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They call us “Nano U.” No wonder when close to 200 faculty members are involved in the study of nanotechnology in some way. Northwestern researchers have been pushing forward the frontiers of nano-knowledge since before the turn of the 21st century. In this issue of CenterPiece, we've collected articles about a number of these research pioneers and the new knowledge they're creating in fields including biomedicine, materials research, and business. And to reassure you that there’s a lot more to Northwestern research than nanotechnology, we’ve also covered exciting historical and medical research projects in this issue.
Twenty (or More) Things You Might Not Know About Nanotechnology

Navigating the Nanoscape

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From University Research Lab to the Marketplace

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FRONT COVER – Channeling the Future: The schematic depicts a thin-film transistor, imagined by the laboratory of Mark Hersam, materials science and engineering. The channel material in the transistor is a meshed network of single-walled carbon nanotubes, which can offer exceptional performance and promise for optoelectronic materials.
Chad Mirkin, chemistry and director of the International Institute of Nanotechnology:

“One of the lessons learned over the first 10 years of nanotechnology research is that every material, when miniaturized, has new properties, and many of these properties can be used to create applications and technologies that solve problems in health care, electronics, energy, and the environment.” So testified Chad Mirkin at a US Senate Subcommittee Committee on Science and Space hearing last summer. “The fastest way to new materials is through the miniaturization of existing materials — a tenet of nanotechnology.”

Mark Ratner, chemistry and director of the Initiative for Sustainability and Energy at Northwestern, and Tamar Seideman, chemistry:

Nanoscale structures have certain properties that are governed not by the classical mechanics that describes a thrown baseball, but rather by quantum mechanics. One quantum prediction that is a bit shocking is that electrons can flow between two sites in such a way that the current flowing through two independent pathways is not twice the value of the current through one of those pathways— or, to put it another way, maybe 1+1 is not always equal to 2. A joint project of the Ratner and Seideman groups has calculated that this is exactly what will happen when...
two molecular wires are lined up next to one another (see picture above). These quantum behaviors have been observed — and might even be the basis for some future electronic devices — but the behavior still seems wonderfully strange.

**BIOMEDICAL RESEARCH**

- **Samuel I. Stupp**, materials science and engineering and director of the Institute for Bionanotechnology in Medicine:

  One of nanotechnology’s specific strategies has been to create biomimetic nanostructures made from natural building blocks used by biological systems to create proteins and genes. Biomimetic nanostructures by definition can emulate some of the functions of molecules in living systems. An interesting area of nanotechnology first developed in Stupp’s laboratory is that of nanostructures built mostly with peptides that can promote the regeneration of tissues and organs. This can include regeneration of the heart, brain, spinal cord, bone, cartilage, and other tissues without using stem cells. **Regeneration** is without a doubt the new medicine in this century, linked to the universal aspiration of humans to have longevity and a high quality of life.

- **Guillermo Ameer**, biomedical engineering (and former student **Eunji Chung**):

  Nanometer-sized structures play a wide range of roles in order to meet the biological and engineering criteria of our tissues and organs. In particular, bone consists of 60 to 70 percent (by weight) hydroxyapatite, a nanometer-sized mineral consisting of ions such as calcium and phosphates. Hydroxyapatite particles are distributed among collagen fibers in bone and provide mechanical rigidity needed for skeletal movement. In addition, these particles can store proteins and trigger biological cues that differentiate local stem cells into bone cells when needed. By incorporating hydroxyapatite nanoparticles into a synthetic, biodegradable, and elastic polymer, researchers in the Ameer laboratory have fabricated a biomaterial that meets both the mechanical and biological requirements of bone. This novel biomaterial can be engineered for use in minimally invasive surgeries and supports new bone formation.

- **John Marko**, molecular bioscience:

  “The thing I find most amazing about the nanoworld is that the most impressive nanoscale machines are the ones that random variation and natural selection have built up inside all living things. By this I mean the enzymes that catalyze metamorphoses of biological molecules,
These images show a stretching experiment on a single chromosome taken out of a cell. The bar is 10 microns (10 millionths of a meter). This photo was taken by Michael Poirier, former graduate student from the Marko lab.

- **Thomas Meade**, chemistry:

  Today’s doctors tweak the dose of prescriptions based on how their patients respond over the course of weeks. Variation in dosage sometimes causes patients to experience unnecessary side effects or to lose valuable time if the dose is suboptimal. With current technology, there is little room to improve this process because each patient is in a different state of health. The doctor cannot visualize the drug once it’s been administered and must wait to observe the effects in order to prescribe a treatment. Iron oxide nanoparticles (essentially nano-sized chips of rust) are tiny magnets that can be visualized by magnetic resonance imaging. Their nanoscale size means that they don’t stick together and clump up like everyday magnets, allowing for their safe use in humans. By attaching drugs to these magnetic nanoparticles, doctors will be able to **track how drugs behave in patients** and design personalized dosing regimens in real time.

- **Margaret Schott**, chemistry:

  The 1968 short documentary film “The Powers of 10” by Ray and Charles Eames provided an early view of the nano realm by “diving down” into a human cell. Using innovative methods for that time, the filmmakers depict a cell nucleus (1000 nanometers), a chromosome (100 nm), an individual gene (10 nm), and finally a DNA base pair (1 nm) that represents the scale of the fundamental building block of the genetic message. Thus the nanoscale is the realm of the simplest **biological structures**, where physics and chemistry meet biology. Beginning in the 1970s Northwestern chemists developed methods for making artificial strands of DNA in the laboratory, building up segments of genes one nucleotide base at a time. Today, artificial yet biologically active segments of DNA can be easily synthesized using automated machines.

- **Lonnie Shea**, chemical and biological engineering:

  “I have been collaborating with **Steve Miller**, microbiology-immunology, and **Xunrong Luo**, medicine: nephrology, on the development of nanoparticles to ‘train’ the immune system not to react to specific antigens (tolerance). This training is useful for autoimmune disease, in which the body’s immune system reacts to self-proteins. Additionally, tolerance is a critical component for **cell therapies**, in which the recipient immune system would normally attack the transplanted cells.”

- **Fraser Stoddart**, chemistry, and **Ross Forgan**, postdoctoral fellow, chemistry:

  Nanomechanics have medical applications. By attaching artificial molecular switches — mechanical components 10,000 times smaller than a human hair — to the surface of a porous nanoparticle, it is possible to prepare **targeted drug delivery devices**. Drugs can be encased within the pores of the nanoparticle and trapped by moving the switches into the “Off” position, so that their components block the pore openings. Careful engineering of the system ensures that the switches will only turn to the “On” position when they encounter a specific change in conditions, such as a change in pH or a chemical marker found in cancer cells, and so the nanocarrier releases its active drug molecules solely at the targeted region of the body.
animal mortality. However, once doxorubicin was bound to the nanodiamonds, all of the animals survived, and the tumors were reduced to the smallest sizes observed in the study. Beyond cancer therapy, nanodiamonds are being explored as wound healing, gene therapy, and imaging agents with marked improvements in performance, signifying the potential of this interesting material to improve several areas of medicine.

**C. Shad Thaxton**, urology:
Humans have natural nanoparticles circulating in their blood stream, and some of them are believed to be beneficial to human health. One such nanoparticle is high density lipoprotein (HDL), which is responsible for transporting “good” cholesterol. In the Thaxton lab, *synthetic nanoparticles* can be made to accurately mimic the structure and function of their natural HDL counterparts. These unique HDL nanoparticles are being studied as potential therapeutics for a number of disease processes including inflammation, cancer, and cardiovascular disease.

**Thomas O’Halloran**, chemistry and director of Chemistry of Life Processes Institute, and medical student **Richard Ahn**:
While arsenic trioxide has a notorious reputation as a poison, it also has a history in medicine that dates to Hippocrates. Recent studies have led to the reemergence of arsenic trioxide as a highly effective, FDA-approved therapy for a specific subtype of leukemia, but clinical trials in solid tumors have failed. To improve the efficacy of arsenic trioxide in solid tumors, researchers in the O’Halloran lab developed a nanoscale formulation in which the arsenic trioxide is trapped in 100-nm fat vesicles called nanobins. These protect normal tissues from toxicity and facilitate tumor delivery by allowing the selective accumulation of nanoparticles in the tumor. The researchers tested the nanobin formulation and the corresponding free drug in a mouse model of human breast cancer. They found that the nanoformulation robustly inhibited tumor growth while the free drug had little effect. The study validates the promise of *nanotherapeutics* as cancer therapies.

**Dean Ho**, biomedical engineering:
To develop *new ways of delivering cancer drugs*, the Ho team examined the use of nanodiamonds, which are tiny carbon particles with diameters between 2 and 8 nanometers. Because of their interesting surface properties, nanodiamonds are capable of binding certain drugs in a very potent fashion that can help increase drug treatment efficiency and simultaneously reduce toxicity. In a recent study in mice, high dosages of doxorubicin, a current standard of chemotherapy, resulted in immediate

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**MATERIALS RESEARCH**

**L. Cate Brinsson**, mechanical engineering, materials science and engineering:
“It’s like fairy dust,” says Brinsson. Both in their beauty and their ability to transform material properties using only tiny amounts, the capabilities of nanoparticles have surprised her. Mixing less than 1 percent by weight of nanoparticles in polymers can dramatically alter the mechanical and electrical properties of these materials, changing thermal degradation temperatures by 40 degrees, improving stiffness and fracture resistance, and making an insulator into a conductor. Nanoparticle diversity is also incredible — from gold to titania to carbon nanotubes and in shapes ranging from tiny dots to tubes to plates, the geometry of the particles and their arrangement in the polymer matrix play an enormous role on *material response*. As with fairy dust, the results can be, at present, unpredictable. Brinsson and her team are working to change that by designing polymer properties a priori by tuning the nanoparticle chemistry and arrangement in the host polymer.
Horacio Espinosa, mechanical engineering:

The Espinosa group has engineered high-performance carbon nanotube-polymer fibers composed of double-walled carbon nanotubes (DWNTs) that are remarkably tough, strong, and resistant to failure. State-of-the-art, in-situ electron microscopy testing methods have been applied to mechanically test and characterize the fibers at multiple length scales — from individual DWNTs and bundles at the nanoscale up to fibers that can be applied to real-world macroscale applications.

Mark Hersam, materials science and engineering:

Hersam's lab is using carbon nanotubes — single atom-thick cylinders of graphite — to make transparent conductors, films that are highly conductive electrically but transparent optically. These films absorb strongly at one wavelength so that, instead of looking clear, they have a tint to them and look more like stained glass than the normal glass. The high electrical conductivity of this film could be used in solar cells, for example.

Matthew Grayson, electrical engineering and computer science:

By strategically stacking 5–10 nm thick layers of semiconductors in what is called a superlattice, it’s possible to create artificial materials with new thermoelectric properties. For example, in superlattices, researchers in Grayson’s lab force heat to flow “perpendicularly” to the direction of electrical current flow, creating a new paradigm for electronic refrigerators that might cool nanostructures to cryogenic temperatures.

Yonggang Huang, civil and environmental engineering and mechanical engineering:

Nanomanufacturing has helped the development of stretchable electronics — soft, elastic, and curved electronics, which are very different from those dictated by the ongoing push toward smaller and faster devices that are still confined to the hard, rigid, and planar surfaces of silicon wafers. Applications of stretchable electronics range from surgical and diagnostic implements that naturally integrate with the human body and provide advanced therapeutic capabilities...
to cameras that use biologically inspired designs to achieve superior performance.

- **Mercouri Kanatzidis**, chemistry:

  Bulk crystals of lead telluride (PbTe) are capable of converting heat to electricity when they are put under a temperature differential. For example, if one end is at 500 degrees (Celsius) and the other at 45 degrees the conversion efficiency can reach around 8 percent. Only a few percent of nanocrystals of lead sulfide (PbS) grown inside bulk crystals of PbTe can reduce the flow of heat through the material allowing a much higher efficiency to be achieved — around 14 percent. The nanocrystals scatter heat waves in PbTe, making it a better **thermoelectric material**.

- **Teri Odom**, chemistry, and graduate student **Wei Zhou**:

  Researchers in the Odom laboratory have successfully created a new type of subradiant or “dark” plasmon (quantum of collective charge oscillation) that exhibits extremely narrow resonance linewidths and can be easily tuned by modifying the height of gold nanoparticles arranged in a large-scale, two-dimensional array. Previous attempts to make dark plasmons have involved structuring single nanoparticles or nanoparticle arrays in complex ways, attempting to take advantage of broken symmetries in the structure. The Odom lab discovered that controlling the out-of-plane dipolar interactions between particles, i.e., tuning the nanoparticle height, was far simpler than trying to manipulate sub-wavelength features in individual particles.

- **Randy Snurr**, chemical and biological engineering:

  Researchers have created a new class of nanoporous materials called **metal-organic frameworks** (MOFs) from metal corners connected by organic linkers in a building-block approach. They look very much like molecular-level Tinkertoys. Because the building blocks can be combined in different ways, there are an enormous number of potential structures that may have interesting properties for different applications. For example, if you consider making MOFs from only 100 different building blocks, there are over 25 million different combinations.
Researchers in the Snurr lab are currently using computational methods to screen the vast number of possible structures and study their potential applications for energy and environmental applications. Almost every atom in these materials is exposed on the internal surface, and some of these materials have incredibly high surface areas. The current record for the highest surface area is a material called MOF-210, which has a surface area of 6200 square meters per gram, equivalent to the area of a football field in something the weight of a paperclip.

**BUSINESS RESEARCH**

- **Barry Merkin**, Kellogg management and strategy, and **Chad Mirkin**, chemistry and director of the International Institute for Nanotechnology:

  Academic exploration in the field of nanotechnology is often driven by federal and state investment, with the hope that this investment will bear fruit in the marketplace. The Small Business Entrepreneur’s Evaluation (SBEE) Program offered through the International Institute of Nanotechnology provides a platform for scientists and engineers to present their newly developed technologies and receive assistance in the development of viable business plans. Each quarter, faculty members are offered the opportunity to present their marketable technology to an audience of students from the Kellogg School of Management, who then may use this as a springboard for writing a complete business plan. The success of the SBEE program, headed by Barry Merkin and Chad Mirkin, is evidenced by the formulation of 17 start-up companies since the inception of the International Institute of Nanotechnology.

- **Chad Mirkin**, chemistry and director of the International Institute of Nanotechnology, **Mark Hersam**, materials science and engineering, with **Mihail Roco**, chair of the US National Science and Technology Council subcommittee on Nanoscale Science, Engineering and Technology (NSET), and Senior Advisor for Nanotechnology at the National Science Foundation:

  “Nanotechnology has been recognized as a revolutionary field of science and technology, comparable to the introduction of electricity, biotechnology, and digital information revolutions,” the authors write in *Nanotechnology Research Directions for Societal Needs in 2020* (Lancaster, PA: World Technology Evaluation Center, 2010). “Between 2001 and 2008, the numbers of discoveries, inventions, nanotechnology workers, research and development, funding programs, and markets all increased by an average annual rate of 25 percent. The worldwide market for products incorporating nanotechnology reached about $254 billion in 2009. Current developments presage a burgeoning economic impact: trends suggest that the number of nanotechnology products and workers worldwide will double every three years, achieving a $3 trillion market with 6 million workers by 2020.”

  —by Joan Naper
We are constantly being experimented on. DDT as an insecticide, lead in paint and gasoline, asbestos in building materials — time and again throughout history, humans and the environment have been exposed to untested substances that turn out to have deadly consequences.

Now a group of researchers is starting to worry about the unknown risks that accompany the new and powerful science of nanotechnology.

“The extraordinary thing about nanomaterials is that they exhibit unusual behaviors and can do unusual things,” says David Dana, law. “The flip side is because they are so unusual, they may do things to the human body and the environment that we didn’t anticipate. The upside is potentially the downside.”

Dana refers to sunscreen as an example. Although skin is porous, it still acts as a strong barrier against topical substances that might seep in, keeping them away from the bloodstream, the lymphatic system, or even the brain. Sunscreens use titanium dioxide and zinc oxide particulates to reflect, scatter, and absorb the sun’s damaging ultraviolet rays. When zinc oxide particles are shrunk to a size between 1 and 100 nanometers, the lotion goes on clear without the streaky, white mess.

“Because the particles are so small, they could travel to places in the body where we don’t want them to go,” Dana says. “There are no conclusive reports about it, but there are some potential effects on human health.”

TOO LATE TO REGULATE?

Human health is one of the topics explored in Dana’s new book The Nanotechnology Challenge: Creating Legal Institutions for Uncertain Risks (Cambridge University Press 2011). Edited and contributed to by Dana, the book is a compilation of essays by legal scholars and social and physical scientists who offer views on how to address the unknown threats of nanotechnology. While the collection does not come to any firm conclusions, its theme is to push for more information and encourage experts to think about creative approaches to regulation.

“If we wait until nanomaterials are produced and then wait to observe an effect, then we’ll never regulate them,” says Kimberly Gray, civil and environmental engineering and a key contributor to Dana’s book. “We need to screen them for their effects during their development, but there isn’t a regulatory approach for these things.”

According to Gray, the vast majority of studies that have examined effects on health have been completed on the
In David Dana’s book The Nanotechnology Challenge, several experts weigh in with their opinions about this new field of science. But what do everyday people think? According to Jamie Druckman, political science, it all depends on how it’s framed.

In 2008, Druckman surveyed people’s opinions toward nanotechnology — specifically carbon nanotubes — as a part of an exit poll during the last US presidential election. He assembled 20 teams of student pollsters and sent them to randomly selected polling locations throughout the northern part of Cook County, Illinois. A pollster asked every third voter to complete a self-administered questionnaire and to provide email addresses for follow-up questions that were sent two weeks later.

Some respondents received surveys that positively framed carbon nanotubes by prefacing the questions with information about how they can lower energy costs and increase energy availability. Others received surveys that negatively framed the science, stating there are unknown implications for human health. A final group received questions that were not framed.

Some of the frames — both positive and negative — included scientific facts as support. The other frames were more general and did not cite specific studies or scientific evidence. The survey for the control group did not include facts.

“In both events, we found that the frames drove opinions,” Druckman says. “And in the follow-up questions, people responded in a biased manner that corresponded with their earlier opinions.”

In every case, the positive frames generated significantly more support for carbon nanotubes than the control group. The negative conditions elicited the least support. Druckman also found that the embedded scientific facts did not significantly strengthen the frames, which he found troubling because “factual information seems to have no effect on the public’s views.”

However, he pointed out that different facts presented more clearly could matter, and he is currently working on research to explore this possibility.

The results of his studies could have implications for which new technologies survive or fail. “It’s important to see how the public responds,” Druckman says. “New technology will only make it through regulation if people think it’s worth it.”

Druckman’s research appears in The Nanotechnology Challenge in the chapter titled “How Scientific Evidence Links Attitudes to Behaviors,” coauthored by Toby Bolsen of Georgia State University. — by Amanda Morris

David Dana

mammalian cellular level, not at a systems level. And there has been very little investigation into the unintended consequences on ecological health.

“The position most people take is just not to worry about it,” she says.

“A lot of literature says we just shouldn’t bother with regulation,” Dana adds. “Nanotechnology development is moving too fast, and it’s too complicated, so we should just take a pass. I understand that view, but I don’t agree.”

Because of these views, there has been little conversation about nanotechnology regulation in the US Congress. However, there has been some effort in the European Union and Australia. Nanoparticles have become popular in the cosmetics industry because they can deliver active ingredients deeper into the skin to fight lines, wrinkles, and uneven pigmentation. The EU now requires increased safety testing for cosmetics containing nanoparticles and demands that the nanoparticles be listed on the ingredients label.

SIZE OVER SUBSTANCE

In her essay “Five Myths about Nanotechnology in the Current Public Policy Debate: A Science and Engineering Perspective,” which is included in Dana’s book, Gray outlines misconceptions about nanotechnology, concluding that most people don’t know what nanomaterials are or understand the hazard.
One of the misconceptions is that nanomaterials are derived from common materials that are already deemed safe, and thus are also safe. Plus, they are used in such small quantities that they are below harmful thresholds. Gray debunks the myth by comparing gold with nanogold. When size is diminished to nanometer dimensions, gold is no longer metallic in nature, shiny, or golden in color. Instead, nanogold is red, blue, or yellow and will not conduct electricity. It is also highly reactive and promising for catalysis. Although these features unlock new opportunities for engineering, scientific, and medical applications, their risks to human health and the environment are unknown.

One of the challenges to regulation is that nanomaterials are used in many different industries. In the United States testing is industry specific. Most of the legal debate surrounding nanotechnology focuses on patent law rather than on science or industry.

“For example, an additive in your coffee would be tested by the Food and Drug Administration,” Dana explains. “It’s tested by its industry. The issue about nanomaterials is that they cut across a huge variety of industries, so it isn’t clear where the testing should take place.”

Despite the challenges, Dana and Gray think there should be further testing for nanomaterials before they hit the market. Both say that although this would cause delays for innovation and cost more money in the short term, stricter regulations would save money and even lives in the long run. Dana says more testing is particularly needed in the areas of food and cosmetics.

“Drugs receive a lot testing,” he says. “But if it’s food or cosmetics, then it doesn’t have much testing at all, really. How much would society hurt if a cosmetic is delayed a bit before entering the market? We should be more sensitive to nanotechnology depending on what’s the conceivable risk and how essential it is to move it ahead quickly.”

The Nanotechnology Challenge is scheduled to be issued in November 2011. Other Northwestern contributors include Daniel Diermeier, managerial economics and decision sciences; Jamie Druckman, political science; John O. McGinnis, law; and Laurie Zoloth, Center for Bioethics.

—by Amanda Morris
Heightened awareness of the problem of sexual abuse has led to deep anxiety over adults touching children — in nearly any context. Though our society has moved toward increasingly strict enforcement of this taboo, studies have shown that young children need regular human contact, and the benefits of breastfeeding have been widely extolled. Exploring the complicated history of love, desire, gender, sexuality, parenthood, and inequality, Erotic Attunement probes the disquieting issue of how we can draw a clear line between natural affection toward children and perverse exploitation of them. Pondering topics such as the importance of touch in nurturing children, the psychology of abuse and victimhood, and recent...
This practical resource highlights the critical importance of diagnosis and design in the work of leading and managing for school improvement. The authors maintain that today’s school leaders and managers, under intense pressure to improve student learning, cannot simply adopt and implement prepackaged reforms manufactured outside the school. Rather, to effect real reform, they must understand how leading and managing for instructional improvement gets done in their school and in turn use their diagnoses as the basis for mindful design and redesign. This book is a must-read for school administrators, teachers, stakeholders, and reformers who seek a new way to improve teaching and learning.

The text draws on over 10 years of empirical study and includes detailed vignettes to examine real-world examples of school social networks. It combines distributed leadership with diagnosis and design and grounds that work in the daily life of schools; looks at both formal and informal aspects of the school organization; and incorporates suggestions and tools for doing the work of diagnosis and design.

_Santiago Billoni: Complete Works_
A-R Music Editions, 2011
Edited by Drew Edward Davies, musicology

This volume presents the complete known works of Santiago Billoni (ca. 1700–ca. 1763), a Roman composer and violinist active in New Spain (viceregal Mexico) between the 1730s and 1750s. One of the most significant composers to work in the Americas during the viceregal period, Billoni was the first Italian-born musician to be named chapel master of a cathedral in New Spain.

His 31 concise works, which include villancicos, cantadas, masses, vespers psalms, and other liturgical pieces, stand as unique in New Spain for their use of chromatic harmony, virtuosic yet unmechanical violin technique, and emotive musical rhetoric grounded in the contemporaneous preference for interior devotion. They witness the diffusion of Italianate music in a variety of styles to Spanish America’s northern frontier and survive exclusively at the cathedral of Durango, where Billoni served as chapel master from 1749 until 1756. This volume is the first complete edition of any composer from New Spain.
WHAT IS AURASENSE? HOW DID IT GET STARTED?

AuraSense is a company that centers around the development of nanoparticles used as therapeutics and intracellular biomolecule detection probes. All of these technologies were either developed in the Mirkin laboratory or in my laboratory. All of the intellectual property was developed here at Northwestern. AuraSense worked with Northwestern to license these technologies, and now it’s our job to commercialize them and develop products from them. That’s the challenge that we are tackling right now.

It really started at the basic science level. For instance, nanoparticles for gene regulation were first investigated in the Mirkin laboratory. After demonstrating that these nanoparticles could work to regulate target genes in human cells, that technology was certainly thought of as a potential therapeutic. The question then was how to take the basic idea and early data and turn gene-regulating nanoparticles into a product. To do that takes a significant amount of money, time, and expertise not typically found in an academic laboratory. To facilitate that, the best approach was to start a company, license the relevant intellectual property, build partnerships with industry to generate capital, make rapid progress, and take advantage of partners’ experience in therapeutic development.

WHAT ARE SOME OF THE COMPANY’S MAJOR MILESTONES?

Formation of the company as a legal entity; negotiating the license with Northwestern and licensing the technology to the company; putting together a core group of people to drive commercialization efforts; hiring scientists to develop and nurture partnerships; building a laboratory that is steadily generating results for partners; and our first, second, and third partnerships with major pharmaceutical companies for technologies being developed at AuraSense.
WHAT ARE SOME OF AURASENSE’S SHORT-TERM AND LONG-TERM GOALS?

The most important short-term goals for the company include making good on the partnerships that we’re currently engaged in; building our relationships with those companies; and continuing to demonstrate the power of the technologies that AuraSense is developing.

Our ultimate goal is to have each of the technologies that have been licensed to AuraSense as commercial products that are benefitting patients, whether as a therapeutic or through our intracellular detection platform.

WHAT ADVICE DO YOU HAVE FOR INVENTORS-TURNED-ENTREPRENEURS?

Having good mentorship and people with experience, especially if you’re doing it for the first time, is very important. Being patient but persistent is also very important. No matter how fast one wants the process to move, there are always “i’s” to dot and “t’s” to cross, and that takes time. I would encourage Northwestern researchers to disclose potential inventions early, and often, and use the INVO office to protect inventions.

WHAT FUNDRAISING TIPS OR ADVICE DO YOU HAVE?

AuraSense has had three main funding sources. The first is private individuals. We started with a round of equity investment. Our second major source is our partnerships. We’ve gone to big companies, interested them in the technology, and then they invested in the technology for codevelopment.

Third is through government funding, including Small Business Innovation Research and Small Business Technology Transfer Grants. AuraSense has submitted a number of these grants and has been successful multiple times. They bring in money to drive forward specific projects that are both scientifically significant and have high commercial potential.

Be as broad and open minded about funding as you can be. Certainly, one would like to keep as much ownership and control over the technology as possible. Venture capital investment is definitely another possibility that can bring in significant capital and really drive the development of the technology.

HOW DO YOU BALANCE RESEARCH AND THE COMMERCIAL DEMANDS OF THE MARKETPLACE?

The research is driven by the intellectual curiosities of the people who are in the laboratory. We’re on the academic side, really driving the technology forward to specifically address the limitations that current technologies face. The commercial side is looking for products and to generate a profit. Their goal is to prepare technologies for the marketplace, taking them well beyond proof of concept or an experiment that meets a scientific milestone. It means a product that can be built reliably, put in a box, and sold to customers.

Those two things are very different, and that’s the challenge for AuraSense — being able to take what is done in the research lab and translate it into a real product that is functional, very easy to use, and addresses specific shortcomings of conventional technology.
WHAT SUGGESTIONS DO YOU HAVE FOR MAKING THE LEAP FROM LAB TO MARKETPLACE?

AuraSense is lucky from a standpoint that a number of different technologies have been licensed to the company. Some of the technologies have promise in the relative short term and some of them on a longer time scale. We’ve been able to leverage some of the near-term opportunities to help support those projects and also build the case for some of the longer-term opportunities.

The longer-term opportunities are more difficult because there can be a significant gap between basic science, proof of concept, and commercial products. Especially in therapeutics, this “valley of death” exists because of the amount of money required to take a proof-of-concept therapeutic into human trials and beyond. You have to be pretty open to all types of funding sources including aggressive partnerships with pharmaceutical companies and other organizations.

As mentioned, government grants are a good way to raise initial money and keep the technology steadily moving forward in the early going.

WHAT ARE YOUR THOUGHTS ON DEALING WITH PARTNERSHIPS?

One of the main things is diligence and patience. Some of these larger companies work much more slowly than you would like. Seek advice from people who have done it before so that one can understand how much the technology is worth at a specific development stage. Experience at all levels from the business, science, and intellectual property side — you really need it to help navigate a successful relationship with a partner.

WHAT IS IT LIKE BEING AN ENTREPRENEUR?

It’s very exciting. And, personally, I’m very excited about the opportunities at AuraSense and the possibility of moving things from the laboratory, where they have promise, to patients, where we have high hopes that they will have a significant and positive impact. Ultimately, seeing a good idea turn into an effective therapy would be amazingly rewarding.

For more intellectual property–related reading, visit invo.northwestern.edu.

— Thanks to INVO for this article.
In 2004, the Research Experience for Undergraduates (REU) program at Northwestern had been humming along successfully for three years. Students came to campus for nine weeks over the summer to work on research projects with various faculty members. At the end of the summer, they wrote reports and gave presentations at the REU symposium. Then the reports were filed away and forgotten — rarely to be seen again.

“Integrate, you are expected to write papers, and you’ve never been taught how to do it. It’s on-the-job training — trial by fire.”

To Mark Hersam, this was a shame.

“I thought it was a significant waste of effort,” says Hersam, materials science and engineering. “We could get greater dissemination of the undergraduate research by making it available to others.”

From this thought emerged Nanoscape: The Journal for Undergraduate Research in Nanoscience. Launched in 2004, it is the first of its kind in the country, giving students the opportunity to distribute their research while exploring the process of publishing.

As editor-in-chief of the journal, Hersam wanted Nanoscape to simulate a real peer-reviewed publication. Not only do students submit their own papers, but they also review papers from their peers with the guidance of an editorial board comprising graduate students, postdocs, and faculty members. Students also learn how to respond to their peers’ comments on the papers as the next step of the publication process.

“The peer review and revision process is central to publishing in a real, academic journal,” Hersam says. “And yet nowhere else in our educational system do we directly expose students to that process.”

While Nanoscape does accept submissions online from undergraduates everywhere, the editorial board does not actively solicit from outside institutions; most of the papers still come from students in Northwestern’s REU program. Hersam says interaction with the journal gives undergraduates an edge when applying to graduate school and during their graduate careers.

“In graduate school, you are expected to write papers, and you’ve never been taught how to do it. It’s on-the-job training — trial by fire,” he says. “Whereas our REU students have been through it before. They know what’s coming. They’ve already made mistakes and learned from them, so they are in a better position moving forward.”

The REU program is funded by the National Science Foundation. Nanoscape is a project of the Nanoscale Science and Engineering Center (NSEC), which is a part of the International Institute for Nanotechnology (IIN), both of which are under the direction of Chad A. Mirkin, chemistry. The journal is published yearly with the next issue due out this spring. Learn more and explore past issues at www.nanoscape.northwestern.edu. —by Amanda Morris
Saints Cosmas and Damian are honored together as the patron saints of physicians and surgery. They are depicted in *Legendary Transplantation of a Leg by Saints Cosmas and Damian, Assisted by Angels*, a painting that Northwestern transplant surgeon Michael Abecassis sometimes shows during his lectures about transplantation. The artwork, from circa 1600s by an unknown artist, shows the saints as they transplant the leg of a deceased Ethiopian man to the body of a white patient. The discarded leg lies on the floor at the foot of the bed. While transplant surgery has certainly come a long way, the concept has been around for centuries. And Northwestern researchers continue to develop the field.
TRANSPLANTS: MORE THAN FINDING THE PERFECT MATCH

Someday transplant recipients will receive livers that are encoded with their own DNA and made from their own cells. But these livers will not have originated in their bodies. They will be livers from deceased donors, from strangers, or even from animals, and yet they will be the perfect match.

“Transplantation is a mature field, relatively speaking,” says Michael Abecassis, founding director of Northwestern’s Comprehensive Transplant Center (CTC). “And yet the future of transplant surgery will not look anything like it does today.”

Currently, when people receive transplanted organs, there is a high risk that the body will react to them as foreign entities. The body’s immune system will attack and try to reject them. While doctors and medications have improved to combat the acute rejection that happens immediately in the body, chronic rejection over time has remained a challenge, especially for kidney, heart, and lung transplants.

“Drugs are really good at preventing acute rejection,” Abecassis says. “We can overcome that in 90 percent of the cases. The milestone for acute rejection is a year. But the goal is to make these organs last 20 years or 30 years.”

Achieving this kind of success requires more than transplant surgeons. Abecassis has assembled a group of experts from many fields within medicine and other academic disciplines, including the basic sciences, law, business, social sciences, public policy, and engineering. By engaging as many fields as possible, the CTC improves the lives of patients using research that stretches from basic science through clinical translation to advanced outcomes measurement that ultimately informs healthcare policy.

One of the most radical CTC projects comes from the laboratory of Jason Wertheim, transplant surgery, who also has a background in bioengineering. The researchers in his lab are literally building livers and kidneys.

Organ shortage is the biggest challenge for transplantation. There is a shortage of donations, but even donated organs are sometimes unusable. Some livers are
doing transplant research in 1962, it would have been inconceivable to think that this type of research would even be contemplated.”

Miller completed his first kidney transplant in 1968 and has been researching transplantation since the field was in its infancy. He has devoted his life to solving the problem of rejection by inducing tolerance, so that the body does not view transplanted organs as foreign, making medications unnecessary.

The problem with anti-rejection medications is they come with a slew of side effects. They work by weakening the body’s immune system, which makes the body more susceptible to infections and cancer. Miller’s goal is to eliminate these medications completely.

Miller starts with patients who have a good match between donor and recipient, usually brothers and sisters who share both parents. From the bone marrow, he derives stem cells, which gives rise to the immune system and are involved with rejection. The bone marrow-derived stem cells are transplanted from the donor to the recipient along with the kidney and create a specific immunological tolerance. As long as they are present in the recipient’s body, the recipient is able to accept organs, such as a kidney, from the donor.

“Wertheim is doing something totally futuristic,” says Joshua Miller, transplant surgery. “When I started
There’s a clone that expands in response to the antigen, so your immune system revs up to react against it. With specific immunological tolerance, something magical happens. The clone is no longer there. It’s eliminated for the rejection reaction but not for other things.”

According to Miller, Joseph Leventhal, transplant surgery, has also been able to achieve this with a different protocol. Leventhal has patients who have been off their medications for one year and have not experienced adverse reactions. Miller has one patient who has been off medication for two years.

“They are off the medicines, so they don’t have side effects. They don’t have rejection,” Miller says. “But what’s going to happen next year? These studies in humans have to go on for a long period of time.”

Part of this success is attributable to the diverse community under the CTC umbrella. Transplant surgeons such as Miller, Leventhal, and Abecassis have access to hepatologists, nephrologists, infectious disease specialists, immunologists, and others. Psychiatrists and psychologists are also available to work with the transplant patients to evaluate their mental and emotional states. And Wertheim has access to engineers as they work together to create tissue-engineered organs.

“Medicine doesn’t move along by itself anymore,” Wertheim says. “Collaboration is needed to move medicine forward. It needs engineering, science, and medicine to work together.”

“Our job is to provide the best possible care to transplant patients,” Abecassis adds. “Surgery is a small part of that. To truly advance the field, we have to bring together these various disciplines in order to better provide the type of collaborative scientific approaches that best address their specific conditions.”

Northwestern’s Comprehensive Transplant Center is located on the 19th floor of 676 North St. Clair Street on the Chicago campus. For more information, visit www.feinberg.northwestern.edu/transplant.

— by Amanda Morris
In 2006 Simpson, French and Italian, was perusing the quiet galleries of the Pinacoteca Provinciale di Bari Corrado Giaquinto, a small museum obscurely tucked away on the fourth floor of a city administration building on Italy’s southeast coast. As he eyed piece after piece of the gallery’s collection of 800 beautiful and valuable paintings, his gaze fell on a large, 1882 oil painting by Francesco Netti.

*In Corte d’Assise* depicts the profiles of stylishly dressed women staring down from the balcony of a courtroom. They watch, peering through opera glasses to get a closer look. They watch, wearing fancy hats and fur mufffs to warm their hands. They watch, holding fans over their mouths to silence gasps and sighs of awe. They watch while snickering and giggling to others on either side. With intent eyes fixed on a solitary, sobbing woman below, they watch.

“It began with this painting,” says Simpson. “I was very intrigued by the painting. I looked into it and found out it was about this fascinating trial.”

Curious to learn more about the painting’s subject matter, Simpson visited legal trial archives in Rome and discovered the strange details of a story that became weirder and weirder with every document he read. The key players of the courtroom drama were a wounded soldier, an angry wife, a circus acrobat, a clown, a prostitute, and an equestrienne. The people and event created a media circus, indeed.

Simpson received a grant from the Department of French and Italian to spend a summer in Rome conducting research in the archives. The archive building sits on a gritty Roman street lined with car repair shops and tire stores. Once inside, Simpson...
hunted down a medium-size box full of manila folders. The folders spilled over with trial testimonies, related newspaper articles, letters, photographs, and more. While the trial was at center stage in late-19th-century Italy, subsequent historians have rarely discussed or analyzed it.

“Historically, it’s been mostly ignored, perhaps because it was embarrassing for Italy,” he says. “After the Italian unification wars ended in 1861, Rome aspired to become an important European capital equal to Paris and London. The trial was felt to expose a savage, primitive underbelly of Italian life. It didn’t speak well about the Italian state.”

The Circus Comes to Town

It all started on Sunday, October 6, 1878 when Giovanni Fadda, a captain in the Italian army and a hero of the wars of national unification, was fatally stabbed while in his downtown Roman apartment. Calling for help and soaked in blood, Fadda stumbled downstairs and outside to the Piazza of the Golden Keys where he collapsed and died. A stranger nearby with blood on his hands was immediately arrested and sent to jail.

That man was later identified as Pietro Cardinali, an acrobat in the Cardinali Equestrian Circus, which toured small towns in southern Italy. Shortly after his arrest, a rumor surfaced that Cardinali was the lover of Fadda’s much younger wife, Raffaella Saraceni. Further rumors claimed that an equestrienne in the circus, Antonietta Carrozza, acted as their go-between, facilitating the affair and murder.

“This happened right at the moment when newspapers moved away from only addressing sophisticated levels of society to selling copies to popular audiences — a generation of people who were just learning to read,” Simpson says. “The new readers weren’t very interested in the political debates of parliament or international issues. They bought newspapers to read human dramas filled with sensation and scandal.”

The newspapers leapt onto the “Fadda Affair,” as it was commonly called, and built it into a huge media circus. Soon, everyone across Italy knew the details of Raffaella Saraceni’s scandalous affair and the murder plot to remove her husband from the picture. Before Italian unification, the Catholic Church controlled Rome’s government and did not grant trials by jury. Public juries were a new phenomenon, and citizens relished the novelty. Seating was set up inside the courtroom and tickets distributed so people could watch the trial.
Crowds lined the streets just to catch a glimpse of Saraceni when she entered the courtroom. She denied all the charges, wept daily during the trial, and played the role of a tragic victim.

**Women Under the Big Top**

Just as shocking as the affair and murder was the strong prevalence of women spectators in the courtroom. Astonished that so many women attended the trial, people worried about what it meant for the Italian state.

“That turned into an even bigger phenomenon than the trial itself,” Simpson says. “Men had a lot to say about the topic, but none of the journalists or commenters ever asked a single one of the women attendees why she was so interested in the trial.”

A rumor surfaced that a war wound had rendered Captain Fadda impotent and unable to perform as a husband. Some said women flocked to the trial because they could identify with Saraceni who married a man who turned out to be not what she thought. They claimed that “frustrated maternity” drove her into the arms of the circus acrobat. Others said large numbers of women attended the trial because a war hero was murdered, and they wanted to see justice prevail. Still others claimed the women audience members were there only for the low-level, soap-opera aspect of the drama.

Simpson, whose research and analysis of the trial were published last winter in the book *Murder and Media in New Rome: The Fadda Affair* (Palgrave Macmillan), says the conversation around the trial unified the Italian nation. People read the newspapers every day to follow the testimony as the trial dramatically unfolded. The articles were even read aloud in bars for those who could not yet read.

“Because the story of this trial was published in every corner of the country, it unified Italy in a way that national efforts to create patriotism hadn’t been able to,” he says. “Even though everyone had differing opinions about the trial, they were still talking about the same thing. That’s what constitutes community.”

**Send in the Clowns**

Damning evidence hinged on the testimony of a circus clown, Carluccio, who was missing and presumed dead until his whereabouts were tipped off by a prostitute toward the end of the trial. The clown claimed that Saraceni offered him money to murder Fadda and that when he declined, Cardinali threatened his life if he didn’t keep quiet. Carluccio’s appearance in court, after missing most of the trial, was further evidence of how enormous the media circus had become.

“When Carluccio arrived, thousands of people wanted to see him,” Simpson says. “Here’s a total nobody — a clown from a third-rate circus — and the whole nation is listening to what he has to say.”

In the end, Saraceni, Cardinali, and Carrozza were all found guilty. Six years later, when her prestigious defense attorney became chief of the justice ministry (the equivalent of the U.S. Attorney General), Saraceni was released from prison even though her initial sentence was to serve for life. Cardinali was condemned to death, but the king commuted his sentence to life imprisonment. Carrozza was found guilty but released because she was portrayed as so psychologically damaged that she was incapable of saying no to Cardinali, who had abused her for years. Three days after the trial’s end, she was hired by Rome’s main circus.

“After being judged guilty of complicity in a murder, she was awarded with a huge advancement for her career,” Simpson says. “She became a media star. Rome’s main circus knew her name would sell tickets because people wanted to see her.”

Above: A photograph of Raffaella Saraceni at the time of the trial. Used courtesy of Ministero dei Beni e le Attivita Culturali, Archivio di Stato di Roma.
An illustration from the 1879 Italian newspaper *Bracco Editore* shows Pietro Cardinali stabbing Captain Fadda in his apartment.

**The Circus Leaves Town**

Simpson says the Fadda Affair was an early, formative media circus in the new nation of Italy where high-profile trials still garner huge media attention. Even today, Italian citizens have passionately followed the lurid details of the trial of Amanda Knox, an American exchange student who was found guilty of murdering her British roommate in 2007 and later acquitted on appeal. But the Knox drama, too, will someday become just another overlooked detail in history. Even though the Fadda Affair grabbed every Italian’s attention in 1878 and 1879, the hype did not last for long.

“The trial was prophetic of a media pattern,” Simpson says. “People seize onto things that respond to their nightmares, wishes, or fantasies. They pay intense attention to it for a period of time and then move on to the next thing. Before it’s over, people are already onto the next scandal.” — by Amanda Morris

The accused assassin, Pietro Cardinali, was an acrobat in the circus. Used courtesy of Ministero dei Beni e le Attivita Culturali, Archivio di Stato di Roma.
The image on the cover of the February 2011 issue of Nano Letters might look like something you haven’t seen before. But the crawling, twisting purple substrate studded with pink teeth is a familiar staple from many people’s childhoods. It’s a scanning electron microscopy image of a Shrinky Dink, the popular arts and crafts material that’s been used by children since the 1970s.

Created by two Wisconsin housewives in 1973, Shrinky Dinks consist of large, flexible plastic sheets that can be drawn on, cut out, and shrunk when baked without altering the shape or colors. Now, 38 years later, this simple toy is contributing to complex science in the lab of Teri Odom, chemistry.

She is using the material as a new, inexpensive way to create, test, and mass-produce large-area patterns on the nanoscale.

“Northwestern is heavily invested in nanopatterning and nanofabrication,” Odom says. “We’re trying to solve some grand challenges by making nanofabrication accessible and usable for a wide range of studies.”

Part of the challenge of nanofabrication is developing tools that can create the patterns in a parallel manner with controlled symmetry. As the pattern shrinks, it must be able to maintain the size of the features and spacing without becoming warped. (This image on the cover of Nano Letters was captured mid-shrink, which gives it a wrinkled appearance.)

“The problem is that most fabrication techniques can’t do this,” Odom says. “And the instruments that can do this are too expensive. For example, electron beam lithography is used to make patterns, but it’s a half a million-dollar instrument.”

Known as solvent-assisted nanoscale embossing (SANE), the method that Odom’s group has created using Shrinky Dinks is inexpensive and is able to control feature size, feature spacing, and feature symmetry in a parallel manner. Because of its cost-effectiveness and accessibility, it can be used by researchers from a wide range of fields who previously wouldn’t have considered experimenting with nanofabrication.

Starting with a single master pattern, the method can be used to create new nanoscale masters with variable spacing and feature size. SANE can increase the spacing of patterns up to 100 percent as well as decrease them down to 50 percent in a single step by stretching or heating the Shrinky Dink material. SANE can reduce critical feature sizes as small as 45 percent compared to the original master.

“Part of the large disconnect between making or controlling structure at the nanometer scale, and then having it be used for the macroscale, is the ability to scale it,” Odom says. “If we can’t scale the technology, then we can’t take advantage of the interesting properties that science offers, and it just remains an academic exercise.”

What was once touted as the “magical world of Shrinky Dinks,” the iconic material continues to live up to its tagline.

— by Amanda Morris