down the degeneration of the cartilage or come up with substitutes to repair worn joints. Cartilage is a highly hydrated tissue. In fact, nearly 90 percent of the cartilage located near the articular surface consists of water. This fluid pressurizes upon loading and supports most of the load transmitted across the joint. As a result, there is very little friction and wear of cartilage under normal conditions.

Traditionally lubrication has been an engineering topic. So this research, which applies engineering to a problem related to physiology, is a perfect marriage of engineering and medicine. The goal: to use tissue engineering techniques to grow artificial cartilage that is as strong and resilient as the native tissue, and equally able to reproduce low friction and wear.

In adulthood, the biological triggers that tell cartilage to regenerate are turned off. Therefore, human cartilage cannot restore itself once it has deteriorated in the joints. But fortunately, the body is unlikely to reject the lab-grown tissue since adult cartilage does not contain blood vessels.

As a result, it is unlikely that recipients of engineered cartilage would need anti-rejection drugs, providing a viable alternative to joint replacement surgery or debilitating pain. In collaboration with Clark Hung from biomedical engineering, Ateshian has applied insights gained from cartilage mechanics and lubrication studies to develop better and stronger engineered cartilage.

Ateshian is director of the Musculoskeletal Biomechanics Laboratory, which he founded in 1996. The lab’s fundamental philosophy is that major scientific breakthroughs can be achieved in biomedical engineering by judiciously combining theoretical analyses with experimental studies. The lab’s research efforts have expanded toward modeling of solute transport and growth processes in biological tissues, the development of computational tools that can address these mechanisms, and the extension of insights gained from musculoskeletal studies to cardiovascular tissues and reproductive cells.

In medical imaging, physicians need high-resolution images with high contrast, so they can see what’s inside the body, down to the submillimeter level. Such images allow physicians to pinpoint treatment, so they can eradicate disease-causing tissue without harming healthy tissue that surrounds it. Researchers use varying techniques to create images of what’s inside the body. Ultrasound techniques, for example, produce high-resolution images but sometimes with little contrast, so it’s hard to discern healthy from unhealthy tissue. Optical tomography, which uses infrared light, produces images with high contrast but poor resolution. Photoacoustic tomography is a new multi-physics modality for obtaining high-contrast, high-resolution images of human tissues.

Guillaume Bal specializes in the field of mathematical inverse problems, working in the theoretical realm and collaborating with scientists and engineers who are exploring ways to develop new methods for imaging. He has developed mathematical models for several modalities of medical imaging, including optical tomography, photoacoustics, and several other novel multi-physics modalities combining ultrasound with optical or elastic waves. Photoacoustics is seen as a promising modality for obtaining accurate imaging of tissue in the human brain. His work also helps inform applications in earth science, where researchers work to create images of what exists below the surface of Earth.

Bal also develops mathematical models to analyze equations with random coefficients. He uses such equations for problems involving water or seismic waves moving through geologic formations, sound waves moving through the ocean, or light streaming through the atmosphere. These models look at phenomena at the macroscopic scale, which is more amenable to computations and parameter estimation. Such analyses are crucial in the field of uncertainty quantification with a wide array of applications ranging from dynamics in nuclear waste disposals to uncertainties in climate modeling.

Bal joined Columbia Engineering in 2001 as an assistant professor of applied mathematics. In the fall of 2003, he was a visiting scholar at the Institute for Pure and Applied Mathematics at the University of California-Los Angeles. Bal has also taught at the University of Chicago and was a postdoctoral research associate at Stanford University. He is the recipient of the 2011 Calderón prize. Other awards include an Alfred P. Sloan Fellowship in 2003 and an NSF Career Award, also in 2003.

Diplôme, École Polytechnique (France), 1993; Ph.D., University of Paris VI (France), 1997
People suffering from brain diseases and conditions ranging from traumatic brain injury to brain cancer to progressive brain disorders could be helped if therapeutic drugs could be easily delivered to the affected areas. The blood-brain barrier (BBB), composed of tightly interacting cells, acts as part of the body’s defense system to block bacteria and other substances carried in the blood from invading the brain. It is extremely effective, which makes it very difficult to deliver important diagnostic and therapeutic agents to the brain.

Scott Banta is working toward solving this problem by using a biochemical engineering approach, creating specific cell penetrating peptides (SCPPs) that can cross the BBB and target specific brain cell populations. Banta and his research group are engineering new peptides that are specific for different cell and tissue types. The plasma membrane protects cells by regulating the access of molecules to the cellular cytoplasm. Only compounds within a narrow range of size, charge, and polarity are able to cross the membrane. Using the process Directed Evolution, the Banta group is creating new SCPPs that are able to both target and penetrate specific cells. These peptide sequences can deliver therapeutic cargos, such as DNA, proteins, drugs, or other exogenous materials, to the targeted cellular cytoplasms.

Collaborating with Barclay Morrison of the Department of Biomedical Engineering, Banta is seeking to create SCPPs that are specific for different brain cell types. There is a narrow window of time following a brain injury where the targeted delivery of neurotrophic agents to injured cells could provide a significant benefit to the head-injured patient. In addition, delivery of neurotrophic factors via SCPPs could be beneficial in slowing down the progress of diseases such as Parkinson’s, Alzheimer’s, and Huntington’s. This project has been supported by the National Institutes of Health and the National Science Foundation.

Banta’s interests and expertise extend beyond the human body. In 2010, Banta was awarded an ARPA-E grant from the U.S. Department of Energy to launch new research on using genetic engineering to create renewable biofuels in collaboration with Alan West (Chemical Engineering) and Kartik Chandran (Earth and Environmental Engineering).

“We are going to use genetic engineering to incorporate a new metabolic pathway into an organism that is currently used for wastewater treatment,” he said. “The bacterium, N. europaea, has the ability to grow on ammonia, oxygen and CO2. We will engineer it to create isobutanol, which is a biofuel that is compatible with the existing transportation infrastructure. The cells will fix CO2 from the atmosphere, and the ammonia will either be generated electrochemically, or it will be obtained during wastewater treatment.”

B.S., University of Maryland (Baltimore County), 1997; M.S., Rutgers University, 2000; Ph.D., Rutgers University, 2002
Malaria kills one million victims each year in tropical countries, most of them children. While drugs exist to combat the disease, the malaria parasite develops resistance to these drugs. An effort is now underway to harness a noninvasive electromagnetic-based treatment in the fight against this disease.

The electromagnetic field used in this innovative treatment is the same that is produced in lightning, is responsible for the Northern Lights, and also causes compasses to point in a north-south orientation. It is also found in high-frequency radio waves that bounce from one part of the world to another via antennas to phone networks, TV pictures, and the Internet.

Understanding electromagnetic fields allows scientists to develop smaller and more powerful antennas useful in emergency communication devices and portable radar, or those made flexible with new alloy materials and applied to implantable medical devices. Electromagnetics also has a direct application at the biological level—as in the treatment of parasitic diseases like malaria.

Malaria is caused by a parasite that is transmitted from one human to another by the bite of mosquitoes. In humans, the malaria parasite travels to the liver, where it invades a red blood cell. There, it consumes the cell’s hemoglobin and produces hemozoin, an iron crystal, as a waste product. It then divides into many more daughter parasites that invade other red blood cells. Researchers now understand that the iron crystal remains with the parasite within the host cell. By applying a suitably designed magnetic field, the iron crystals can be made to agitate, rotate, and churn, destroying the parasite before it can multiply further.

Paul Diament is the lead inventor of the magnetic resonance method of treating the malaria parasite, and is working with biologists at the Columbia Medical Center in pursuing this application. He is an eminent researcher in electromagnetics and wave propagation. His teaching and research focus includes microwaves, antennas, optics, radiation statistics, plasmas, wave interactions, relativistic electron beams, and transient electromagnetic phenomena. Along with biomedical applications, his research interests include attempts to make mutual coupling among antennas beneficial rather than detrimental, potentially achieving smaller antenna sizes.

Diament is a member of the Institute of Electrical and Electronics Engineers, the American Physical Society, the Optical Society of America, Tau Beta Pi, Eta Kappa Nu, and Sigma Xi.

B.S., Columbia, 1960; M.S., Columbia, 1961; Ph.D., Columbia, 1963

Employing Electromagnetics to Treat Malaria

Paul Diament
Professor of Electrical Engineering
Ten million Americans suffer from osteoporosis, a gradual weakening of the bones that can lead to fractures, loss of mobility and independence, and depression. Another 18 million suffer from low bone mass. No cure exists for either condition. Doctors simply tell patients to consume enough calcium and vitamin D, to do weight-bearing exercise, and to avoid smoking. Sometimes they also prescribe medications, including bisphosphonates (Fosamax, Actonel, and Boniva), selective estrogen receptor modulators (Evista), or hormones such as parathyroid hormone (Forteo). But all come with side effects, and none are free. The only bone builder on the market, Forteo, costs $8,000 a year and requires daily shots for two years.

X. Edward Guo, director of Columbia’s Bone Bioengineering Laboratory, is trying to figure out how to prevent and treat osteoporosis from both engineering analysis and biological perspectives. To do so, he and his team are analyzing high-resolution 3-D images of bone from both laboratory samples and non-invasive patients’ images to figure out how to better predict fracture risk in patients and monitor efficacy of anti-osteoporosis treatment. With several multi-million-dollar grants supported by the National Institutes of Health (NIH) and working with endocrinologists Drs. Elizabeth Shane and John Bilezikian at Columbia University’s College of Physicians and Surgeons, and Dr. Felix Welsch at the University of Pennsylvania, they have developed novel imaging analysis and modeling techniques to identify microstructural deteriorations in bone and have translated these technologies in clinical assessments of osteoporosis. Guo and his team also plan to use their knowledge to better understand osteoporosis and bone loss experienced by astronauts in outer space.

During the last two years alone, Guo, as principal investigator, has received four new NIH grants totaling $6.3 million to support his innovative bone bioengineering research. These include a highly competitive NIH Challenge Grant, which was ranked in the top two percent in the review process. This two-year $915,108 grant will support Guo’s work in testing the novel hypothesis that an osteocyte network may function in a similar way as a neuronal network and plays an important role in mechanical memory.

The current yearly research expenditure in Guo’s laboratory is over $2 million, one of the top funded bioengineering laboratories in the country.

In the future, Guo and his team hope that doctors can prescribe drugs that would help mature bone cells recruit more bone-forming cells and snub the bone-destroying ones. Such drugs would be a boon to an aging population. After all, women over 50 can lose as much as 20 percent of their bone mass around menopause. Perhaps someday everyone could get drugs at a younger age to prevent later bone loss.

B.S., Peking University, 1984; M.S., Harvard-MIT, 1990; Ph.D., Harvard-MIT, 1994
Artificial limbs are being used with increasing frequency to replace missing body parts, such as arms and legs. Typically, patients need them because of infection, circulatory disease, congenital defects, accidents, cancer, or, increasingly, war-related injuries. Right now, nearly four million Americans have a prosthetic device.

Henry Hess and his collaborators are working with molecules to figure out how to build artificial muscles that are as good as the real thing. In a system that’s far more efficient than anything manmade, the human body takes glucose and uses the sugar to power muscles that enable people to move and talk. But if Hess and his team can figure out how to duplicate Mother Nature, they can make better prostheses, and ultimately, better car engines, too. Imagine a car engine that worked like a big, artificial muscle.

The team is also working on novel “smart dust” biosensors, which may be used to detect cancer earlier or detect pathogens like anthrax in the environment. In these devices, the artificial muscles play the role of miniature pumps that collect and transport the molecules of interest.

Hess, who was raised in East Germany, joined the Columbia Engineering faculty in 2009 and teaches Tissue Engineering. The course introduces students to the field of biomaterials, and in particular to the many factors important in the selection, design, and development of biomaterials for clinical applications.

He directs Columbia’s Hess Laboratory on Nanobiotechnology – Synthetic Biology. His lab focuses on the engineering applications of nanoscale motors. Such microscopic motors with the ability to create forces and drive active movement with high efficiency enable new approaches to a wide range of nanotechnologies, including biosensing, drug delivery, molecular assembly, and active materials.

“We have successfully utilized motor proteins in synthetic environments for the controlled transport of nanoscale cargo,” said Hess, ”and continue to advance the design of such hybrid bionanodevices and materials.

“The hybrid approach has the advantage that techniques, materials, and devices unique to either biology or technology can be merged into a revolutionary combination. Applications particularly suited to hybrid systems are found in medicine and biotechnology, where biocompatibility is critical and the environmental conditions are favorable for biological nanomachines.”

His other research interests include engineering at the molecular scale, in particular the design of active nanosystems incorporating biomolecular motors, the study of active self-assembly, and the investigation of protein-resistant polymer coatings.

B.S., Technical University Clausthal (Germany), 1993; M.Sc., Technical University Berlin, 1996; Ph.D., Free University Berlin, 1999.
Rheumatoid arthritis (RA) is an autoimmune disease that affects nearly 20 million people worldwide, striking young people as well as old, causing pain, stiffness, and swelling of the joints. Early diagnosis and treatment can slow or prevent joint damage and increase the likelihood of leading an active and full life.

Leading an international team of engineers, scientists, and physicians from Germany and the United States, Andreas Hielscher has developed a 3-D optical tomographic (OT) imaging system that displays disease activity in joints. “Shining light through the finger allows us to see the disease before X-rays can find any changes,” explained Hielscher, showing the latest results from a recent clinical trial.

In another project that relies on the same harmless light transmission measurements, members of his laboratory have built an optical imaging system for the diagnosis of breast cancer. Breast cancer afflicts one in nine women during their lifetime and is the second leading cause of cancer deaths in women. Hielscher’s patented imaging technology has been licensed by a New York company and promising clinical pilot studies using the new imager are underway.

Hielscher also employs OT imaging to localize green fluorescent proteins (GFPs), developed by Columbia’s 2009 Nobel laureate Martin Chalfie. GFPs and their derivatives make it possible to see and monitor cell and tissue behaviors during development, including observation of cancerous tumors in vivo. Hielscher and his colleagues use GFP to study the growth of cancers in the stomach, liver, and brain. Most recently, he is applying this technology to monitor drug effects in difficult-to-treat early childhood cancers, such as neuroblastoma and Wilms tumors.

Before joining Columbia Engineering in 2001, Hielscher was a postdoctoral fellow at Los Alamos National Laboratory and was on the faculty at the State University of New York Downstate Medical Center. Now he directs Columbia’s Biophotonics and Optical Radiology Laboratory, which works towards establishing optical tomography as a viable biomedical imaging modality. To this end, Hielscher’s team is developing state-of-the-art imaging hardware and software that provide 3-D distributions of physiologically relevant parameters in biomedical systems. The work of the laboratory is supported, among others, by the National Institute of Arthritis and Musculoskeletal Skin Diseases, the National Institute of Biomedical Imaging and Bioengineering, the National Cancer Institute, and the New York State Foundation for Science, Technology and Innovation.

B.S., University of Hannover (Germany), 1987; M.S., University of Hannover, 1991; Ph.D., Rice University, 1995
Walk into any clinical research lab and you will undoubtedly find one or more microscopes. The problem with conventional microscopes, however, is they can only show images of thin slices of dead tissue or cells in a dish. It takes a special kind of instrument to produce images from inside the living body, which is exactly the kind that Elizabeth Hillman is building.

“It is a significant technical challenge to build imaging systems capable of studying cellular or molecular processes in living organisms,” said Hillman. “You need devices that can image very fast and in 3-D and that show you lots of different things at once. It’s a complex problem, one that forces you to think about physiology and physics at the same time.”

One such optical imaging technique is microscopy to investigate the brain, particularly the relationship between blood flow and neuronal activity. Functional magnetic resonance imaging (fMRI), one of the most ubiquitous tools used to investigate neuronal activity, relies on detecting subtle changes in blood flow in the brain.

“The problem is, we really don’t understand why these changes in blood flow occur,” said Hillman. “Even the best neuroscience textbooks only devote a page or so to blood flow in the brain.”

Hillman’s work is beginning to tease out this complex process, improving our fundamental understanding of how the brain functions, and also raising the possibility that fMRIs will one day prove even more useful and revealing. In another project, she is developing a technique that permits her to create images of the organs in live lab mice, which she hopes will allow pharmaceutical companies and researchers to study diseases and treatments without sacrificing large numbers of animals. She has also developed techniques to make images of living human skin and is using optical imaging to investigate how the electrical activity in cardiac tissue changes during a heart attack.

Because all of these measure different wavelengths of light, none require the heavy shielding or careful dose monitoring necessary in radiologic imaging. Hillman hopes that ultimately many of her imaging tools will prove useful in the clinic and as laboratory research tools. She is quick to point out, however, that she does not expect her techniques to entirely replace MRIs.

“Optical imaging isn’t going to be the next MRI,” she said. “MRIs do some things well, but they can’t tell you things like how bad the burn on your arm is or whether you have good blood flow in the back of your eye. Our systems can.”

M.Sci., University College London, 1998; Ph.D., University College London, 2002
Early four decades after it first emerged, AIDS is still a deadly disease, killing more than 25 million people worldwide. More than 2.5 million people a year are newly infected with HIV (human immunodeficiency virus), a virus that almost always leads to AIDS (acquired immunodeficiency syndrome).

HIV is one of many diseases, like cancer and other viral and bacterial illnesses, that attacks the immune system, the body’s defense against infection and disease. Even for healthy people with a normal immune system, improving that system would make an individual healthier.

James Hone and his team want to take some key immune-system cells and genetically modify and immunize them outside of the body. A small percentage of people are born with certain genes that make them immune to HIV. Ideally, scientists would harvest their good HIV genes. Then they would modify other people’s genes to look the same way. They would grow a supply of these HIV-resistant genes and put them back into the human body. It’s a potential alternative to shots and traditional vaccinations.

Hone’s goal is to create the basic tools needed to engineer the immune system outside the body, and then to put it back inside the body.

Hone, whose work focuses on carbon nanotubes (CNTs), nanoelectromechanical systems (NEMS) and nanoscale structures with applications in cellular and molecular biology, solar and fuel cells, electronics, and sensors, teaches Carbon Nanotube Science and Technology to graduate students.

Hone is also working with IBM and Professors Ken Shepard and Tony Heinz—as well as two professors in the Department of Chemistry—on a project funded by the U.S. Department of Defense to develop field-effect transistors using graphene to determine if they are more efficient than III-V and silicon semiconductor technologies. Recent research by Hone and Columbia Engineering professor Jeffrey Kysar has shown that graphene is the strongest material ever measured and holds great promise for the development of nanoscale devices.

In addition, Hone is the co-investigator of a team led by researchers at the Mt. Sinai School of Medicine. The group won six million dollars over five years to look at how cells interact to form tissue in the kidneys.

“The specific thing we’re looking at is part of the kidney that acts as a filter,” said Hone. “You have cells that come together like interlocking fingers. The question is: What is it that gets cells to do that?”

Hone’s lab will build microscopic scaffolds—three-dimensional structures that will allow scientists to artificially control the environment for cells to begin to form these tissues.

B.S., Yale, 1990; Ph.D., University of California-Berkeley, 1998
Arrhythmogenic right ventricular cardiomyopathy (ARVC), which affects one in 5,000 people worldwide, is a leading cause of sudden death. With this disorder, fibro-fatty tissue replaces healthy heart muscle, and the heart’s beating becomes uncoordinated. As a result, the heart can’t pump well.

With ARVC as their inspiration, Hayden Huang and his team are figuring out how heart cells respond to physical stresses. ARVC can be caused by genetic mutations that affect proteins which link cells together. Huang is testing whether changes in these proteins interfere with how cells stick together and send signals, making the heart less able to withstand the stresses associated with constant pumping and ultimately damaging its tissue.

To do so, he looks at factors such as cell stiffness (how hard it is to deform the cell), cell adhesion (how well cells stick to surfaces or to each other), cell structure (what the cell is made of and how the components are arranged), and cell response (how cells react to physical stresses like being stretched).

Once Huang and his team unravel the mystery of how heart cells work and how ARVC progresses, they can help develop a diagnostic test to determine who suffers from the condition, which can be asymptomatic for a long time, and formulate a treatment to repair or prevent changes in the heart muscle. They also want to solve the mystery of why ARVC primarily affects the right heart when the left heart apparently does most of the heavy work. This research will help scientists better understand the differences between the two sides of the heart and heart function in general.

Huang teaches the Tissue and Molecular Engineering Laboratory and Fluid Biomechanics. He came to Columbia from a position as associate biophysicist and instructor of medicine at Brigham and Women’s Hospital, Harvard Medical School.

Huang directs the Biomechanics and Mechanotransduction Laboratory, which studies cellular mechanics and mechanotransduction in cells and cell clusters. While the current scope of the projects are focused on the cardiovascular system, the techniques and insight are relevant to any number of cell and tissue systems.

“The current interest of our laboratory is in determining how cell-cell interactions, especially at the junctions where cells make contact, influence cellular mechanical behavior,” Huang said. “Several techniques are used for studying cell-cell interactions, including fluorescence microscopy (wide-field and two-photon), time-lapse microscopy, cell stretching, magnetic micromanipulation, and physical micromanipulation (pipette aspiration, for example).”

B.S., Johns Hopkins University, 1995; S.M., Massachusetts Institute of Technology, 1997; Ph.D., MIT, 2002.
For many people, stiff, aching joints are the first sign of age. For more than 20 million Americans, it is also the first sign of osteoarthritis, a disease characterized by loss of the lubricating and load-bearing tissue that lines the joints and that is behind an estimated $128 billion each year in health care costs and lost productivity.

"Since the lifespan of most joint replacements is limited typically to 15 or 20 years, restoring joint function with living tissue is almost always preferred," said Clark Hung.

The trouble is, that this tissue, known as articular cartilage, is made up of a network of chondrocyte cells embedded in a stiff matrix of collagen and other substances that is subjected to daily, repetitive mechanical deformation and a lack of nutrient-rich blood flow. Because of this, damaged tissue does not heal easily and replacement cartilage with natural properties has proved difficult to grow in a lab. Until now.

By growing chondrocytes under mechanical loads that mimic the conditions inside joints, Hung and Gerard Ateshian, professor of mechanical engineering and biomedical engineering, have been able to culture tissue that is almost identical to the body’s own. The tissue loading helps transport nutrients to the chondrocytes. As a result, their engineered tissue grows faster, is more durable, and, they anticipate, will provide better restoration of the joint.

Hung has so far succeeded in growing bovine and canine articular cartilage and foresees a near future in which human cartilage will routinely be produced in the lab using his method. Good news for anyone who plans on growing older.

In August of 2010, the American Society of Mechanical Engineers (ASME) named Hung to its most recent class of fellows.

“Becoming a fellow in ASME is particularly fitting,” Hung says, “as I came to Columbia to build a research program in cell and tissue engineering that capitalized on the institution’s long-standing strengths in the area of biomechanics.”

Hung serves on the ASME’s executive committee of the bioengineering division and he is an associate editor for its Journal of Biomechanical Engineering. The organization has more than 100,000 members. Hung joins the group’s select group of fellows, which includes just 3,012 members.

Hung is also a member of Columbia’s Bioreactor Core faculty that includes Gordana Vunjak-Novakovic, Elisa Konofagou, Helen Lu, and Jeremy Mao. Their group is funded by the National Institutes of Health to support advanced research into functional tissue engineering, stem cells, and the study of disease.

Osteoporosis is a major public health threat for more than half of all Americans. An estimated 10 million already have the disease and another 34 million are at high risk of developing porous bones, shortening lives, and increasing health care costs.

Christopher Jacobs is working to unlock a stem cell mystery that could provide significant advances in the treatment for osteoporosis. He has received a $1 million New York State grant to research stem cell behavior related to the condition. Osteoporosis occurs when bone marrow stem cells fail to produce bone-forming osteoblasts in sufficient numbers. Very little is known, however, about the cellular mechanism by which bone marrow stem cells sense and respond to changes in their mechanical loading environment.

Jacobs’ Cell and Molecular Biomechanics Laboratory will determine whether a novel cellular sensor, the primary cilium, is responsible for the stem cell’s ability to sense mechanical loading. His lab was one of the first to show that primary cilia act as mechanical sensors in bone cells. The project will characterize the ability of transplanted stem cells to home in on sites of bone loading and form new bone and then determine whether the stem cells retain this ability if their primary cilia are first disrupted.

“If the hypothesis is proven to be true, it will be a breakthrough in skeletal mechanobiology and suggest approaches for new anti-osteoporosis drugs,” Jacobs said. “It will also be a significant advance in relating primary cilia dysfunction to human disease.” Jacobs describes the overall focus of his lab is to understand how cells sense and respond to changes in their mechanical environment.

“Although a wide range of tissues are known to be regulated by physical signals, outside of sensory mechanisms, the cellular apparatus responsible for the initial ‘mechanotransduction’ event is poorly understood,” he said. “Our group is primarily focused on mechanosensitivity of bone cells as it relates to osteoporosis, stress fractures, and disease bone loss associated with spinal cord injury and space flight.”

The group’s active projects include Mechanotransduction in Bone via Oscillatory Fluid Flow; Mechanosensitive Primary Cilia in Osteogenic Differentiation of Stem Cells Due to Loading; Primary Cilia as Mechanosensors in Bone; and Primary Cilia Mechanics and Mechanobiology.

Jacobs was an assistant professor in the Department of Orthopaedic Surgery at Pennsylvania State University and an associate professor in the Department of Mechanical Engineering at Stanford University before coming to Columbia.

B.S., Washington University, 1988; M.S., Stanford, 1989; Ph.D., Stanford, 1994

Combating Bone Loss
CHRISTOPHER R. JACOB
Associate Professor of Biomedical Engineering
Creating Personalized DNA Chips for Everybody

JINGYUE JU
Samuel Ruben-Peter G. Viele Professor of Chemical Engineering

Genes play an important role in nearly every disease—a major reason why scientists spent $1 billion sequencing the entire DNA of one individual for the Human Genome Project. This astronomical cost of decoding the code of life makes mapping the three billion base pairs of DNA in each person seem like a pipe dream. However, advances in science and engineering made by Columbia scientists should make this dream come true in the near future.

Jingyue Ju and his team are developing revolutionary technologies to dramatically reduce the cost of DNA sequencing so that each person’s genome can be routinely decoded on a chip the size of a credit card for just $1,000. Ju co-invented the fluorescent labeling technology that made the Human Genome Project possible. The new sequencing technology uses different colors of fluorescent dyes to label the four letters of the genetic alphabet for decoding on a chip.

Such a chip should be possible in a few years, said Ju, who directs the Center for Genome Technology and Biomolecular Engineering at Columbia and who collaborates with a group of interdisciplinary scientists including chemistry professor Nicholas Turro on this research. Working with Nobel Laureate Eric Kandel and Professor Ian Lipkin at the Columbia University Medical Center, Ju and his team are using the new genome technologies to study the genetic networks for long-term memory, and to rapidly and accurately detect pathogens.

In the future, every newborn could get his entire genome sequenced on a tiny chip. With this information, doctors could easily look up each person’s genetic predisposition to various diseases and could tailor their medical advice. This technology would help doctors better prevent, diagnose, and treat diseases based on each person’s genetic profile. It would also make it easier for pharmaceutical companies to develop personalized drugs for diseases like depression and breast cancer.

Drugs for anti-depression, for example, currently only work in about half the patients. With personalized gene chips, doctors would know in advance which drugs would work (and not work) for each patient.

The National Institutes of Health has supported Ju with a three-year, $1.8 million grant for his proposal, “Single Molecule DNA Sequencing by Fluorescent Nucleotide Terminators.” His project aims to sequence a human genome with high accuracy and speed at a low cost, an achievement that would be critical to the emerging field of personalized medicine.

B.S., Inner Mongolia University, 1985; M.S., Chinese Academy of Sciences, 1988; Ph.D., University of Southern California, 1993
The immune system’s ability to detect and counter infectious agents is among the body’s most remarkable—and welcome—capabilities. Durable as this response may seem in the face of internal and external invasions, it is extremely intricate, and small disruptions can have large implications to the body’s response.

However, the immune system sometimes needs help. Lance Kam seeks to improve immune response by combining cellular and molecular biology with technology adapted from the microelectronics industry. These techniques may one day allow doctors to retrain a patient’s immune system to combat cancer, treat autoimmune diseases, and prevent transplant rejection.

Their research has shown that T lymphocytes, key regulators of the body’s ability to recognize previous threats and adapt to new ones, respond in specific ways to patterns of proteins and other biomolecules they come in contact with. By recreating these patterns at a scale as fine as tens of nanometers, Kam’s group, together with colleagues in an NIH-sponsored Nanomedicine Development Center, has been able to manipulate the activation of T lymphocytes to combat specific threats.

One of the threats of particular interest is cancer. A normally functioning immune system is able to weed out cancer cells that periodically arise in the body. Over time, people appear to lose that ability, making us more susceptible to cancerous mutations as we age. Identifying the patterns that produce cancer-fighting T lymphocytes would allow doctors to produce more of them and effectively retrain a patient’s immune system to fight the disease naturally.

Kam directs Columbia University’s Microscale Biocomplexity Laboratory, which focuses on understanding proper development, function, and repair of biological systems at scales of the intercellular level (tens of micrometers and hours) reaching down to those of supramolecular assemblies (tens of nanometers and milliseconds).

“Micro- and nano-scale systems have an ever increasing role in biomedical science and engineering,” said Kam. “My research group focuses on the use of these systems to understand how cells read and respond to the complex presentation of cues in their extracellular environment.

“We focus particularly on the use of fabrication approaches, which offer a level of control over multiple spatial scales that is not possible through traditional molecular and self-assembly approaches; these are the scales at which cells operate and the realm of an increasing range of biological phenomena.”

Kam did postdoctoral research in chemistry at Stanford University prior to coming to Columbia Engineering.

B.S., Washington University, 1991; M.S., University of Hawaii, 1994; Ph.D., Rensselaer Polytechnic Institute, 1999
More than a quarter of U.S. adults live with chronic pain caused by both injuries and a host of diseases. In fact, this physical suffering is the leading complaint of older Americans—and the reason one in five of them takes pain killers. (Back pain leads the list, followed by headaches.) Unfortunately, in 70 percent of cases, medication does not work. As a result, patients miss work and increase health care costs by frequently visiting doctors.

Jeffrey Koberstein and his team are figuring out how to deliver pain relief drugs to the right place. With Richard Ambron from the Columbia University Medical Center, they are creating tiny, easy-to-swallow particles—known as drug-delivery vehicles—that would carry medication to its target. Ordinarily, a mass of nerve cells, called ganglia, shuttles a pain signal to the central nervous system. For them to send this pain signal, they need to create a certain protein. If scientists can stop production of this protein, they can prevent the transmission of pain. They stop production of this protein through a process called RNA interference, which helps control which genes are active and how active they are.

In the future, Koberstein and his team plan to use their “molecular toolbox” to help deliver other drugs. As a result, they should be able to more efficiently and cost effectively treat patients with many conditions and diseases.

Koberstein has also collaborated with colleagues Jingyue Ju and Nicholas Turro on a project that has firmly established the feasibility of using novel fluorescent nucleotides, surface chemistry, and molecular engineering for DNA sequencing on a chip.

“This is a key step to advancing the field of DNA sequencing by synthesis through fluorescence imaging or by single molecule detection,” said Ju.

Koberstein’s other research interests lie in developing fundamental relationships between molecular structure and properties of polymers and other soft matter, and particularly how polymer surfaces and interfaces can be designed from a molecular perspective. The goal of this work can be generally considered as gaining a molecular design capability to change the chemical composition of a polymer surface through external controls.

Koberstein is a former department chair and is currently co-director of a National Science Foundation IGERT grant on Soft Materials. In 2006, he was awarded the Charles M.A. Stine Award of the American Institute of Chemical Engineers, Division of Materials Science and Engineering, its highest award. He taught at Princeton University and the University of Connecticut before coming to Columbia Engineering in 2000.

B.S., University of Wisconsin, 1974; Ph.D., University of Massachusetts, 1979
A study in the New England Journal of Medicine showed that two-thirds of adults underwent medical tests in the last few years that exposed them to radiation and, in some cases, a higher risk of cancer. Elisa Konofagou is pioneering new uses for an imaging technology that is radiation free, less expensive than CT scans and MRIs, yet just as effective: ultrasound. Moreover, she is going beyond ultrasound’s traditional application as a diagnostic tool, using it to treat diseases like cancer, Alzheimer’s, and Parkinson’s.

In the area of oncology, Konofagou is developing a tool that could identify and destroy tumors without the need for surgery. Her technology, called harmonic motion imaging, uses ultrasound to probe soft tissue in search of abnormal growths.

“You’re basically knocking on different parts of the organ until you detect a different amplitude in one particular location,” she said.

She has found that ultrasound can distinguish benign from cancerous tumors and that its beam can be aimed with extreme precision to detect and ablate, or destroy, the abnormality. If proven effective, the technique could be used in inoperable cancers of the brain, prostate, pancreas, and kidneys.

In the area of neurology, Konofagou is deploying ultrasound to temporarily open the blood-brain barrier to help treat patients with diseases like Alzheimer’s, Parkinson’s, and ALS. Currently, physicians have few good options when it comes to treating these patients. Their choices include direct injection deep into the brain or IV drugs, which flow across the entire brain, not just the diseased areas, causing severe side effects in some cases.

The technique Konofagou has pioneered sends ultrasound waves through a millimeter-specific brain region and the intact skull, causing that part of the blood-brain barrier to open. Medicine would be injected by IV and would reach only its intended target.

Konofagou has also deployed ultrasound in the field of cardiology. Konofagou’s myocardial elastography can identify and localize the portions of the heart that trigger atrial fibrillation. Following diagnosis, the same technique can be used to evaluate treatment, such as after using radiation-free ablation to restore the heart’s natural rhythm. In the future, she hopes her innovations may allow for an inexpensive, noninvasive screening test for heart disease.

“I believe ultrasound can do anything,” she said. Each day, her research is bringing that statement closer and closer to reality.

B.S., Université de Paris VI (France), 1992; M.S., University of London, 1993; Ph.D., University of Houston, 1999

Treating Tumors Without Radiation

ELISA E. KONOFLAGOU
Associate Professor of Biomedical Engineering and of Radiology
Heart disease is the nation’s leading cause of death. About 80 million Americans suffer from at least one form of cardiovascular disease, and each year about 900,000 people die from it. To understand stages of this disease, Andrew Laine and his team are analyzing real-time video 3-D ultrasounds of the heart. Ultrasound echoes are high-frequency sound waves that bounce off tissues and can be converted into sonograms.

“Recent advances in real-time 3-D ultrasound (RT3-D or 4-D) imaging give us a wealth of dynamic information captured in seconds over the entire cardiac cycle,” said Laine. “With the proper analytic tools it can provide a novel and clinically effective 3-D strain-and-torsion measuring tool that will allow cardiologists to routinely measure cardiac wall motion and strain with reliable accuracy.”

The modality of real-time 3-D ultrasound imaging has many advantages since it is portable, non-invasive, and doesn’t require exposure to X-rays as in CT imaging systems. Cardiac MRIs by contrast are far more expensive and lack real-time processing. By using real-time 3-D ultrasound technology for both screening and treatment of heart disease, we can reduce health care costs while improving the quality of patient outcome.

Ultimately, Laine and his colleagues will develop software that will be able to measure the strain on the muscles of the heart in real-time 3-D and localize infarcted or ischemic tissue that could be salvaged by intervention and thus recognize at an early stage what tissue is damaged or at risk.

“By visualizing and evaluating strain exerted by functioning heart muscle comprising the cardiac wall using 4-D ultrasound,” he said, “we hope to detect previously undiscovered cardiac myopathies, as well as more subtle changes over time that will allow us to better quantify cardiac function.”

Laine, who received his D.Sc. degree from Washington University in computer science, teaches courses on Medical Image Analysis to graduate students and Wavelet Applications in Medicine to undergraduate students. He serves as vice president of publications for IEEE Engineering in Medicine and Biology Society (EMBS), the largest professional society in the field, and is chair of the Technical Committee on Biomedical Imaging and Image Processing for IEEE EMBS.

Laine holds two patents related to 3-D processing of ultrasound, has authored over 300 peer-reviewed papers, and has graduated over 20 doctoral students in the field of medical image analysis. He is a fellow of the IEEE and fellow of the American Institute of Medical and Biological Engineering.

B.S., Cornell, 1977; M.S., University of Connecticut, 1980; M.S., Washington University (St. Louis), 1983; D.Sc., Washington University, 1989
Working with fruit flies, Aurel A. Lazar and his team are trying to understand how insects’ brains discriminate one smell from another. The brain gets information as “spike trains”—brief electrical pulses that respond to a stimulus, such as a smell. Lazar is working on how a fruit fly’s brain acquires and processes such smells.

Building on a well-developed genetic understanding of the anatomy of its olfactory system, he uses time encoding machines—computer models of olfactory sensory systems—to represent odors as “spike trains.” He is investigating the sense of smell as a memory-based, odor-object recognition system.

Lazar is the founder and leader of the Bionet Group of the Department of Electrical Engineering. The group is an interdisciplinary research team bringing together faculty and students from the biological and engineering sciences to address questions that arise in the field of computational neuroscience. The group is an active and integral part of the world class Columbia neuroscience community.

Lazar’s team has developed a novel in vivo experimental setup with precise and reproducible delivery of airborne stimuli to fruit flies that has enabled them to map out the process of odor encoding in olfactory sensory neurons. This research is performed in collaboration with Richard Axel, University Professor, in The Axel Laboratory.

In addition, the team is pursuing the implementation of massively parallel models of sensory systems in vision and hearing. The team has demonstrated for the first time the faithful recovery of natural video (movies, animation) and auditory scenes (speech, sounds) encoded with neural circuits. This has the potential to enhance next-generation artificial retinal and cochlear implants.

Lazar describes his research interests as being “at the intersection of computational, theoretical, and systems neuroscience. The computational/theoretical work builds on methods of communications/networking, information theory, machine learning, nonlinear dynamical systems, signal processing, and systems identification. The experimental work employs methods of genetics, neurophysiology, and systems biology.”

Lazar teaches Computational Neuroscience: Circuits in the Brain, an advanced undergraduate/graduate introductory-level course, along with follow-up graduate-level courses. He joined Columbia Engineering in 1980.

B.S., Bucharest Polytechnical Institute, 1971; M.S., Darmstadt Institute of Technology, 1976; Ph.D., Princeton, 1980

Understanding How Flies’ Brains Identify Odors

AUREL A. LAZAR
Professor of Electrical Engineering
Nearly 500,000 Americans depend for their lives on thrice-weekly, in-clinic kidney dialysis to remain alive. The treatment is costly ($23 billion a year or about $46,000 per person), very demanding, and provides only a low quality of life. Some 80,000 Americans are on waiting lists for kidney transplants, with 4,000 dying each year before they get one. A steadily operating, ambulatory blood purification system would decrease patients’ burdens and increase quality of life for all of these patients. At present no ambulatory blood processing system exists. Dialysis patients are particularly affected by water accumulation over the typical two-day interval between treatments and thus often experience wide, dangerous, and uncomfortable swings in blood pressure.

Edward Leonard and his team have been working with government and investor support to devise a water extractor for these patients, and also for heart patients who accumulate water. The device, smaller than a lemon, spreads flowing blood into a layer only 100 microns thick. This layer passes between two thin sheets of silicon nitride perforated with many millions of precisely formed nanopores. Cell-free blood plasma is collected from the pores, is processed to extract water, and then is returned along with the cells to the patient. Blood cells move quickly and contact the filter for less than a second. The device, together with the plasma processor, two pumps, and a battery is expected to be about 4 inches square and 1 ½ inches high. It is designed to be worn by the patient at all times, removing water slowly and nearly continuously. This novel blood-cleansing system will not require anticoagulants and will keep treatment costs well within current, federally-mandated cost-containment limits for kidney patients. Testing is underway and first trials on patients are expected in 2013.

Leonard directs Columbia’s Artificial Organs Research Laboratory, a component of the Department of Chemical Engineering since 1968. Its mission has grown with the evolution of modern biology and with the increasing sophistication available for the construction of medical devices. Thus, current projects have a wide range: innovations to traditional artificial organs effecting transport (kidney, liver, lung, cardiovascular implants) with special emphasis on the artificial kidney, to regenerative medicine, especially the development and study of methods for introducing stem cells into adult tissue. Leonard, who directs the NSF-sponsored course cluster in Genomic Engineering and is a member of the Columbia Genome Center, is one of the first Columbia Engineering faculty members to engage in bioengineering research. He has worked in the dialysis field for more than 50 years and has been on the Columbia faculty since 1958. His principal medical collaborator is Dr. Stanley Cortell, professor of clinical medicine and chief of nephrology at St. Luke’s-Roosevelt Hospital.

B.S., Massachusetts Institute of Technology, 1953; M.S., University of Pennsylvania, 1955; Ph.D., University of Pennsylvania, 1960
Nearly three million people in the United States are infected each year with the hepatitis C virus, the major cause of liver cancer. Worldwide, roughly three percent of the population is infected. Jung-Chi Liao is making progress toward the effort to find an effective treatment for the virus. He has focused his research on exploring the DNA helicase—or enzymes—of the hepatitis C virus.

Liao’s work is related to the recent discovery of a peptide that inhibits the functioning of the hepatitis C virus enzyme NS3 helicase, providing new insights. Specifically, several hot-spot residues have been identified to convert ATP energy to separate the virus’s DNA. Liao is currently conducting comparative studies among different helicases to better understand the variations of coupling mechanisms.

Based on his discovery of dynamical coupling mechanisms and the resulting different conformations, pharmaceutical companies may now be able to identify better drug candidates to inhibit ATP binding sites of hepatitis C virus NS3 helicase. In 2007, Liao was invited by InterMune Inc., one of the major biotechnology companies focusing on drug development for hepatitis C virus infections, to give a seminar presentation of this work.

Liao, who heads Columbia’s Liao Research Group, joined Columbia Engineering in 2008 after posts as a research associate in the Department of Bioengineering at Stanford University and as a postdoctoral fellow in molecular and cell biology at the University of California, Berkeley. He says his lab integrates the knowledge of theoretical modeling, molecular and cell biology, and advanced imaging techniques to understand how single molecules play roles in cellular functions as well as the underlying protein structure-function relationship. Their research areas include nanoscale optics, molecular motors and Induced Pluripotent Stem (iPS) Cell Reprogramming.

“Our lab is interested in shedding light on the molecular pathways involved in this process of reprogramming,” said Liao. “We hope to identify important transcription factors and signaling pathways crucial to the process to help better understand the specifics of reprogramming and to better control it for clinical use. In an innovative interdisciplinary approach of combining mechanical engineering with biology, we are using high-resolution microscopy to shed light on this event by tracking single molecules.”

His research interests are concentrated on how mechanical forces play roles in molecules and cells, using both computational and experimental methods to study molecular motors and related cellular functions. “The focus of my work is to integrate computational modeling and simulation with biological imaging techniques to study dynamics of molecular motors,” he said.

B.S., National Taiwan University, 1993; M.S., Massachusetts Institute of Technology, 1997; Ph.D., MIT, 2001

Seeing Proteins at Work

JUNG-CHI LIAO
Assistant Professor of Mechanical Engineering
More than a million people with type 1 diabetes—an autoimmune disease that is life-threatening unless treated with frequent doses of insulin—will soon be able to check their blood sugar levels without the daily drawing of their own blood.

A team of researchers, led by Qiao Lin, has invented a microfabricated, miniature sensor that can eventually be implanted in a patient’s body for long-term, continuous glucose monitoring. It will be part of a closed-loop system that will automatically deliver insulin to diabetic patients based on blood sugar levels.

There are 17.9 million people in the United States of America diagnosed with diabetes, according to the American Diabetes Association.

Lin’s glucose sensor consists of a microscopic diaphragm, which vibrates under remote magnetic excitation in a microchamber filled with a glucose-sensitive polymer solution. When glucose enters the chamber through a semipermeable membrane, it binds reversibly with the polymer, changing the viscosity of the solution. As the viscous damping on the diaphragm vibration directly depends on the viscosity, the glucose concentration can be determined by wireless vibration measurements. Depending on the result, insulin can be injected to maintain a normal glucose level.

The reversible binding of glucose to the polymer is key. “It is a physical process and the glucose is not consumed,” said Lin. This is a key difference between his device and current, less reliable, sensors that use an irreversible electrochemical reaction of glucose with an enzyme.

The project has been carried out by an interdisciplinary team including Lin and his mechanical engineering Ph.D. student Xian Huang at Columbia, biopolymer chemists Qian Wang and his Ph.D. student Siqi Li at the University of South Carolina, and Jerome Schultz at University of California, Riverside, an expert in biosensors.

Lin also directs the Columbia BioMEMS Laboratory, which conducts research in microelectromechanical systems (MEMS) as applied to biological sensing and manipulation, with an emphasis on controlling, sensing and characterizing biomolecules and cells by integrating MEMS transducers with microfluidics. The goal of these systems is primarily to facilitate understanding of fundamental biophysical phenomena and to enable practical biomedical applications.

Lin was a postdoctoral scholar in Caltech’s electrical engineering department and an assistant professor of mechanical engineering at Carnegie Mellon University prior to joining the Columbia Engineering faculty.

B.S., Tsinghua University (Beijing), 1985; M.S., Tsinghua University, 1988; Ph.D., California Institute of Technology, 1998
Many sports-related injuries involve soft tissues such as ligaments, which connect bone with bone, and tendons, which join muscle to bone. Each year, more than 200,000 people suffer damage to their anterior cruciate ligament (ACL), the primary ligament that stabilizes the knee joint. With the rate of ACL tears and other soft tissue injuries increasing in all segments of the population, it is a hopeful sign that Helen H. Lu has developed a new approach to help the body heal after these debilitating soft tissue injuries.

One of the major hurdles preventing healing lies in integrating soft tissue grafts with the body, and Lu’s group has focused on engineering the interface that connects soft tissue to bone. While tissue engineering has traditionally involved a single-tissue approach, Lu is growing multiple tissues to build functional organ systems that will integrate with the body.

“With the ACL-bone interface, we see three distinct yet continuous tissue regions—ligament, fibrocartilage, and bone,” said Lu. “As we understand how the biological interfaces between these different types of tissues are formed and how to reestablish these distinct tissue-to-tissue boundaries post-injury, we can regenerate the native soft tissue-to-bone interface and promote integration.”

Lu has developed a novel “scaffolding” to grow these three different tissue types within one functional system. This interface scaffold is stratified, with each layer differing in architecture, porosity, and composition to best nurture each particular cell type, while integrating seamlessly with the adjacent tissue. Each portion of the scaffold is biocompatible and biodegradable, and will ultimately be replaced by living tissue, thus becoming part of the body.

Lu and her research group are working on the design of an integrative interference screw. The interference screw, used to fix an ACL graft in place, is usually made of titanium alloys, but a tissue-engineered screw has none of the drawbacks of a permanent metallic implant and promotes integrative repair. This new method will move ACL repair from traditional mechanical fixation to biological fixation, resulting in longer-lasting and stronger repair.

Lu’s group is extending the interface tissue engineering approach to the repair of another critical soft tissue-to-bone transition area, the rotator cuff. Tears in the rotator cuff are one of the most debilitating and common injuries of the shoulder. In collaboration with Dr. William Levine, a shoulder surgeon at Columbia, Lu is developing special nanofiber-based scaffolds that mimic the native tissue in organization as well as functionality for integrative rotator cuff repair.

B.S., University of Pennsylvania, 1992; M.S., University of Pennsylvania, 1997; Ph.D., University of Pennsylvania, 1998

Repairing Torn Ligaments

HELEN H. LU
Associate Professor of Biomedical Engineering and of Dental and Craniofacial Bioengineering
Motor vehicle accidents account for more than half of the 1.5 million traumatic brain injuries (TBIs) that occur each year. Finding ways to prevent, treat, and repair TBIs is the basis for the research of Barclay Morrison and his Neurotrauma and Repair Laboratory team.

At the moment of injury, some brain tissue is instantaneously destroyed and can never be saved by post-injury treatment, so prevention becomes all the more important. Using an atomic force microscope, Morrison is measuring material properties of anatomical structures within the brain that can be used by the National Highway Traffic Safety Administration to set standards for automotive manufacturers.

“We’re determining the safe limits of brain deformation, which is the underlying cause of TBI, to learn what the brain can withstand, so safety systems can be designed to minimize the trauma,” said Morrison.

Morrison’s group is also working with the aftermath of TBIs. One approach investigates the brain’s own initial response, which is an attempt to repair the damaged neural connections and replace lost tissue. For reasons yet unknown, this repair process is aborted. If Morrison can find a way to short-circuit this response, it may be possible to harness and control the brain’s innate potential for repair. It may even be possible to grow replacement neural tissue from a patient’s own stem cells via neural tissue engineering.

In a scenario directly from “The Six Million Dollar Man” or “The Bionic Woman,” Morrison sees the possibility of interfacing neurons directly onto silicone circuitry to control a prosthesis. While this technology is now only imagined, he continues to investigate the factors that influence the ability of neurons to form connections with silicone circuitry, hoping for a breakthrough that can immediately impact the lives of thousands.

WIRED magazine explored this research in the spring of 2010: “Engineers have now designed silk-based electronics that stick to the surface of the brain, similar to the way a silk dress clings to the hips. The stretchable, ultrathin design would make for better brain-computer interfaces (BCIs), which record brain activity in paralyzed patients and translate thoughts into movements of computer cursors or robotic arms.”

“This will significantly improve recording by conforming the electrode array to the surface of the brain,” Morrison said in the article. “It will move forward the field of flexible electronics.”

Before coming to Columbia Engineering, Morrison was a postdoctoral researcher in TBI at the University of Pennsylvania and later at the University of Southampton, U.K.

B.S.E., Johns Hopkins University, 1992; M.S.E., University of Pennsylvania, 1994; Ph.D., University of Pennsylvania, 1999
In recent times, degenerative joint diseases, low back pain, cardiovascular diseases, osteoporosis, and sports injuries have become the focus of biomedical engineering.

An overwhelming number of people today suffers from one or more of these clinical problems. As the average age of our population increases, this group of clinical diseases will affect an ever-increasing percentage of the population, worldwide.

The detailed understandings of this group of diseases have been, and are being successfully addressed by bioengineers using advanced engineering methodologies and mathematics. By far the largest subgroup of the family of diseases known as arthritis is degenerative joint disease (osteoarthritis), and it has attracted engineers to study this medical problem. Indeed, engineers have been successful in developing laws that govern the fundamental stress-strain behaviors of articular cartilage (the soft lining covering the bony ends in a joint). This tissue is the major constituent of joints (hip, knee, shoulder, intervertebral disc, meniscus, etc).

"After more than 35 years of concentrated efforts by bioengineers, we now have detailed knowledge on how tissues such as articular cartilage are formed biologically by chondrocytes (cartilage cells), deform under heavy and rapid joint loading, and fail," said Van C. Mow. "Failure of articular cartilage as a bearing material of our joints always leads to osteoarthritis."

Based on this relatively recently gained engineering knowledge, engineers are learning how to influence the cartilage cells to form and shape cartilage within joints, repair the damaged cartilage, and, in general, make the cartilage stronger against the natural wear and tear processes that often result from the activities of daily living, or from extreme loads, such as performing competitive sports.

Currently Mow’s lab is developing new models to understand how cartilage cells receive signals (mechanical, electrical, and chemical) to maintain tissue health and to stimulate the cellular repair processes to mend the micro-damages on and in the cartilage that result from excessive and repetitive loading.

Mow, a member of the National Academy of Engineering, the Institute of Medicine of the National Academy of Sciences, Academia Sinica of Taiwan, and the Academy of Sciences for the Developing World, is the founding chair of Columbia Engineering’s Department of Biomedical Engineering. He has served as professor of mechanical engineering and orthopedic bioengineering, director of the New York Orthopedic Hospital Research laboratory at Columbia University Medical Center, and is currently director of the Liu Ping Laboratory for Functional Tissue Engineering.


Reconstructing Cartilage

VAN C. MOW

Stanley Dicker Professor of Biomedical Engineering and of Orthopedic Engineering

In recent times, degenerative joint diseases, low back pain, cardiovascular diseases, osteoporosis, and sports injuries have become the focus of biomedical engineering.

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Mechanical engineers think about the design, construction, material properties, and operation of mechanical devices that allow functionality. They have responsibility for understanding how engines work, how buildings can be more efficiently built, and how the environment affects bridge architecture. They also apply their knowledge to the workings of the human body.

Consider the structure all humans have had their first experience with: the womb. Much more than a structure that protects a growing fetus, the womb is made up of many parts that work together to incubate and then birth the baby. One of those parts is the cervix—the lower end of the uterus—and its strength holds a baby inside the mother while it is developing. To prepare for birth, the cervix must dramatically soften. When the cervix fails as a structure and dilates prematurely, miscarriage or premature birth can be the result. By better understanding the mechanical properties of the cervix, better prenatal diagnostic and screening techniques can be developed to reduce premature births, which is the leading cause of fetal deaths.

Kristin Myers investigates the mechanical behavior of soft tissues in order to understand how their tissue architecture influences constitutive behavior and disease development and to aid in early diagnosis and treatment. One of her main focuses is the characterization of the cervix during normal pregnancy and the pre-term labor condition known as cervical insufficiency. A woman with cervical insufficiency has a softer, weaker, or abnormally short cervix, which may efface and dilate without contractions in the second or early third trimester as the weight of a baby puts increasing pressure on it. Myers works to identify abnormal extra cellular matrix components that lead to the altered mechanical function of the tissue and is developing new instruments that can test the strength of the cervix.

Myers joined Columbia after completing her doctoral work at Massachusetts Institute of Technology and post-doctoral work at Johns Hopkins University. In addition to her cervical research, she also studies glaucoma and examines the strength of the collagen fibers that make up the white part of the eye, or sclera. In this research area she works to determine if corrections to the mechanical structure of the eye can correct glaucoma. She is exploring whether people who are diagnosed with glaucoma have a weaker eye structure, and if so, could there be a way to correct the structure mechanically.

B.S., University of Michigan, 2002; M.S., Massachusetts Institute of Technology, 2005; Ph.D., MIT, 2008
Sometimes the building blocks of life—DNA—get knocked askew. The double-helical form that nucleic acids are customarily known for can change and, when it does, the transmission of genetic information is affected. Unfortunately it can be almost impossible to observe, in a laboratory setting, how these different conformations occur.

When experimental attempts fail to capture the details of super-microscopic mechanics like that of DNA, computer simulations on the macromolecular level can deliver valuable insight into what drives assembly in biology. For example, mutations in spectrin proteins are linked to muscular dystrophy and other genetic diseases. These mutations change the way in which the protein unfolds on length-scales that are too small for experimentalists to see. Computer simulation of the process provides atom-by-atom detail about the interactions that occur. This type of research holds promise in providing guidance for the development of better and more efficient biomedical technologies, as well as for innovative disease treatments.

Vanessa Ortiz applies the fundamentals of physics and engineering to understand biological phenomena. She works to describe these phenomena with a multi-scale hierarchical modeling approach, rooted in the use of advanced, state-of-the-art sampling methods, to investigate the behavior of nucleic acids in solution and when in contact with other macromolecules (proteins, nanotubes), surfaces, or assemblies (membranes). Using these models, she is able to predict how a physical system will behave under different conditions, helping scientists draw closer to devising therapies that can treat or even prevent disease.

Her primary research interests are in the development and application of advanced multi-scale computational modeling techniques for the study of biological macromolecules. The goal is to provide insight into the molecular mechanisms that drive assembly in biology, thereby providing guidance for development of better and more efficient biomedical and environmental sensing technologies. In particular, Ortiz concentrates on developing the use of nucleic acids for templating directed organization of nanomaterials, including biomolecules, templating of inorganics, and approaches combining preformed and template materials for use in the areas of nanotechnology and materials.

She has been instrumental in investigating the stability under stress of cytoskeletal proteins and in understanding the stability of diblock copolymer vesicles and worm-like micelles as a function of different design parameters for the development of efficient drug carriers.

B.S.E., University of Puerto Rico, 2002; Ph.D., University of Pennsylvania, 2007

**Using Physics and Engineering to Understand Biological Phenomena**

**Vanessa Ortiz**

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Each year as many as one in five Americans get the flu. More than 200,000 end up in the hospital for complications, and 36,000 die from flu-related causes. And those statistics are for only one family of viruses.

Ben O’Shaughnessy and his team are figuring out how viruses invade cells so they can help develop anti-viral drugs to prevent diseases like the flu and AIDS. Like detectives, they’re tracking down how viruses break through their own wall-like membranes and those of healthy cells. That is, how do they open up their own barrier and that of the cell they’re trying to attack? A virus uses a finger-like protrusion to poke a hole in the cell it is attacking.

The long-term goal of this research is to keep the virus from invading (most likely through preventing the fusion of the virus and healthy cell wall), and then to come up with virus-fighting medications. These drugs are especially important for infections such as AIDS, Ebola hemorrhagic fever, and dengue fever, which have no vaccine.

The research may also help the search for effective anti-viral drugs to treat viral diseases such as flu. While flu vaccines exist, they are imperfect as flu viruses mutate rapidly, which makes it difficult for scientists to decide on the best cocktail to protect against the strains that will appear each November. There is particular urgency to develop anti-viral drugs to protect people from both “regular” flu and from H1N1 or “swine” flu.

The National Institutes of Health awarded O’Shaughnessy a $1.5 million grant in 2010 for a project that takes a closer look at a process essential to all life: cell division. His team is investigating how a muscle-like ring inside the cell is assembled and how it works on a molecular level to complete the closure as the cell physically splits, a process called cytokinesis.

“We are mathematically modeling this machine to establish a quantitative understanding of how it works,” he said. The research has potentially far-reaching implications.

“Failed or improper cytokinesis due to improper ring construction can result in cells with zero or many copies of the genome,” O’Shaughnessy added. “Understanding the mechanism of cytokinesis is essential to help combat cancer, neurological disease, and birth defects associated with such failed cytokinesis.”

O’Shaughnessy teaches Molecular Phenomena in Chemical Engineering to undergraduates and Statistical Mechanics and Topics in Biology for Physical Scientists and Engineers to graduate students.

B.Sc., University of Bristol (England), 1977; Ph.D., University of Cambridge (England), 1984
Nearly 50 million people nationwide struggle with type 2 diabetes or high cholesterol, and rates are increasing annually. The clues to why some people are more susceptible than others are being discovered on a small Pacific Island, where Columbia Engineering researchers are discovering new genetic variation and associating it with metabolic disease.

Itsik Pe’er, who leads the Itsik Pe’er Lab of Computational Genetics, is developing analytical methods for analysis of DNA sequence variants. Recent technological breakthroughs now allow high-throughput observation of these genetic alterations along the genome (an individual’s collection of genetic material).

Such heritable changes are thought to be responsible for 40 to 90 percent of population risk to a wide variety of health conditions, from diabetes to schizophrenia. The Pe’er group is studying a population from the Pacific Island of Kosrae, in the Federated States of Micronesia, which suffers from increased rates of metabolic disorders, such as obesity, type 2 diabetes, and high cholesterol.

The unique genetic makeup of the islanders, who have been isolated for thousands of years, makes them ideal for genetic studies, but their interrelatedness makes analysis of their DNA extremely complex.

The Pe’er group has developed computational tools to decipher remote family ties between individuals based on identity of genomic segments inherited by descent from a recent unknown ancestor. These analytical methods enabled examination of 500,000 polymorphic sites along the genomes of 3,000 Kosraeans, representing most of the adult population.

The lab was thus able to discover multiple new disease genes for health traits. Based on these disease associations, the researchers were able to sequence the entire genome of representatives of the Kosraean population, resulting in discoveries that have broad implications for anyone with these metabolic diseases.

The unprecedented scope and uniqueness of this recently completed dataset expose the effects of population isolation, and pinpoint severe mutations in individual genomes that are likely associated with disease. The combination of these genome sequences with the precompiled map of segments that are identical by descent delineates large groups of mutation carriers to confirm such associations.

Before joining Columbia, Pe’er was a postdoctoral researcher at several institutions, including the Weizmann Institute of Science and Massachusetts General Hospital. His research group is a home to an interdisciplinary team attracting diverse academic backgrounds, analytical talents, and skill sets to effectively promote computational understanding of human genetics.

B.S., Tel Aviv University (Israel), 1990; M.S., Tel Aviv University, 1995; Ph.D., Tel Aviv University, 2002
Countless times a day—often without realizing it—humans make split-second decisions based on what we see and on our subjective knowledge. It might be as simple as clicking a link that catches our interest online, or recognizing a friend from a 50-millisecond glimpse of his or her face across a crowded room. But no matter how effortless the decision-making process may seem, the effort to translate that into an automated system has proved daunting.

“We can build a computer that’s good at very constrained decision making, but general purpose, rapid decision making is difficult,” said Paul Sajda. “It might be able to detect what is interesting or novel, but it doesn’t always know what’s interesting or novel to you.”

Those two tasks—rapid decision making and identifying subjective interests—are, however, exactly what Sajda and his team are succeeding in building. At the same time, Sajda is attempting to reveal the most basic neural structures in the brain that process visual information. In his Laboratory for Intelligent Imaging and Neural Computing, Sajda connects subjects to an EEG and flashes a series of images on a computer screen to record the neurological equivalent of the “Aha!” moment signaling interest or recognition. Once the “cortically coupled computer vision system” is calibrated to recognize the things that interest an individual, it can present more images that are likely to pique that person’s interest.

His work has drawn the attention of the Defense Advanced Research Projects Agency for its potential to help conduct a sort of visual triage by sifting quickly through petabytes (that’s a million gigabytes) of satellite imagery or hours of surveillance tapes. He also works with researchers at Columbia University Medical Center on techniques that enhance the brain’s ability to make quick decisions. But the question that most fascinates Sajda is what his studies of the brain’s visual recognition networks can do to reveal the organ’s fundamental ability to process massive amounts of information.

“It’s still unclear at what scale the brain processes information,” said Sajda. “It could be groups of neurons, it could be the whole brain. We don’t know.” But he and his research group stand a good chance of finding out.

Growing up on Long Island, Sajda knew he wanted to be an engineer, but was also fascinated by anatomy and physiology. That fascination with living systems continues to infuse his work, at the same time that his engineering perspective is helping redefine what we know about the human brain.

B.S., Massachusetts Institute of Technology, 1989; M.S., University of Pennsylvania, 1992; Ph.D., University of Pennsylvania, 1994
Welcome to the post-modern biology lab. It’s made of silicon, measures 5mm on a side and costs just $20. It can also be deployed to harsh or distant locations and when an experiment is complete, it can be discarded. Welcome to Ken Shepard’s lab—or at least one of the many he is designing. This new research combines expertise in chemistry, biology, and integrated circuit design in a manner that gives Columbia unique, high-impact capabilities. While most of the semiconductor industry is focused on continuing to try to scale integrated circuit technology according to Moore’s Law, Shepard’s lab is focused on “more than Moore” applications of IC technology.

Shepard and his team at the Bioelectronics Systems Lab employ the integrated circuits technology to build their own micrometer-scale arrays of sensors that can detect biological molecules or select strands of DNA. “There are definitely other techniques for doing these things, but they’re difficult, time-consuming, and expensive,” said Shepard. “The goal here is to come up with something that’s as sensitive as the most sensitive instruments, if not more, and reduce everything else about it.”

Very often, in order to detect a particular molecule, they have to first be labeled—physically attached to something such as a fluorescent dye that permits detection. Shepard and graduate student Matthew Johnston aim to circumvent this laborious process by directly detecting the weight of individual molecules.

When target protein molecules bond to the surface of one of their chips, it causes the frequency of a vibrating piezoelectric crystal to change. The magnitude of the change quickly confirms the presence of their target.

In their first test of the lab-on-a-chip, Shepard and Johnston are using a sensor designed to search dust samples for common airborne allergens that have been linked to high childhood asthma rates in urban areas. Shepard also envisions a day when his chip-based labs could be used to quickly and easily detect blood-borne cancer proteins.

Shepard’s “more than Moore” activities have been funded by corporate sources (Semiconductor Research Corporation) and state and federal grants (New York State Foundation for Science, Technology, and Innovation; National Science Foundation; National Institutes of Health; and the Defense Advanced Research Agency). He is also a principal investigator on a large NSF Ph.D. training grant in the area of bioimaging technologies.

Shepard was given a Faculty Development Award in 2006 by the New York State Office of Science Technology and Academic Research. In 2008, he was named a finalist for the Blavatnik Award for young faculty by the New York Academy of Sciences. He is a fellow of the Institute of Electrical and Electronics Engineers.

Doctors in developing countries will soon be able to use handheld devices to collect and analyze blood tests at a patient’s bedside to diagnose infectious and other diseases, thanks to research by Samuel K. Sia.

The devices, now undergoing field tests in Rwanda, require only a finger prick of blood and provide quantitative results in less than 20 minutes. The aim of the new technology is to significantly reduce the time between testing patients and treating them, without increasing costs or regulatory burdens.

“Nowhere is the need for new diagnostic technologies greater than in developing countries, where people suffer disproportionately from infectious disease compared to the U.S. and Europe,” said Sia.

The “lab-on-a-chip” technology uses microfluidics—the manipulation of small amounts of fluids—to miniaturize and automate routine laboratory tests onto a handheld microchip. The devices are being developed in a collaboration between Sia’s lab and Clanos Diagnostics Inc.—a venture capital-backed startup company that Sia co-founded in 2004—as well as with the Mailman School of Public Health at Columbia University. Sia’s work also focuses on developing new high-resolution tools to control the extracellular environments around cells, in order to study how they interact to form human tissues and organs. His lab uses techniques from a number of different fields, including biochemistry, molecular biology, microfabrication, microfluidics, materials chemistry, and cell and tissue biology.

His device, known as mChip (mobile microfluidic chip), significantly reduces the time between testing patients and treating them and provides medical workers in the field results that are much easier to read at a much lower cost. The microchip inside the device is formed through injection molding and holds miniature forms of test tubes and chemicals; the cost of the chip is about $1 and the entire instrument about $100. Sia’s research has recently been featured in Popular Science and Nature Medicine.

In August of 2010, MIT’s Technology Review magazine named Sia to its prestigious listing of the World’s Top Young Innovators for 2010 for his groundbreaking work in biotechnology and medicine.

Sia received a CAREER Award from the National Science Foundation that supports his work in developing biocompatible microelectromechanical systems and implantable medical devices, such as glucose sensors. A recipient of the Walter H. Coulter Early Career Award in 2008, Sia participated in the National Academy of Engineering’s U.S. Frontiers of Engineering symposium for the nation’s brightest young engineers in 2007.

B.Sc., University of Alberta (Canada), 1997; Ph.D., Harvard, 2002
Childhood vaccines are one of the great success stories of medicine. With timely vaccination, many childhood illnesses have been nearly eradicated. Yet this battle against common childhood epidemics requires constant vigilance and planning. In particular, a steady supply of vaccines needs to be made available to children. This task is especially difficult because the supply of vaccines is inherently fragile. Just in the last decade, the United States has experienced six major protracted disruptions of its vaccine supply. The Centers for Disease Control plans for such emergencies by maintaining a national stockpile. An important decision is how to set stockpile levels in order to minimize cost and the risk of a shortage in a dynamic and uncertain environment.

Such uncertainties exist in many real systems. To make a system more efficient requires an understanding of how to effectively account for uncontrollable random factors. Industrial engineers build mathematical models to capture the behavior of these systems, with the goal of simulating system behavior and optimizing system performance under economic and technological constraints.

Van-Anh Truong studies decision problems that arise in many health care systems and supply chains. Her work has application in the management of pediatric vaccine stockpiles, the allocation of operating room capacity to emergency and elective surgeries, the structuring and pricing of health care services, the tactical purchase of equipment for semiconductor fabrication facilities, and the strategic use of inventory in retailing. She develops scientific theory to design smarter systems, and to help deploy machines, staff, and materials more efficiently. By drawing on mathematics and engineering analysis and design, she develops representative models of real systems, how they interact over time, and how they are affected by random events in the environment. Her analysis of these mathematical models yields insights and algorithms for finding decisions that optimize system performance.

Truong’s theoretical interests include separation methods for stochastic dynamic programming, approximation algorithms, and learning-based optimization. Prior to teaching at Columbia University, Truong was a quantitative associate at Credit Suisse and a quantitative researcher at Google. She is a member of the Institute for Operations Research and the Management Sciences (INFORMS).

B.S., University of Waterloo (Canada), 2002; Ph.D., Cornell, 2007
Approximately 35 million men and women in the United States suffer from TMJ problems, and as many as one in four people experience symptoms of TMJ disorders, including pain in the chewing muscles, jaw stiffness, clicking, popping or grating, or the pain of arthritis. The temporomandibular joint, or TMJ, is the jaw joint that lies in front of each ear, connecting the mandible (lower jaw) to the skull, providing the mobility necessary for biting, chewing, swallowing food, speaking, and making facial expressions.

Gordana Vunjak-Novakovic and her research team have been able to grow bone grafts that will match a patient’s original jaw bone for facial reconstruction surgery to repair injuries, disease, or birth defects. This spectacular advancement in bone tissue engineering provides all the advantages of the body’s original jaw bone. The team used real bone as a scaffold to grow the new TMJ graft. Taking the knee joints of calves, they stripped them of all their living cells and carved them into cubic centimeter-size parts of a human jaw joint. Using mesenchymal stem cells, which can differentiate into many cell types, to seed the scaffolding, they fed them with streams of nutrients, growth factors, and oxygen in a bioreactor. The next step will be to determine the best way to grow blood vessels in the bone grafts to continue their viability.

In another research area, Vunjak-Novakovic is engineering thick, vascularized, and electromechanically functional cardiac tissue, by culturing stem cells, the actual “tissue engineers,” on a channeled elastomer scaffold perfused with culture medium containing oxygen carriers, to mimic blood flow. This research may lead to a heart patch that could be laid over injured heart tissue to restore normal function in someone who has suffered a heart attack. “As a biomedical engineer actively involved in this field, I look forward to unlocking the full regenerative potential of human stem cells, so we can cure disease and live longer than our failing organs,” she said.

Her lab hosts the Bioreactor Core of the National Institutes of Health (NIH) Tissue Engineering Resource Center. “This sophisticated bioreactor and imaging instrumentation has moved stem cell research from the ‘flat biology’ of petri dishes to controllable models of high biological fidelity, which can be studied in real time to observe the interacting factors mediating self-renewal and differentiation of stem cells,” said Vunjak-Novakovic. “We now have the capacity to develop entirely new research paradigms and approaches to engineering human tissues.”

In 2002, Vunjak-Novakovic was elected a fellow of the American Institute for Medical and Biological Engineering. In 2007, she gave the Director’s lecture at the NIH, as the first woman engineer to receive this distinction. She was inducted into the Women in Technology International Hall of Fame in 2008, elected to the New York Academy of Sciences in 2009, and, in 2010, received the Clemson Award of the Biomaterials Society for contribution to literature.

B.S., University of Belgrade (Serbia), 1972; S.M., University of Belgrade, 1975; University of Belgrade, Ph.D., 1980
The key to unlocking complex problems like the biological cause of cancer—the second-leading cause of all deaths—may be found in the fundamental building blocks of life. How genes control each other—and how to predict that activity—is a research focus of Chris Wiggins. He is working to develop models that predict how genes behave to explain how some cells become cancerous.

“The relationship between biology and mathematics has completely changed in the last decade,” said Wiggins. “New technologies have transformed biology into a data-rich science, and advances in algorithms have made possible data-driven predictive modeling in biology. At the same time, the World Wide Web made it possible for any biologist to share their data with the entire mathematical community with the click of a mouse.”

Wiggins and his collaborators have shown how one can use these data, along with the appropriate math, to learn which genes are controlling which other genes and why.

“The problem is a bit like watching stocks go up and down, and trying to predict which stocks are driving each other,” he said. “In this case, our models are also constrained and guided by the hard work of decades of bench biologists and medical scientists.”

While the architecture of the underlying genetic network is a basic biological topic, Wiggins said, “it is at the root of numerous biological diseases, including cancer, and we are now on the threshold of finding more of those genetic links.”

Wiggins, who was a National Science Foundation postdoctoral research fellow in biomathematics at the Courant Institute, was profiled in Scientific American in 2008. In recent months, numerous publications have explored his work trying to lure the school’s top math students to tech startups instead of joining Wall Street banks.

The influx of new talent would expand the city’s technology sector, the brain drain of math and engineering students to West Coast schools and companies would ebb, and New York City’s intellectual environment would be enriched. “I want young people to realize the creative things they can do with math,” he said.

Wiggins received the Janette and Armen Avanesians Diversity Award in 2007. The award was established to recognize outstanding performance of engineering faculty in enhancing diversity in departmental, school, and university programs at Columbia. The award winner receives a cash prize of $1,000 and a plaque. Nominations are evaluated on the basis of excellence in advancing diversity at Columbia Engineering.


“Turning Off” Cancer Genes

CHRIS H. WIGGINS

Associate Professor of Applied Physics and Applied Mathematics
In the realm of national preparedness, few scenarios are as scary as the possibility of a “dirty bomb.” The National Institutes of Health (NIH) is funding a $25 million grant to find new technologies that will provide rapid mass-screening of radiation exposure.

Y. Lawrence Yao, together with researchers from Columbia University Medical Center and department colleagues, is part of a multi-institute consortium that, among other tasks, is charged with developing a high-throughput “biodosimetry” device capable of rapidly testing a large swath of the population in the event that an RDD (radioactive dispersal device), commonly called a “dirty bomb,” is detonated in a major metropolitan area. This group is collaborating on an effort to design the most effective and quickest technologies that involve advanced imaging, lasers, and robotics.

Radiation affects cell division. When cells divide under normal conditions, the break is clean, with no extraneous cellular material. After radiation exposure, however, pieces of damaged chromosomes, micronuclei, appear along with divided cells and can be tested for DNA breaks.

The advances in these technologies being pioneered by Yao and his colleagues will accelerate the screening process based on blood from a finger stick. With the help of a highly automated, efficient, and eventually portable device—a prototype of which is already whirring in Mudd’s basement—doctors can quickly determine the scope of radiation exposure and whether medical treatment is needed by processing tens of thousands of samples per day, instead of only a few hundred.

Yao and his colleagues, and the NIH, are confident that this device can operate at high volume and full throttle, with the hope that it is never needed.

Yao, who also directs Columbia’s Manufacturing Research Laboratory (MRL), engages in multidisciplinary research that includes nontraditional manufacturing, laser materials processing, laser assisted material removal, shaping, and surface modification, laser applications in industry and art restoration, and robotics in industry and health care.

In 2009, he received the Janette and Armen Avanessians Diversity Award, established to recognize outstanding performance of engineering faculty in enhancing diversity in departmental, school, and university programs at Columbia. The award winner receives a cash prize of $1,000 and a plaque. Nominations are evaluated on the basis of excellence in advancing diversity at Columbia Engineering.

Before joining Columbia in 1994, Yao served as a senior lecturer in the School of Mechanical and Manufacturing Engineering at the University of New South Wales, Sydney, Australia.

B.E., Shanghai Jiao Tong University (China), 1982; M.S., University of Wisconsin-Madison, 1984; Ph.D., University of Wisconsin-Madison, 1988