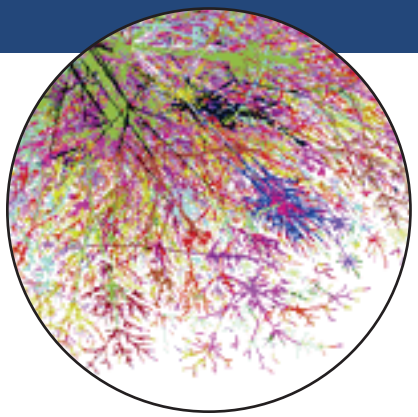
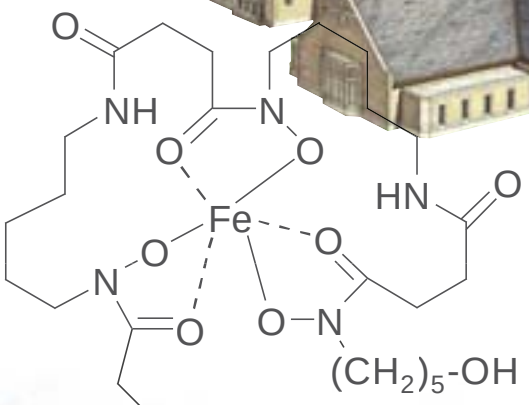
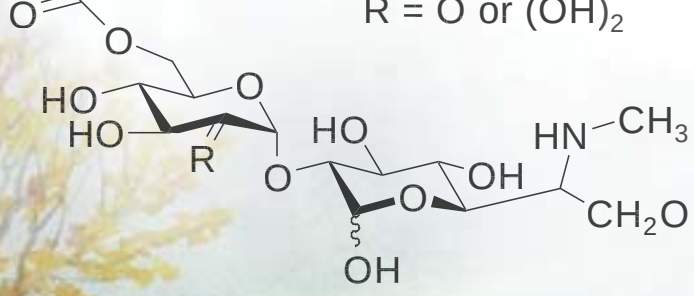
The Journal of the University of Notre Dame College of Science
Spring 2004, Volume 1, Number 1

Renaissance







Construction begins on the Jordan Hall of Science

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From the Dean

It's my pleasure to introduce you to the inaugural issue of *Renaissance*. This journal is our way of heralding the teaching, research, and student accomplishments at the University of Notre Dame's College of Science.

"Renaissance" means "rebirth" in the French language. We in the College of Science are in the midst of such a "rebirth." In the years ahead, the College of Science will continue to make significant positive changes in faculty hiring, curricular revisions, and—above all—exciting improvements in the physical plant.

In this issue, we highlight the recent groundbreaking of a new $70 million science building named the Jordan Hall of Science, in recognition of a major gift from Trustee Jay Jordan III and his family. This state-of-the-art teaching building will house the undergraduate teaching labs for the College of Science and will also contain major University lecture halls with the latest technology. In a sleeve within the front cover of this issue is a CD with a "fly through" of the new building. It is truly a major event in the history of Notre Dame to construct such a building. Generations of future students will experience new teaching approaches and greater excitement in the learning of science. We are all indebted to the Jordans and the many other donors who made this building happen.

We all know that buildings alone don't produce greatness and quality in a university. The faculty and the students will define the advances in teaching and learning that will result from the new Jordan Hall of Science. This will require innovative and stimulating pedagogy for both science majors and nonscience majors on the part of the faculty. The College of Science is committed to increasing the exposure of all students to science and providing a more relevant and expansive experience to those choosing science as a major through efforts to revise and streamline curricula and undergraduate research experiences.

This issue of *Renaissance* also highlights the research programs of some of our faculty holding endowed chairs. The stature of the departments and collectively the College depends heavily on attracting and retaining the best faculty both for teaching and research. We firmly believe that outstanding teaching and research go hand in hand because our undergraduates benefit immensely by being exposed to research. In this past year, we added a dozen outstanding new faculty to the College of Science. They and the existing faculty have been increasing our federal funding by 16 to 18 percent a year, which is a top increase for any university.

Above all, it is important that science serve humanity. Notre Dame is especially proud of the way its scientists have undertaken important missions worldwide to improve the human condition. One example is the efforts of Rev. Thomas Streit, C.S.C., with the Notre Dame "Haiti Program." (*See page 20*).

Finally, we hope to use *Renaissance* to inform you of the accomplishments of our students and graduates. In this issue is a reprint of an article written by Notre Dame's 14th Rhodes Scholar, Andrew C. Serazin, who was a student in the Department of Biological Sciences.

In forthcoming issues, we hope to continue reporting on the graduates and award-winning undergraduates of the College. *Renaissance* belongs to everyone in the College of Science. In that spirit I extend an invitation to alumni of the College of Science to send us word of their newsworthy accomplishments, exciting career changes, or significant professional awards. We will incorporate these items in future issues of *Renaissance*.

We plan to publish *Renaissance* three times a year: in early fall, winter, and in the spring after commencement.

I look forward to working with faculty, alumni, and friends to truly make the next decade and beyond a renaissance for the College of Science.

Joseph P. Marino
William K. Warren Foundation Dean
College of Science

UNIVERSITY OF NOTRE DAME

College of Science

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Design: Notre Dame Media Group

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One Bold Step for Education: The Jordan Hall of Science

WHEN IT IS COMPLETED IN 2006, THE JORDAN HALL OF SCIENCE IS BOUND TO MAKE A BOLD AND POWERFUL STATEMENT, REDEFINING THE ROLE OF THE NOTRE DAME COLLEGE OF SCIENCE, THE FUTURE OF SCIENCE EDUCATION AND RESEARCH ON CAMPUS, AND EVEN THE EASTERN EDGE OF CAMPUS, WHERE IT WILL STAND.

One look at this prominent edifice will be sufficient to impress upon even the casual observer the realization that science instruction has undergone the most profound and fundamental transformation in its history at Notre Dame.

Nearly 25 years will have elapsed from the first groundswell of support within the College of Science for a new and modern science teaching facility. It was envisioned as not just a brick-and-mortar building, but a structure destined to reshape the future, the curriculum, and the self-image of the scientific community on campus.

When chemistry professor **Paul Helquist** arrived at Notre Dame in 1984, a movement was already afoot to update the University's science facilities. A fellow chemistry professor had the vision and conviction to modernize every aspect of science teaching and stimulate the expansion of a small group of scientists who were already performing influential scientific research. "The person who deserves full credit for planting the seeds in our minds was Rudy Bottei," Helquist said. "As early as 1982, he was talking to anyone who would listen to him."

For 48 years, until his death in April 2003, Bottei taught analytical and environmental chemistry at Notre Dame. The movement begun by Bottei gathered momentum throughout the 1980s, a period that coincided with a great leap in growth at Notre Dame. This building spurt on campus had huge implications for the College of Science as well. The more that the College of Science lagged behind compared to the development and expansion of the other colleges on campus, the more resolute the Notre Dame scientists became that the College of Science needed to have its turn too—and soon.

By 1988 the movement reached escape velocity. After working through the summer and fall of 1988 on a document outlining the needs of the College of Science, the department chairs of chemistry and biochemistry, physics, mathematics, biological sciences, and preprofessional studies were ready to take their mission to the next level.

On December 7, 1988, they presented their findings to College of Science Dean **Francis J. Castellino**. "Simply renovating the present laboratories once again is not a feasible solution to the problem when one takes into account the needs for much greater ventilation, fume hood space, instrument rooms, and other improvements," they wrote. The groundwork had been laid, but extensive fund-raising lay ahead.

Other circumstances shifted in the College of Science's favor. By the time the Notre Dame Board of Trustees approved the planning of the new science facility in 1993, the United States economy was in the early stages of one of its greatest growth spurts in history. But, boom times could not speed up the incremental and deliberate planning process that is required for a building the size of the new science hall.

There was widespread recognition that something had to be done immediately to upgrade many aspects of teaching within the College of Science. At the top of the list was the state of the chemistry and physics laboratories in Nieuwland, which "simply were not suitable for teaching purposes," Helquist said.

The science hall will be a 201,783-square-foot building that will cost $70 million.

It will include:

40 undergraduate laboratories for biology, chemistry, and physics

two 250-seat lecture halls

a 150-seat multimedia lecture hall

two classrooms

22 faculty offices

offices for preprofessional (premed) studies

a greenhouse

an herbarium

and an observatory

It will be built on Juniper Road in front of the Rolfs Sports Recreation Center

The $70 million Jordan Hall of Science "will enable us to teach science at a level that simply has not been possible…"

—Paul Helquist

Notre Dame President Rev. Edward A. "Monk" Malloy, C.S.C., John W. "Jay" Jordan, Gretchen Jordan, Goldie Jordan, and Dean Joseph P. Marino break ground for the new Jordan Hall of Science.

A fund-raising effort begun in 1991 raised $8 million for a crash renovation of Nieuwland labs in the summer of 1993. The plan to overhaul the laboratory facilities was carried out with near-military precision, as work crews demolished the old labs on Nieuwland's second, third, and fourth floors. Throughout that summer, workmen rebuilt the labs and by the start of the fall semester, the major upgrade had been completed.

Meanwhile, the new facility was taking shape—at least on the drawing boards. The winning design was awarded to the architectural firm of S/L/A/M Collaborative of Glastonbury, Connecticut. The Indianapolis firm Geupel Demars Hagerman won the construction contract.

Final plans were approved in December of 2002. But, a shaky national economy at the time temporarily delayed progress on the Jordan building until October 2003, when the University Board of Trustees gave the go-ahead for construction, with a completion date set for summer 2006.

The $70 million Jordan Hall of Science "will enable us to teach science at a level that simply has not been possible," Helquist said. It will have a powerful influence on the easternmost edge of the Notre Dame campus—an area that historically has been dominated by Notre Dame sports facilities.

Notre Dame physicist **Kathie E. Newman**, who was associate dean in 1988 and an important cog in the early stages of planning, speculates that the existence of the Jordan Hall of Science will have a far deeper effect on the University than most people realize. "As I look to the future, it will be very interesting to see how the students react to the new building. I'm talking about not just science majors, but nonscience majors too. I am anxious to see how the new building becomes integrated into campus life," she said.

Helquist and Newman believe that College of Science Dean **Joseph P. Marino's** dictate that the entire science curriculum be modernized in parallel with the construction of the Jordan Hall of Science will almost certainly begin to draw some of the country's brightest students. At the same time, the atmosphere for scientific research that has already made enormous strides in the 1990s is expected to position Notre Dame to enter the same league with the top scientific universities in the United States.

This same vision is shared by the building's chief benefactor, **John W. "Jay" Jordan**, a Chicago businessman and founder of The Jordan Company (TJC), a private investment firm that acquires, manages, and builds companies for the TJC partnership account.

Jordan arrived on the Notre Dame campus on a chilly and drizzly Saturday, October 18, 2003, to dig a first spade of earth along with Notre Dame President **Rev. Edward A. "Monk" Malloy, C.S.C.**, Dean Marino, and Jordan's wife, Gretchen, and daughter, Goldie.

At these groundbreaking ceremonies, Jordan stepped up

to the microphone. A 1969 Notre Dame graduate and a member of the University's Board of Trustees since 1993, Jordan not only downplayed his own role but sought to temporarily draw attention away from the magnificence of the new building.

"This structure is not what's important. [Compared to] continuing education and advancing the legacy of Notre Dame, the structure is irrelevant. What happens inside is," he said. "We have a world-class dean, a world-class faculty, and a world-class student body. They deserve the best. Folks like us have the resources to give them the best. That's all we do. What is really important is what *they* do."

South Bend Center Moves out of the Dungeon and into the Light

Indiana University's low-profile medical school on the Notre Dame campus is poised to break out of obscurity in a big way.

One day in 2005, IU's satellite medical school will emerge from the basement of Haggar Hall, where it has been quartered for the last 33 years.

The 7 faculty members and 32 students of the medical school, the South Bend Center for Medical Education (SBCME), will move, lock, stock, and barrel, to a new $15 million building on Angela Boulevard across from the Marie P. DeBartolo Center for the Performing Arts. Construction of the three-level building began in August at the site of the former Northern Indiana State Hospital.

For Biological Sciences Professor **Kenneth R. Olson**, the move is akin to being released from three decades of confinement, in more ways than one. The combination of cramped quarters, dark hallways, and seedy rooms earned the facility its nickname "The Dungeon" many years ago.

Haggar was the original site of the Department of Biological Sciences before it moved to the new Galvin Life Science Center in the mid 1960s.

In 1970, the Indiana State Legislature established seven regional sites for teaching preclinical medicine, with South Bend as one of those sites. The following year, the SBCME rented Notre Dame's post–World War II-era Stran Steel Building, which was originally constructed as a temporary building. Then, two years later, the IU program moved into a large section of the Haggar basement to begin its program there.

By the time Olson arrived in 1975, it was already a well-established fact that the IU program was sorely in need of larger and more suitable quarters. "My first office was a little box. I had a little tiny corridor for my lab," he said. Even the men's room in the Haggar basement was converted into a lab. To this day, only three people can squeeze themselves into the room.

"We talked long ago about the need for a new building, but there was no money for it," said Olson, who is chairman of the building committee. The IU staff implored Indiana politicians and the General Assembly for new quarters without any success. "So we have just been hanging out waiting for something to happen for over 20 years," Olson said.

Olson recalled an earlier instance when IU and Notre Dame floated a trial balloon to create new quarters when the Department of Biological Sciences added the Hank Wing to the Galvin Center. But, after months of discussions, it became apparent that the money was not going to be forthcoming from the state. In addition, the IU medical school needed more room than the new Hank Wing could give. So the "guest" with the two-year medical program had to continue to wait in the Haggar basement.

The new building, called the Raclin–Carmichael Hall, will be a boon to Notre Dame as well as IU.

Backed by $5 million in funding from Notre Dame, the W. M. Keck Center for Transgene Research will move out of Stepan Chemistry Hall to occupy much of the second floor of the 66,000-square-foot building.

Francis J. Castellino, the Keck Center director and Kleiderer/Pezold Professor of Biochemistry, is counting the days as Olson is. "Space is such a huge, huge issue on this campus," Castellino said. Currently the Keck Center's research faculty, post-docs, and graduate students are sprawled among various buildings and floors.

"It's not the most efficient way to get work done," Castellino said. "A lot of science is done as you pass somebody in the hallways. We don't get together as much as we should, so the move will solve a major problem for us."

However, the separation of about 30 Keck Center personnel from the Chemistry Department is a downside "that I think about a lot," Castellino said. Yet, the positives far outweigh the trade-offs.

Joseph Marino, dean of the Notre Dame College of Science, sees the joint Indiana University/Notre Dame partnership as a significant step in bringing biomedical research to a new level at Notre Dame. "There are terrific opportunities to collaborate and make joint hires that will benefit Notre Dame science and the IU medical school," he said.

The new building will house a state-of-the-art 250-seat auditorium and two "almost-in-the-round" classrooms. "The classrooms will have three tiers. They are large enough to give our students plenty of room, but small enough that we can really

"There are terrific opportunities to collaborate and make joint hires that will benefit Notre Dame science and the IU medical school."

—Joseph P. Marino, dean of the Notre Dame College of Science

interact with them," Olson said. Laboratories, seminar rooms, offices, and four examination rooms round out the main features of the building.

IU medical students spend their first and second years of medical school at the Notre Dame facility before continuing their education in Indianapolis. "We have had 70 or so students come back to this area and begin their practice," Olson said. "That was the idea behind these centers when the General Assembly created them in 1970— the hope that the students would experience local communities other than Indianapolis. That has certainly been the case."

Furthermore, many of the students have become primary care physicians, thus filling a need that had grown acute in the 1980s and 1990s.

Olson envisions that the SBCME will serve as a magnet for medical education programs for physicians of both Memorial Hospital and St. Joseph Regional Medical Center.

But, for now, he will have to wait in the basement of Haggar for the day when the moving vans show up. Olson has already thought about the day when the SBCME leaves Haggar. He won't shed a tear and he won't look back.

And what will become of the "temporary" Stran Steel Building that was erected when Harry Truman was President?

It will finally be leveled.

Patient Tailored Therapies:

KECK CENTER PUTS NOTRE DAME AT THE FOREFRONT OF CANCER RESEARCH

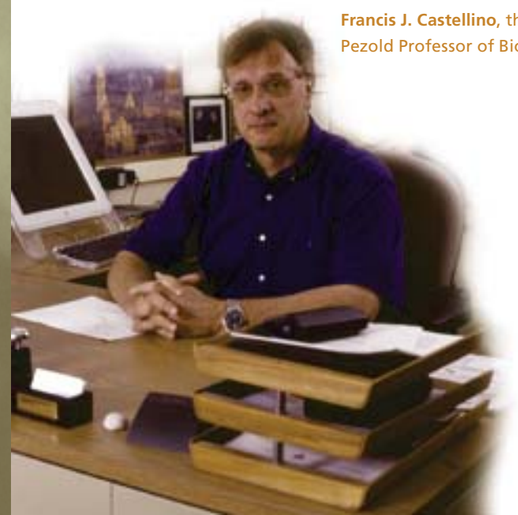
Biomedical research at the University of Notre Dame is producing a foundation for the production of a new generation of so-called designer drugs that target the molecular alterations that begin the cascading events toward carcinogenesis.

A small cadre of scientists on campus is probing the circuitry of the human cell in hopes that future therapies will be more effective in killing tumor cells without harming normal, healthy cells.

"The day is going to come where every cancer is going to be profiled for its genetic composition," said **Francis J. Castellino**, the Kleiderer/Pezold Professor of Biochemistry. "In other words, one person's colon cancer or prostate cancer may have some slight differences from another patient's in terms of the cancer's genetic makeup, and those differences could dictate the therapeutic regimen."

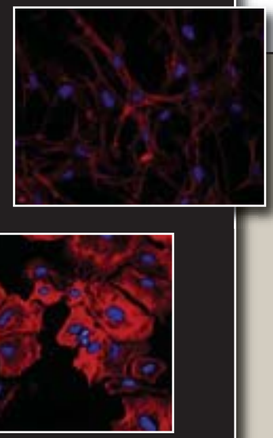
The term "patient-tailored therapies" will soon supplant old concepts associated with chemotherapy. "In the not-too-distant future, a regimen of tailor-made chemotherapeutics will be designed for different people, based on their susceptibility to certain side effects, or perhaps even the genetic makeup of their unique tumors," Castellino said. "These subtleties are going to drive therapy, outlook, and even diagnoses."

As part of this effort, 10 Notre Dame researchers are looking at the gene profile in colon tissue in colon adenomas and carcinomas and asking the question, "What genes are turned on or off when a benign polyp moves to malignancy?"



Francis J. Castellino, the Kleiderer/Pezold Professor of Biochemistry

Phalloidin AlexaFluor 594 stain of wild type (top) and urokinase receptor deficient (bottom) endothelial cells demonstrating altered cellular morphology of urokinase receptor deficient cells adherent to vitronectin.



Notre Dame's evolution from a small midwestern university renowned for its undergraduate program into an emerging powerhouse in cancer research is a recent phenomenon. It is a story with more interlocking themes, twists, and turns than a Robert Altman movie.

The founding of the W. M. Keck Center for Transgene Research, followed closely by the creation of the Walther Cancer Research Center in the mid to late 1990s, is regarded by many as the development that has thrust Notre Dame into national prominence as a premier player in several fields within the genetics of molecular medicine, including cancer.

Notre Dame is a true rarity in advanced research because it does not have a medical school. Instead, both centers operate within the Department of Chemistry and Biochemistry. This unique arrangement of research in interdisciplinary fields has produced a special niche worldwide for Notre Dame's College of Science.

Cancer research at Notre Dame focuses on using mice that are genetically altered in a targeted fashion to be predisposed to cancer. Whole mouse research is a very effective way to study cancer because it provides insights into a wide range of possible physiological changes that are not possible through growing cancerous cells in a culture dish, implanting tumor cells in mice, and awaiting an outcome.

In general, this targeted approach to gene alterations differs from the more common transgenic approach in that the targeted gene is altered in its appropriate chromosomal location and can thus remain under appropriate control mechanisms. The usual transgenic approach involves insertion of the gene into the chromosome in a random fashion.

"Just inserting a gene and letting it randomly go into chromosomes will interrupt the function of other genes and skew results," said Castellino. "We change genes in their appropriate location, and that's difficult work."

Four major areas of investigation are underway:

1 ***molecular biology and gene targeting in collaboration with the Keck Center***

2 ***drug design and development in collaboration with the organic synthesis group in the Department of Chemistry and Biochemistry***

3 ***cell biology and cell signaling involving the Cell Biology Group within the Department of Biological Sciences***

4 ***activities in clinical oncology in the Department of Preprofessional Studies***

> "Just inserting a gene and letting it randomly go into chromosomes will interrupt the function of other genes and skew results. We change genes in their appropriate location, and that's difficult work."
>
> —Francis J. Castellino

The Keck Center has 40 or 50 different strains of mice with altered and targeted germ lines. "We have one mouse model that we are particularly interested in—one that has a genetic defect that causes the mouse to develop first polyps and then colon cancer," Castellino said.

In a new study involving the Northern Indiana Cancer Research Consortium and cancer patients in two hospitals in nearby South Bend, Indiana, Notre Dame researchers are obtaining live tumor cells and using a laser to pick out the cells where a defective gene, known as the APC gene, has been shown to be vital in the development of precancerous polyps in humans.

Identifying genes involved in coagulation and inflammation as they relate to the development and progression of cancer is of special interest at the Keck Center. How does the removal of a pro-inflammatory gene affect the growth of polyps that are formed by the mutation of the parent gene? What other genetic linkages contribute to the development of the tumor?

"The beginning of every disease is inflammation," Castellino said. "There is a profound relationship between coagulation and inflammation. It is probably the hottest topic in the field of blood clotting."

All this would not be possible if Notre Dame did not take a huge leap in 1997 when its scientists produced a genetically altered mouse line that was the first in the world to be deficient in the coagulation factor VII (FVII). This factor is involved in a complex series of enzymatic reactions leading to the formation of a blood clot. "It was a seminal event that gained Notre Dame international prominence," Castellino said. "No one at Notre Dame had ever done this before." Careers were on the line, especially those of the graduate students.

The development of FVII required key steps along the way, not the least important of which was a $2 million grant from the Keck Foundation.

Notre Dame senior faculty member Eliot Rosen and four graduate students chosen by Castellino then became resident scientists at the Flanders Interuniversity Institute for Biotechnology at the Katholieke Universiteit Leuven, Belgium. The Belgian scientists were highly skilled in molecular medicine. The Notre Dame researchers brought their own unique set of research skills to Belgium. The result was an ideal marriage.

"Eliot handled a lot of the molecular biology aspects. I handled a lot of the protein chemistry," Castellino said. "So, everybody merged and everybody learned from each other."

Having a modern animal facility at Notre Dame was essential for carrying out a long-term study. "The animal facility here may not be the biggest, but it is among the better ones," Castellino said.

The traffic between South Bend and Leuven continued for two years. "I remember I was in a meeting when I was called out to take a phone call with news that this first altered mouse strain had been generated," he said. It was the third or fourth mouse that had ever been genetically altered to be deficient in a major blood coagulation factor.

The first paper that was ever published on a factor-VII-deficient mouse appeared in the best journal in the field, *Nature*. "It probably cost upwards of $500,000 to publish that paper," Castellino said.

The work with the Belgian scientists started a chain reaction that continues today. "We modeled our whole transgene center after the way they built their research infrastructure," he said.

The creation of the Keck Center drew the interest of the Walther Cancer Center in Indianapolis, a private philanthropic organization whose goal is to fund the cancer research efforts of major universities and hospitals in Indiana and neighboring states.

"I clearly remember sitting in my office with one of the Walther representatives invited up here by Chuck Kulpa, who was an associate dean at the time," said Castellino, who is founding director of the Keck Center. "Notre Dame already had some presence in cancer research, particularly with Morris Pollard."

That meeting eventually led to the establishment of a research center on campus in 1997. Cell biologist **Alan L. Johnson** and two postdoctoral students received Walther funding to pursue research on cell death as it relates to ovarian cancer. Johnson focused on identifying genes that play a key role in allowing ovarian epithelial cells to avoid apoptosis, or cell death, and begin the formation of malignant tumors.

The appointment of oncologist **Rudy Navari**, a Notre Dame graduate and a member of the Science Advisory Council, as director of the Walther Center gave the center even wider recognition. "Rudy left his practice in Birmingham, Alabama, and got his master's degree in clinical ethics at the University of Chicago," Castellino said. "He made an entire career change to take over the Walther Center here."

In recent years, the Walther Center at Notre Dame has launched interdisciplinary projects with 25 faculty members and 15 fellows in the departments of Chemistry and Biochemistry, Biological Sciences, and Preprofessional Studies in the College of Science.

In 2004, the Keck Center is embarking on a major project to model diseases that are related to the inflammatory and coagulation disorders. "One of the key problems we will be focusing on is sepsis," Castellino said. "Sepsis is the body's response to infection that has spread throughout the blood and tissues. It is the leading cause of death in trauma units."

"These dissemination bacterial infections are very dangerous. They cause a systemic inflammatory response, which turns on coagulation. Then coagulation reinforces inflammation. Once this cycle begins you can end up with multiple organ failure and death." Sepsis can affect infants and people whose immune systems are compromised, such as the elderly and those with chronic illnesses.

The group pursuing this research will include **Takayuki Iwaki, Kazuo Asada** and **David Joyce**, the head of the clinical trial program at the Eli Lilly Company. "Dr. Joyce brings important clinical experience to the Keck Center. He will be an key member of the inflammation group," Castellino said.

Another focus of the center is atherosclerosis as well as inflammatory and coagulation diseases related to asthma.

Associate director of the Keck Center, **Victoria Ploplis**, will spearhead a fourth project examining the inflammatory relationships in cancer.

Collaborations will continue with Eliot Rosen, now at Indiana University. "Though he is not at Notre Dame any more, Eliot will be joining us on projects. His going to Indiana University will open up more vistas for us," said Castellino.

At press time, Notre Dame's Keck Center was a finalist for another major competitive NIH Program Project grant. Word of that grant is expected in early February.

Celebration and bonhomie permeated McKenna Hall Auditorium, when dozens of scientists and engineers from around the world gathered in September at Notre Dame for Jacek K. Furdyna's 70th birthday.

Testimonials flowed easily from friends and colleagues of the professor of condensed matter physics, whose name at Notre Dame is synonymous with molecular beam epitaxy, the development of the blue laser, and spintronics.

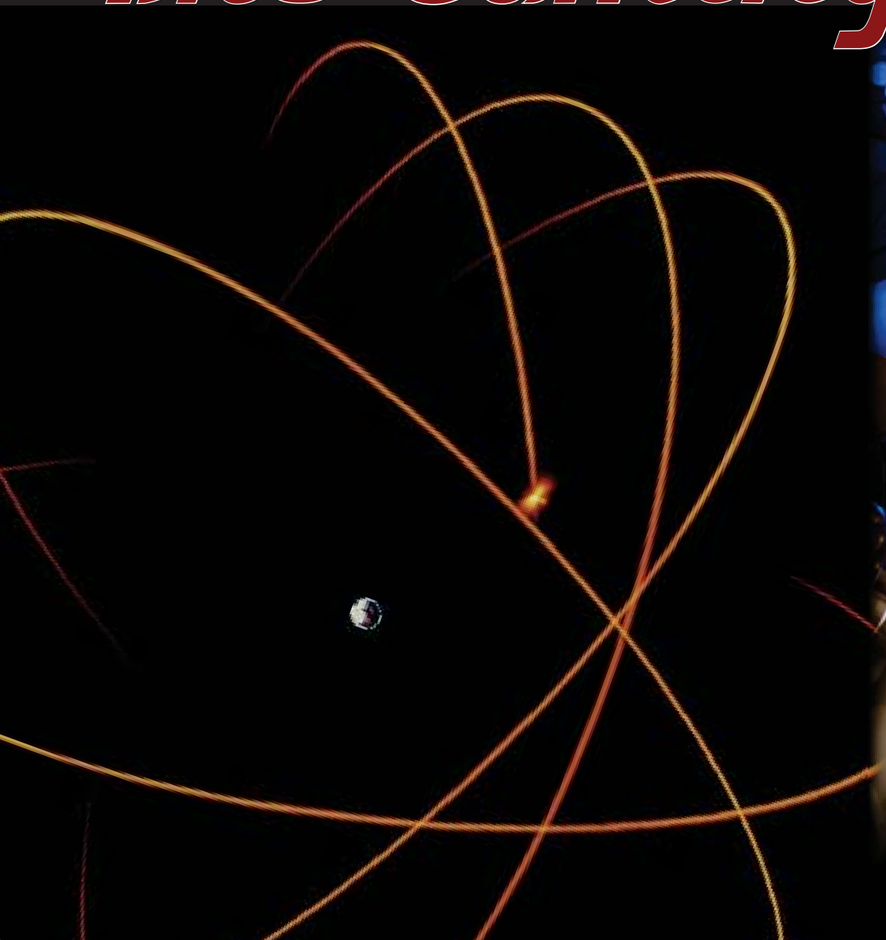
Over the course of 40 years (the last 16 of which have been at Notre Dame), Furdyna, The Aurora and Thomas Marquez Professor of Information Theory and Computer Technology, has put his signature on over 500 published papers within the field of semiconductors and their nanostructures.

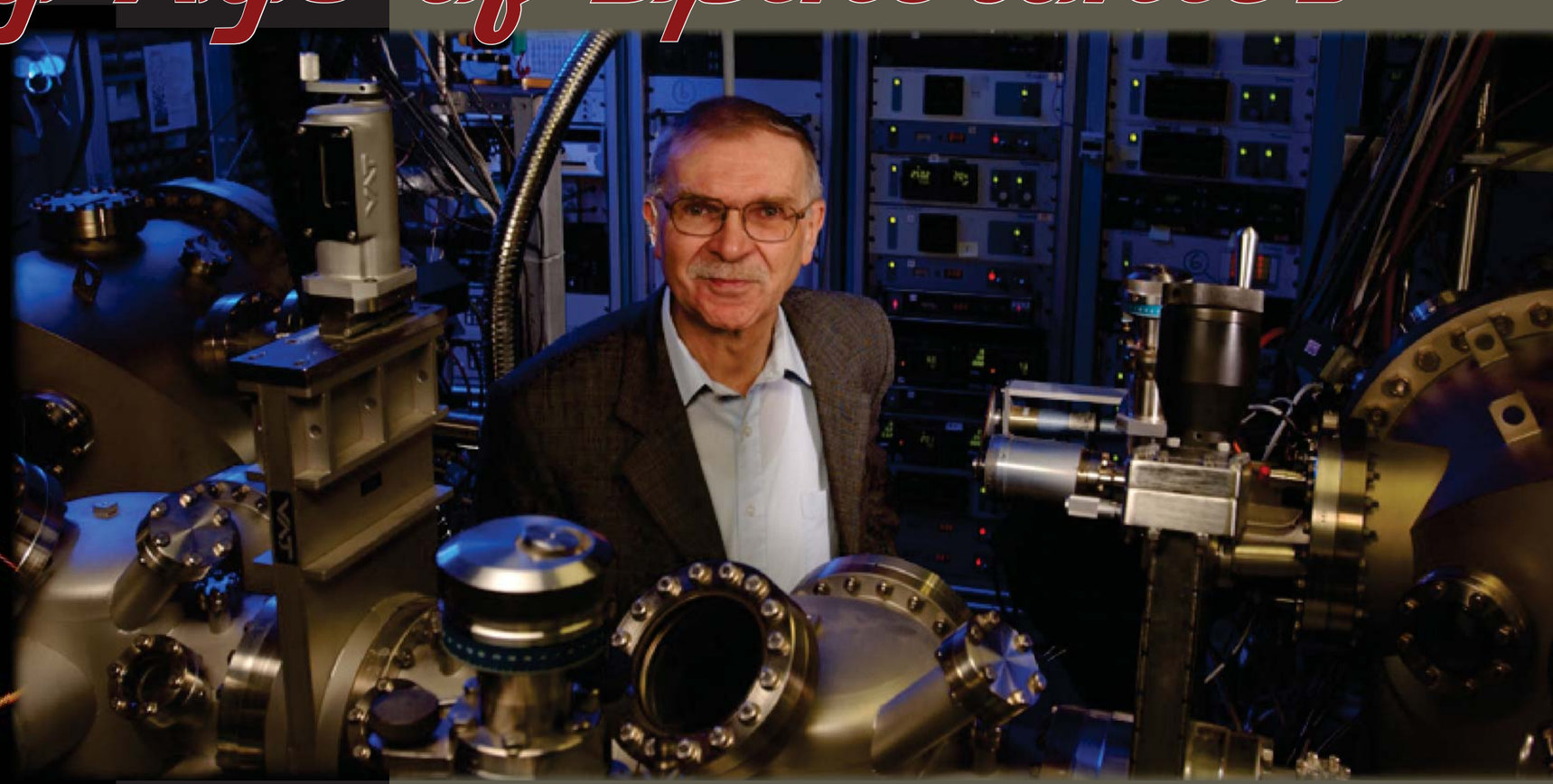
As director of Notre Dame's $2 million molecular beam epitaxy laboratory since 1988, Furdyna has played a key role in research projects involving his Notre Dame colleagues, as well as those at 70 different institutions worldwide.

Aside from all the accolades and good cheer one would expect at the birthday party, a careful listener at the festivities might have also picked up on a sense of excitement that has been building in the realm of semiconductor research for the past 15 years.

Scientific interest in magnetic semiconductors has intensified since the late 1980s because of critical discoveries that promise to usher in the next generation of quantum computers and communication in this century. These discoveries use the spin of the electron in much the same way that the electron's charge properties were harnessed to launch the revolution in communications technology in the 20th century.

The Coming Age of Spintronics





The forthcoming "Age of Spintronics" is at hand, many believe. Or, at the very least, the opportunities that it offers must be looked into and thoroughly researched. If these assessments are right, then spintronics could transform the microelectronics industry, paving the way for new technology that increases the functionality of present-day devices by combining logic, storage, and sensor applications. This next generation of semiconductors will function at higher speeds, with less power, and with the potential for more robust memory functions.

But before the new technology's potential can be realized, the disciples of spintronics will need to produce new materials, new handling and processing techniques, and altered circuit design in order to exploit the electron's spin properties.

Furdyna's early research in magnetic semiconductors puts him in the forefront of this emerging field. As early as 1991, the National Research Council asked him to chair a panel on diluted magnetic semiconductors. That panel brought together giants from both academia and industry: MIT, Harvard, the IBM Corporation, AT&T, Purdue University, Ford Motor Company, and General Motors Research Laboratories.

Just very recently, *Discover* magazine in its January 2004 issue has listed Furdyna's joint project with **Professor Roberto Merlin** of the University of Michigan on spin-entanglement in magnetic semiconductors as one of "100 Top Science Stories of 2003." *Discover* refers to this work as "a giant leap toward quantum computing."

As one of the founding fathers of spintronics, Furdyna foresaw the future of this radical approach to communications technology. He recently discussed with Renaissance his 40-year career as a condensed matter physicist and educator.

Friends and colleagues celebrate Jacek Furdyna's 70th birthday in McKenna Hall

Q: Professor Furdyna, you came to Notre Dame after 20 years at Purdue University. What brought you here?

Furdyna: I was director of the Materials Research Laboratory, a multimillion dollar materials science project at Purdue, when the National Science Foundation decided in 1987 to do away with smaller materials research labs. When I came to Notre Dame, I brought a part of Purdue's Material Research Laboratory activity with me. About the same time that I was leaving Purdue, I also received a rather large grant from the Defense Advanced Research Projects Agency (DARPA). That money, and funding from Notre Dame, allowed me to set up the molecular beam epitaxy laboratory that we now have operating at Notre Dame.

I think it was a wise move to set up this facility, because it acts as a "magnet" for a whole variety of programs. Not many institutions have a multimillion dollar machine that allows you to custom-design materials one atomic layer at a time, and thus to fabricate materials systems with predesigned functions. So, this allowed us to act as a resource and to jump-start many extremely fruitful collaborations.

Q: You also gained fame in 1990 when you developed the first semiconductor blue laser. Could you describe that event?

Furdyna: When the blue laser was a hot item, we were doing really well at Notre Dame. We were very visible then. We used zinc selenide at the time to create the blue laser. Our material was the only game in town until gallium nitride came along. But gallium nitride is still a rather messy (structurally complex) material, so that you can't really make very neat integrated structures with it. Using gallium nitride you can fabricate single-laser units. This by itself is very important, particularly for optical memories such as CDs, because you can "cram" more information on a disc using blue light than you can using the near-infrared lasers that are presently used for that purpose. But if you want to make arrays of these things, gallium nitride is not a suitable material, and it may be that zinc selenide's time may still come. This is what materials science is all about: you need to explore materials on a wide front, look for functionalities, and then invest in what works best.

Q: You have stated that you are most proud of your contributions to the field of magnetic semiconductors. Could you describe these contributions?

Furdyna: An enormous amount of new physics occurs when you bring two disciplines together. Consider the field of semiconductors: there is transistor electronics, the semiconductor chips that you have in your laptop, and the semiconductor lasers that you have in your CD player or laser printer. On the other hand, you have the field of magnetism (in terms of everyday life, think of magnetic tape and magnetic memories in larger computers). Both disciplines are extremely important, but they don't "talk to each other." What we started at Purdue back in the very late 1960s is that we married magnetism and semiconductor physics. We did this by putting magnetic atoms into the body of a semiconductor.

There are certain magnetic atoms that are especially easy to substitute for the nonmagnetic atoms of the semiconductor "host" (like manganese). Consider, for example, the zinc selenide we discussed in connection with the blue laser. We can readily replace a fraction of the zinc with manganese, thus forming a magnetic semiconductor alloy that has both attractive semiconductor (especially optical) and magnetic properties that are governed by the electron spin.

So, we have invested an enormous amount of time and money into developing these magnetic semiconductors. The result is that the physical phenomena that one observes both in electrical and optical properties of these magnetic semiconductors are now determined by the electronic charge, as well as by the spin of the electron.

The opportunities that the presence of spins in semiconductors hold out for both basic science and future applications have now become very important. We have learned what spin does in the context of semiconductivity. Just very recently it has caught on like wildfire, first in Japan. This came about when it was discovered that by substituting manganese for gallium in gallium arsenide (a very important semiconductor, the heart of many semiconductor devices) and forming a gallium manganese arsenide alloy, one obtains a *ferromagnet*—and ferromagnets constitute the heart of magnetic devices. While this discovery was made in Japan, we at Notre Dame were the first in the United States to produce this system (again, using our molecular beam epitaxy method, with a bit of tweaking). We are now fairly well recognized among the leaders in this new ferromagnetic semiconductor field.

Q: So what you are doing is to go beyond the electron's charge and utilize its spin state as well?

Furdyna: Yes. Traditional electronics is based entirely on the electron charge, and yet it can be shown that the electron's spin state is much more long-lived (robust) than its charge state.

The electron does not "forget" its spin so easily when it travels through a semiconductor crystal, even if it scatters back and forth thousands of times. So people are speculating that "spintronics"—short for spin-based electronics—may play an important role in memories. That in turn may open possibilities of new formats for computing: what is now referred to as quantum computing. Think of how we have used the electron's charge state to (without exaggerating) change civilization. Harnessing the electron spin may bring similar—or even greater—rewards.

Q: How close are we to reaching that goal?

Furdyna: My guess is that we have another 10 years down the road before we reach our goal in this area. But let me comment here that a scientist tends to be a bit of a pessimist when making predictions—that is because he or she knows all the difficulties that must be overcome. This self-critical attitude often shortchanges how fast things develop. I had this experience with the blue laser. When we were developing it, I thought it would take five years to resolve the problem of introducing positive charges (so-called holes) in the semiconductor structure because of some inherent difficulties in zinc selenide. But I greatly underestimated scientific ingenuity—the solution came in just two years.

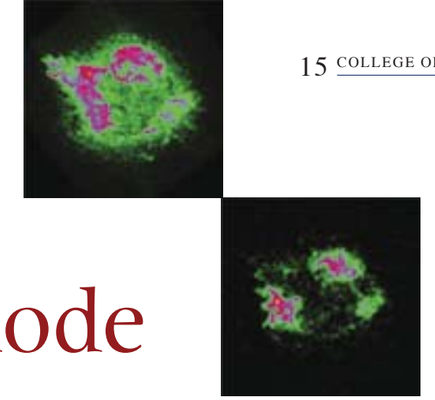
Q: What obstacles lie ahead for spintronics?

Furdyna: There are two major challenges. The ferromagnetism in semiconductors now only occurs at low temperatures. So, the first challenge is to make semiconductors ferromagnetic at room temperature. We are inching up in this category. We can now make materials where ferromagnetism occurs around 170 degrees kelvin (about 100 degrees below zero degrees Celsius). But note that this is already well above the temperature of liquid nitrogen, so one can contemplate liquid-nitrogen-cooled devices even as we speak. And the second is a challenge more in the engineering area—how to package spin-dependent materials into viable device structures. Thus far we are still at a stage where we are developing a materials science of these new materials.

We Are Stardust: Exploring the Mysteries of the Cosmos

Ever the showman, Carl Sagan came into our homes and touched us with the poetry of the cosmos. “We are made of stardust,” he would say with boyish wonder, as he revealed our true essence.

We are indeed children of stars and supernovae explosions, those violent eruptions in which the heavier elements on the Periodic Table were made. Physicists want to dig deeper and will not be content until they understand the precise mechanisms by which the elements were created within these blast furnaces deep in space.



Pictured are two X-ray photos of supernovae Cassiopia A, which exploded about 350 years ago. At top, the image Casa-Si shows the silicon distribution in the ejected material. At bottom, the image Casa-Fe shows the iron distribution. Both elements are formed in nucleosynthesis during the explosion.

How do supernovae explode and were they really the sites where our HEAVY elements were made?

This is just one mystery they want to solve. Others include: What triggers thermonuclear explosions of binary star systems? How do supernovae explode and were they really the sites where our heavy elements were made? “At present, there is no self-consistent model for a supernovae explosion,” says nuclear astrophysicist **Michael C. F. Wiescher**, who is Freimann Professor of Physics at Notre Dame.

In order to resolve these issues, Wiescher and his fellow physicists at the Joint Institute for Nuclear Astrophysics (JINA) are beginning an ambitious campaign to understand the underlying processes of nucleosynthesis in stars like our sun, as well as in supernova events. It is a huge effort that will challenge both physicists and supercomputers.

Wiescher is leading a collaborative effort involving Notre Dame, Michigan State University, and the University of Chicago that will recreate stellar processes using particle accelerators at the Institute for Structure and Nuclear Astrophysics (ISNAP) at Notre Dame, the National Superconducting Cyclotron Laboratory (NSCL) at Michigan State, and the Argonne National Laboratory, a DOE facility near Chicago.

JINA crossed a critical threshold in 2003 when the National Science Foundation (NSF) awarded $10 million for the project, which will bring together two distinct communities—astrophysics and nuclear physics—in a venture that will continue through this decade and beyond.

“Today, no university research group can do everything alone. Our projects are too ambitious and expensive,” Wiescher said. “So, the NSF is establishing frontier centers where, through cooperative efforts, new discoveries will emerge.”

The JINA collaboration, now entering its fifth year of conceptual existence, is something of a test case for the Department of Energy and the NSF to show how collaborative systems might work in the future.

JINA has already brought international teams of scientists from the United States and 10 other countries to the Notre Dame campus to use the university’s three accelerators. In 2003 alone scientists came from Brazil, Bulgaria, Canada, Germany, Hungary, India, Mexico, Russia, Turkey, and the United Kingdom to conduct research projects using the Notre Dame accelerators.

Accelerator experiments allow researchers to simulate processes that could otherwise only take place deep inside of a star. They can be slow processes, which take billions of years at 15 million degree temperatures in the core of stars like our sun, or they can be rapid processes, which take less than a thousandth of a second at 15 billion degree temperatures inside exploding supernovae.

The measurements made by physicists seek to unravel the nuclear processes that control the evolution and lifetimes of stars and the processes that drive the explosion of novae and supernovae.

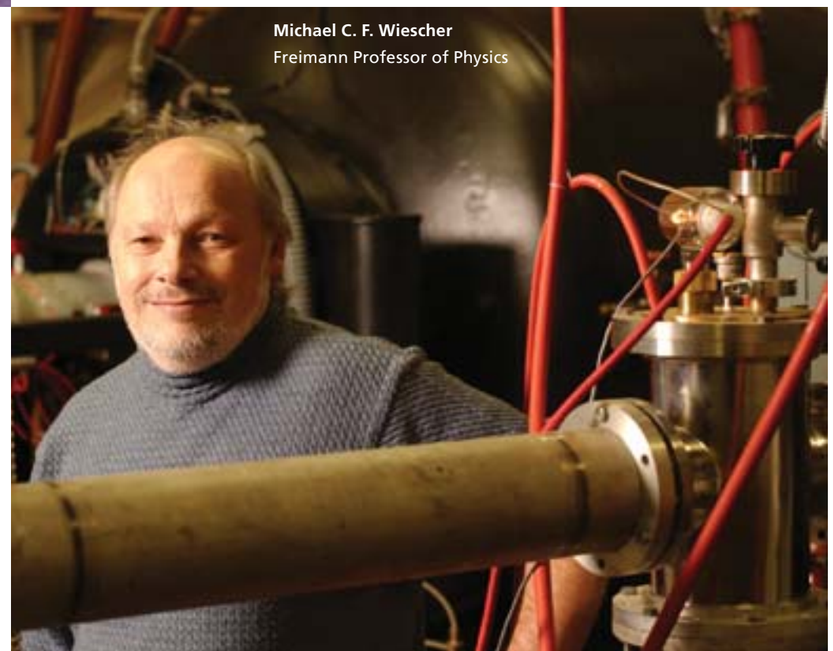
JINA has formed new collaborations between theorists at Notre Dame and the University of Arizona, the University of Chicago, and the University of California to develop new models that take into account the influences of a rapidly changing environment when a star collapses or erupts. Within this collaboration a new generation of theoretical models are being designed that will enable supercomputers to simulate what happens, for instance, when an incredibly dense neutron star sucks away the outer atmosphere of a regular companion star that had the misfortune of invading the neutron’s star space.

Gigantic thermonuclear explosions from this transfer of matter produce strong X-ray radiation bursts that have been observed by space-based observatories like the Rossi X-ray Timing Explorer or Chandra X-ray Observatory.

In the future, JINA will play an important role in designing an experimental program in nuclear astrophysics at the Rare Isotope Accelerator (RIA), a proposed $900 million facility that will explore radioactive nuclei and the nature of nucleonic matter at the limits of stability. Two JINA principals, Michigan State University and Argonne National Laboratory, are competing to become the future site of RIA.

For another future project, the National Underground Science and Engineering Laboratory (NUSEL), the JINA collaboration will participate in the design of a high-intensity accelerator laboratory. This lab will be located more than 3,000 feet underground in order to shield it from cosmic radiation and therefore improve the sensitivity of its measurements by orders of magnitude compared to what is possible using the laboratories available today.

As events unfold, Notre Dame and JINA will have the opportunity to play a role in answering the mysteries of the origin of the elements. It wouldn’t be surprising if somewhere in the cosmos, Carl Sagan is still asking those same questions.



Michael C. F. Wiescher
Freimann Professor of Physics

Andrew J. Sommese
Vincent J. Duncan and Annamarie Micus Duncan
Professor of Mathematics

Solving Mechanical Problems One Equation at a Time

A long robotic arm featuring Canada's red maple leaf is the star performer of every IMAX movie ever filmed from our space shuttles.

Gleaming white against the backdrop of our blue–green Earth, the mechanical arm swings, rotates, and turns satellite payloads with a loving touch that only a mother could duplicate.

Yet we know it is not a mother's instinct, but mathematics, that gives robotic arms their precise and delicate movement.

Behind the seemingly effortless movement of these steel arms lies the work of complicated mathematical equations. In fact, mathematics makes possible the function of many of the mechanical devices that pervade modern life.

"This collaboration is not about just solving specific problems, but creating a whole technology for solving problems of this sort."

Charles Wampler

"James Watt, of steam engine fame, said his greatest accomplishment was finding a way to make four hinged bars give him almost a straight line," says **Andrew J. Sommese**, Vincent J. Duncan and Annamarie Micus Duncan Professor of Mathematics at the University of Notre Dame. Watt's straight-line mechanism, patented in 1874, avoided friction and wear in guiding the steam engine's piston, a crucial step at the dawning of the industrial revolution.

From Watt's engine to the space shuttle robot, the motion of any collection of rigid links connected by hinged joints can be described using polynomials, a certain type of mathematical expression (see box).

Polynomials are Sommese's forte. With his collaborators **Jan Verschelde** and **Charles Wampler**, Sommese has been developing a series of ever more powerful algorithms to solve tough polynomial problems that mechanical engineers face when designing robots and other machinery.

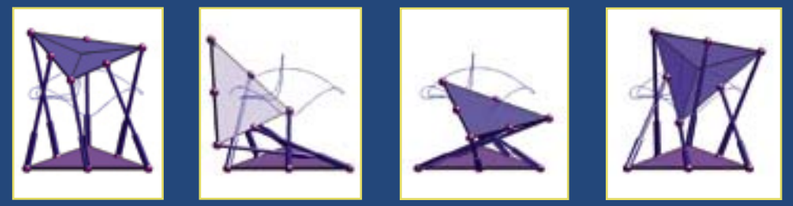
"Predicting the motion of a machine before it is built is relatively easy," says Wampler, a mechanical engineer with General Motors Research Laboratories. "It's when you try to create a machine with special motion characteristics that the game gets really interesting."

This leads to polynomial systems with dozens of variables and equations. What's more, such systems typically don't have just one solution. In fact, they can have billions and billions of solutions. According to Sommese, "there could be so many solutions no computer on earth could ever find them all."

A polynomial is any mathematical expression whose unknowns are combined with just the operations of addition, subtraction, and multiplication. The equation of a circle, $x^2 + y^2 = 1$, is an example. (Recall that x^2 is just shorthand for *x times x*.)

The simplest type of mechanism, a single bar on a hinge joint, has circular motion—think of the bob on a pendulum clock or the tip of a rotating propeller.

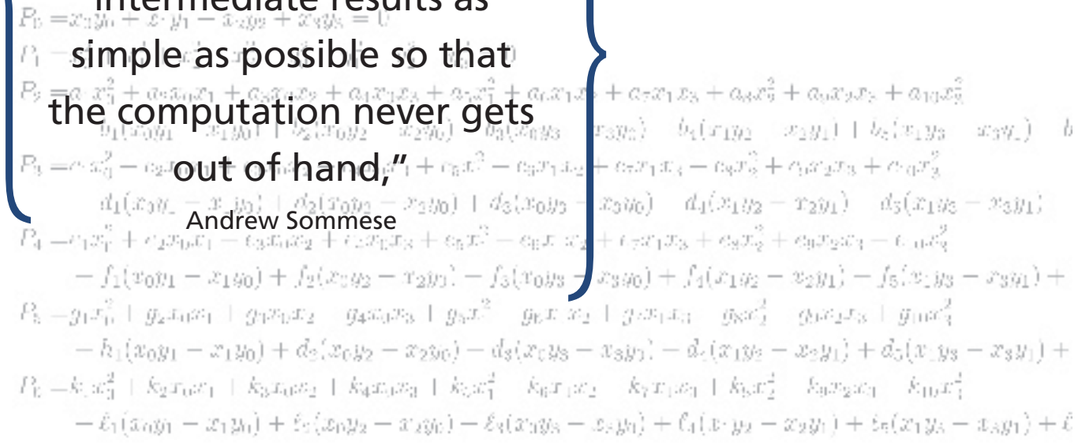
So far, that may sound pretty simple, but add a few more links and joints and the situation quickly becomes complicated. So much so that even with today's super-fast computers certain problems concerning the design of robots with just four or five links can push the limits of current computational algorithms.



This mechanism consists of a moving upper triangle supported over a stationary lower triangle by six telescoping struts, with ball joints where the struts meet the triangles. A general mechanism of this type is a rigid structure when the strut lengths are held constant, but due to a special arrangement of equilateral triangles, this one moves along the path illustrated. The constraint imposed by each strut can be written as a polynomial, and the motion can be found by simultaneously solving the entire set of polynomials.

"Our method numerically examines a few equations at a time, keeping the intermediate results as simple as possible so that the computation never gets out of hand,"

Andrew Sommese



Fortunately, the problems relating to robotic systems tend to be special and have far fewer solutions than a mathematician might expect. The trouble is, even the best computer algorithms have trouble figuring out what is special about the equations, so a tremendous number of possibilities have to be explored to find the solutions that count.

"Back in 1992, we solved a mechanism design problem that had stumped engineers for over 70 years. But the computer had to check more than 400,000 possibilities just to find 1,442 answers," reports Sommese. (The paper detailing that solution, written with Wampler and fellow GMer **Alexander Morgan**, was published in the ASME *Journal of Mechanical Design*.) "It was pretty cool that we could do it, but the inefficiency of the approach limited further progress."

Now Sommese, Verschelde, and Wampler have scored a breakthrough in efficiency. They recently proposed a new equation-by-equation approach. It may open up a way to find solutions of polynomial systems in engineering and science that up until now were far beyond the range of even today's fastest supercomputers.

Sitting in his second floor office in Hurley Hall on campus, Sommese describes the importance of their approach. "Our method numerically examines a few equations at a time, keeping the intermediate results as simple as possible so that the computation never gets out of hand," Sommese says. "This now opens the door to resolving polynomial problems with many, many equations." Software engineers will soon be able to incorporate these methods into their programs, so computers can achieve a sophisticated answer to a design problem.

Mathematicians everywhere have been working on finding example solutions to problems using polynomials. Sommese, Verschelde, and Wampler took a different approach to the conundrums. An important feature of the approach is that it is purely numerical. "We don't alter the original equations; we just keep track of their numerical properties," says Sommese.

That's a big advantage compared to competing approaches using computer algebra to combine equations. These can founder when intermediate results become too voluminous for the computer to handle.

"Also, we use probabilistic methods," says Sommese. "Suppose some polynomials describe a curlicue curve in space and some others describe a wavy surface. If you can find all the points where the curlicue meets a random plane and all the points where the wavy surface meets a random line, then it turns out to be rather easy to find all the points where the curlicue intersects the wavy surface."

"Instead of curves and surfaces in our familiar three-dimensional space, try imagining shapes in 10 or 20 dimensions and you have a hint of the objects we deal with," suggests Sommese with a smile.

"If that blows your mind, don't worry," reassures Wampler. "Nobody can really visualize such things, but our computer algorithms can keep track of them all the same."

The route to this breakthrough started in the middle 1980s for Sommese, who has specialized in theoretical algebraic geometry through much of his career at Notre Dame. "In the 1980s I became interested in numerical computation. I still use my background in algebraic geometry to guide me because it studies the deep structure of polynomials that we use to get numerical solutions," he said.

The first step toward the recent breakthrough came in 1995, when Sommese and Wampler announced the birth of "Numerical Algebraic Geometry" at a SIAM (Society for Industrial and Applied Mathematics) conference in Park City, Utah. They proposed the idea of numerically slicing the solution sets with linear subspaces to reduce higher-dimensional components down to just a few representative points.

But it wasn't until 1999 that Sommese and Verschelde, a computer scientist at the University of Illinois, Chicago, broke ground on the construction of practical algorithms in the paper, "Numerical Homotopies to Compute Generic Points on Positive Dimensional Algebraic Sets," which appeared in the *Journal of Complexity.*

After that, the threesome pitched in together and refined their methods in a half-dozen articles that appeared in various journals, including the SIAM *Journal on Numerical Analysis* in 2001 and 2002, and articles just accepted for publication in the ASME *Journal of Mechanical Design* and in the SIAM *Journal on Numerical Analysis.*

This breakthrough approach will likely find its way into mechanical engineering courses and eventually into industry, where robots and machines move in exquisite synchrony. It may change the way university professors in mechanical engineering conduct design studies. "Eventually it will be incorporated into the software design packages that industry used to design robots and other mechanisms," Wampler said.

What's next? The team is now addressing what is termed "systems of polynomials with parameters." "Suppose you have a platform robot and engineers want to configure it to move in way that is more productive. That sort of question will become amenable to our methods," Sommese said.

A general-purpose robot can move in almost any way an engineer may wish, but at a price. Having more motors than necessary often means the device uses extra energy and has more ways to break down. A simpler machine might do the job much better, if you can find one that gives the right kind of motion.

Wampler sums up the work this way: "This collaboration is not about just solving specific problems, but creating a whole technology for solving problems of this sort."

Curing the Elephantitis Syndrome in Haiti

Playing in the streets amid the squalor of his hometown of Léogâne, Haiti, a young **Jean Marc Brissau** was inured to the oppressive odor of human waste and the wretched living conditions around him. Fear came with the appearance of a disfigured man that Jean Marc and his playmates called "the monster." The sight of this man, Maurice, shambling his grotesque body through the streets of Léogâne sent Jean Marc and his friends fleeing in all directions.

Only when virtually all Haitians are informed about LF and its cure will the transmission cycle be broken.
—Rev. Thomas Streit, C.S.C.

Léogâne was—and still is—one of the world's hot spots for lymphatic filariasis (LF), a parasitic disease that, if left untreated, turns a normal leg into an elephantine mass of flesh and causes a male scrotum to balloon to grotesque proportions. Once bodily fluids accumulate and swell the arms, legs, breasts, and genitals, LF has advanced into elephantiasis. Eventually the skin thickens to resemble the hide of an elephant.

Unlike other victims who retreat into a world of self-imposed isolation, Maurice had reached that point of despair where he was numb to the pain of ostracism and deaf to the jeers and taunts from villagers. To uneducated Haitians, Maurice was haunted by a voodoo curse.

But the cruelest joke of all was on those same villagers, for they were unaware that they too probably carried the same "curse"—a microscopic worm called *Wuchereria bancrofti*. Transmitted by a *Culex* mosquito, the filarial worm can fester inside the body for six, seven, or eight years before the first signs of LF appear.

For Maurice, the progression from LF to elephantiasis had all but ruined his chances of a normal life. The open sores on the man's legs oozed fluid and insects flew to the sores to lay their eggs in the unkempt folds of the skin. "The poor fellow had both legs affected as well as his scrotum," said **Rev. Thomas Streit, C.S.C.**, a Notre Dame priest–biologist who, for the past 10 years, has been working among impoverished Haitians as part of Notre Dame's Haiti Program.

Compassion was in abundance, but money was scarce in 1994, when Streit left a certain career as a biology research scientist at Notre Dame and began working in Léogâne under the auspices of the federal Centers for Disease Control and Prevention but still retaining the position of research assistant professor at the University. Léogâne residents, like most of Haiti's 8.3 million, were accustomed to well-fed whites entering their black world to preach the gospel and spread their charity.

Two organizations in particular, the Christian Brothers School and the Hôpital Ste. Croix, run by the Episcopal Church, have done much to improve the lives of thousands in Léogâne. But foreigners can only do so much to change entrenched social behavior with reason, education, and science. Be it Haiti or Harlem or Hoboken, biology doesn't stand a chance when suspicion and illiteracy hold sway.

Streit knew that if he was to make any progress against LF, he needed to recruit and train young, modern Haitians who would not be bogged down by ignorance and cultural obstacles, like voodooism. "We would hire kids off the street for a dollar a day," he said. Streit placed his hopes on God and the Haitian young.

At age 17 Jean Marc Brissau came to the Haiti Program to look for a job. Startled when the young Brissau started speaking to him in fluent English, Streit seized his opportunity. "I hired him the next day," he said.

Brissau was smart. Unlike so many other young Haitians, he had the good fortune to be educated at the Christian Brothers School. When he appeared at the Notre Dame center to get a job, Brissau had no inkling that he was going to become swept up in a history-making endeavor to rid his town and Haiti of LF for the first time in four centuries. Today he is an administrator of the Notre Dame Haiti Program, which was infused with a $5.2 million grant from the Bill & Melinda Gates Foundation in 1999.

Nicholas Orelus is slightly older than Brissau and, like Brissau, had studied at the Christian Brothers School. Now 27 and an entomologist, he is in charge of Notre Dame's laboratory.

Both Orelus and Brissau have an opportunity to change Haiti forever. Their education and their eagerness to improve the lives of their fellow Haitians make them perfect candidates for the job. "They both know more about filariasis than most people in the world," Streit said.

The problem lies in transferring that knowledge to Haitians living in remote and nearly inaccessible areas of Haiti. Only when virtually all Haitians are informed about LF and its cure will the transmission cycle be broken. And that, Orelus said, "takes a lot of education."

Michele Sexton, the manager of the Notre Dame Haiti Program, describes how groups of Haitian health workers

will climb into the backs of pickup trucks and venture into the Haitian outback, using every tool they can muster to spread the word about LF. “These guys in the pickup trucks will use sound systems and megaphones to blare out the message,” Sexton said. “They will go out in the middle of nowhere, put up sheets for a screen, and hook up a movie projector to a car battery to tell the story.”

Villagers will surround the truck 50 or 100 at a time, just for the entertainment value. The health workers then try to drive the message home with catchy chants and songs to make an impression. “Once we hired a comedian who told jokes about guys with affected genitals,” Streit said. The people liked and remembered that.

Wiping out LF is eminently achievable, but only if virtually everybody is reached, Streit notes. Luckily LF’s mosquito-worm-man transmission cycle has distinct weaknesses that make its eradication entirely possible. It’s been done before in developed countries in ways that seemed almost effortless, such as in the United States in the 1900s. “Simple things like sanitation and screen windows probably eliminated LF in Charleston, New Orleans, and parts of Florida,” Streit said.

The *Culex* mosquito breeds in water polluted by human waste, explains Orelus. So, a new design for a toilet in which mosquitoes can’t breed would go a long way to stop the cycle dead in its tracks.

Another proven technology is the bed net. Bed nets impregnated with bug repellent will keep mosquitoes away during the nighttime hours when the *Culex* mosquito feeds. It is at night when the larval forms (microfilariae) of the worms inside the body swim in the human bloodstream and congregate at the skin’s surface.

It is as if they are greeting their bloodsucking co-conspirators for a nocturnal rendezvous. And that, said Streit, is exactly how the two species evolved together in Haiti since the first parasitic worms were likely carried from Africa during the slave-trading days. This is the sophisticated arrangement these parasites have created with humans for centuries, dating back to 4,000 B.C. In time, humans will have the last laugh.

Dog heartworm medication (albendazole) developed 20 years ago and now approved for human use is at the forefront of the attack against LF. However, all current drugs have one major drawback: they do not kill adult worms. This will make the elimination of LF more challenging, until a more advanced drug can be developed.

Drugmaker GlaxoSmithKline is donating its entire supply of albendazole as its part in a far-flung effort called The Global Alliance to Eliminate Lymphatic Filariasis. The drug regime recommended by the Alliance involves delivering a single dose of either diethylcarbamazine (DEC), or ivermectin. A two-drug treatment (choosing among albendazole, DEC, and ivermectin, administered concurrently) can be more effective than giving one drug alone. “Albendazole is very effective,” Streit said. “It kills juvenile worms by the millions within hours.” Furthermore, an infected person needs only one concentrated treatment per year to interrupt the transmission cycle.

Despite the effectiveness of the drugs, a huge public relations task faces health workers like Brissau and Orelus. People whose bloodstreams are loaded with tiny dead juvenile worms can get violently sick in hours as the medication performs its job. One case involved a little girl whose worm count reached 278 in just a single drop of her blood.

Streit described what happened next: “One hour after taking the drug, she started getting sick. So many worms died in her that she had this huge reaction. For a couple of days she was laid out flat with headache, sweating, vomiting, and diarrhea while the body was ridding itself of millions of dead worms.” He added, “the people who most need the medicine get the sickest.”

The trouble is that only about 9 percent of the 60 percent of those infected in Léogâne show some outward symptom of LF. For instance, one healthy Haitian man, the best player on the Haitian national soccer team, was able to lead his team to many victories while harboring loads of juvenile worms in his bloodstream.

Convincing uneducated Haitians to become violently ill when they feel fine underlies the difficulty of knocking down LF. But, the Notre Dame Haiti Program and other Global

Alliance members in Léogâne have made so much progress in the last 10 years that now 80 percent of the population—124,000 people out of a community of 150,000—are receiving annual medication for LF.

Finding a way to get worm medication to Haiti’s remote hinterlands was problematic. The solution? Fortify the Haitian salt supply with the medication along with diet supplements like iodine. “All the medications and supplements are heat stable, so when people use the salt to cook with, they remain active,” Streit said. The fortified salt is much like a booster shot. “The dosage is so low that people will not have side effects,” Streit said. Iodine alone will raise the IQ of a Haitian child by 10 points, Streit added.

The rub is that Haitians use salt produced cheaply from the sea. So fortifying the salt must not add to its cost.

Science has done its part to make serious inroads into ridding Haiti and some 80 other countries of LF. “What we really need is administrative and logistical help to get the job done,” Streit said. In the meantime, a steady stream of Notre Dame students continue to help in Haiti, knowing that they are making substantial headway.

Notre Dame senior biology major Michael Porco, of Wallkill, New York, will make a trip from South Bend to Haiti this summer for a one-year stay.

“Mike is a good representation of the kind of student who goes to Haiti. He was highly recommended by his professors. He is a superior student who clearly could go to any medical school he wants,” Streit said. “This unmatched experience will give Mike not just the tools to be a great physician, but the background to work toward a greater good, for world public health.”

In time, Porco will get that medical license. Orelus will go on to study in England. And Brissau? He plans on a career in law in Haiti. But first, they know they have a job to do. A historic job.

Last fall, University of Notre Dame biologists hosted Melinda Gates and members of the Bill & Melinda Gates Foundation in Haiti to view firsthand the progress made in Haiti resulting from the Foundation’s $5.2 million grant awarded Notre Dame in 1999.

Gates and Patty Stonesifer, president of the Foundation, met with Father Tom Streit, C.S.C., Ph.D., associate professor of biology, and program manager Michele Sexton.

The group had a chance to visit the laboratory in Léogâne, Haiti in addition to meeting with Haitians affected by lymphatic filariaisis and those working on the project to eliminate it.

Melinda Gates meets with Haitian officials Dr. Madsen Beaude Rochars, Director Programme Filariose and Joseph Dorvil, Administrator, Planification and Development.
Photo by Wesly Pierre

Antibiotics That Resist Bacterial Protective Armor

Bacteria, those clever single-cell creatures that are the dominant life forms on earth, have been busy altering their structures to make themselves invisible to our immune systems and our cache of antibiotics.

This situation received front-page coverage in 2002 when a particular strain of Staphylococcus aureus, called "hospital staph," became resistant to the antibiotic of last resort, vancomycin.

Members of the Mobashery computational and organic chemistry group are, from left to right, Samy Meroueh, Shahriar Mobashery, Jennifer Zaher and Dugan Hesek.

"We designed and developed a molecule that binds smack in the middle of the A Site. By binding to that location it prevents the normal physiological function of the ribosome."
—Shahriar Mobashery

Genes that make bacteria resistant to antibiotics like vancomycin or tetracycline can spread quickly through bacterial populations. Because only one new type of antibiotic has been introduced to clinics since the 1970s, scientists throughout the world are urgently working to develop innovative classes of antibiotics that will kill bacteria of all kinds.

Among them is Notre Dame bio-organic chemist **Shahriar Mobashery**. Mobashery reports that he and his team of researchers are making progress on a synthetic molecule that kills bacteria by going straight to the heart of the bacteria's protein-making machinery, the ribosome. "Every living organism—plants, fungi, bacteria, humans—has ribosomes," said Mobashery, the Navari Family Professor of Chemistry in Life Sciences.

How the ribosome takes its orders from our genes to produce proteins is a very elaborate process that Mobashery calls "one of the marvels of the natural world." Evolution has brought about a process called translation, which takes the genetic information and produces proteins.

With high-resolution pictures of the ribosome now available, researchers can see its structure clearly. "The components are like gears in a car. Everything works beautifully to make protein synthesis possible," Mobashery said.

Seeing this machinery in an amount of detail never before possible has given scientists like Mobashery an opportunity to develop a new class of antibiotics. "We used this structural information to create a molecule that would bind to a very specific place on the ribosome, called the acyl transfer site," Mobashery said. The "A Site," as it is known, is the precise place where amino acids are added, one at a time, to the nascent protein.

Mobashery's concept for a new antibiotic is simple: go straight to the heart of this machinery and knock it out. "We designed and developed a molecule that binds smack in the middle of the A Site," he said. "By binding to that location it prevents the normal physiological function of the ribosome."

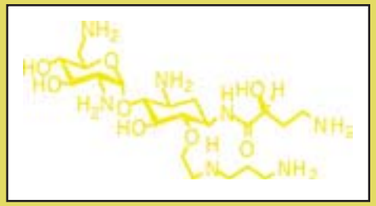
When the molecule disrupts the ribosome's protein-making machinery, the bacteria die. "Our molecule works. It is nontoxic to humans," Mobashery said.

His molecule, yet to be named, has an excellent broad-spectrum level of activity. It kills a full range of bacteria, including Gram-positive and Gram-negative bacteria. "We are very excited about the potential of our molecule," he said.

Having already proved its capabilities, Mobashery and his Notre Dame colleagues are working on ways to simplify the synthesis of this compound. Currently, 14 steps are required to synthesize it. This time-consuming process has prevented the team from making it in quantities that pharmaceutical companies would like.

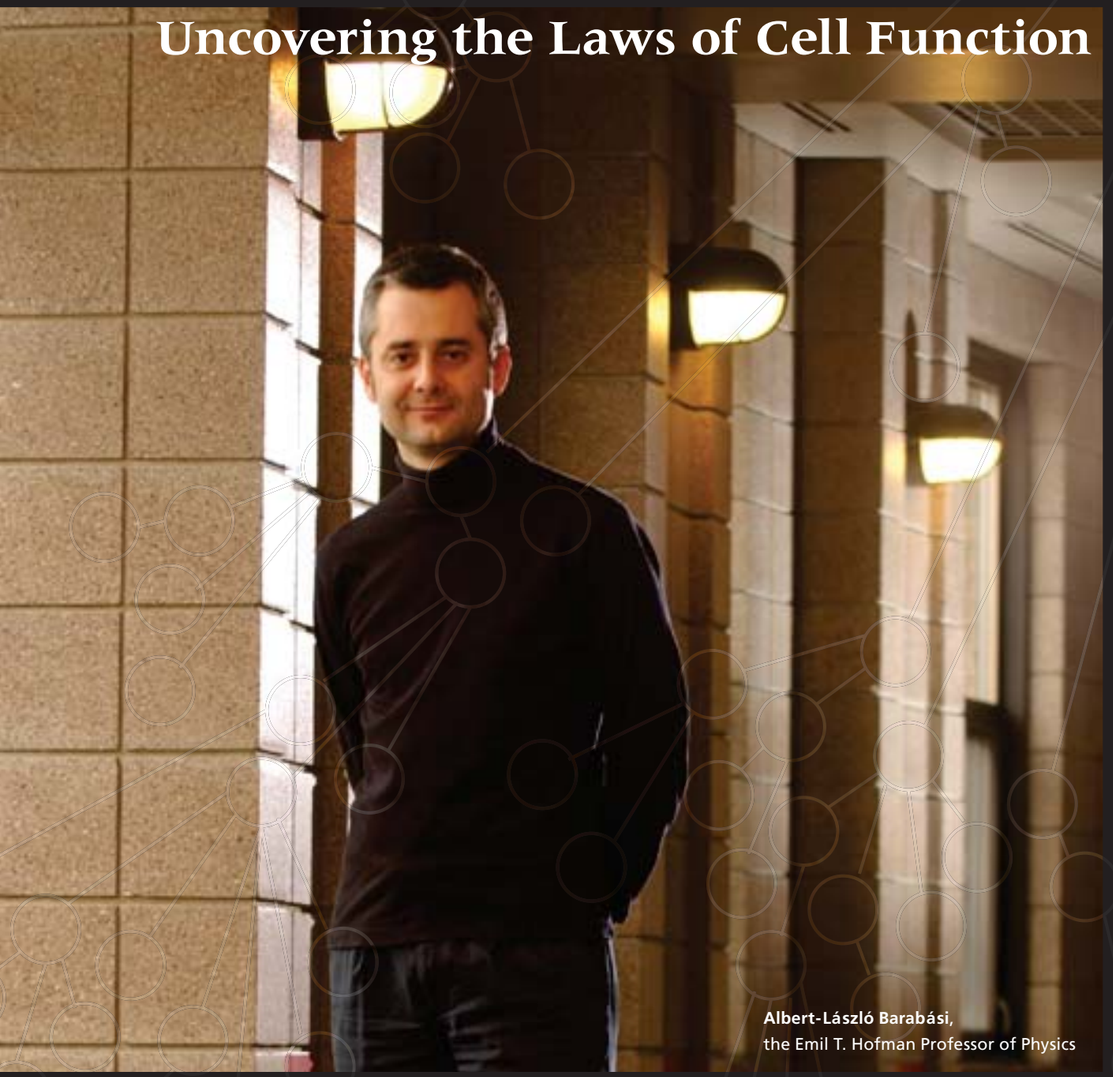
The Notre Dame team has a way in mind to expedite the synthesis of their protein. When they can make multiple grams of their molecule, they will start testing it in animal experiments. Drug companies who have expressed interest in Mobashery's molecule are eager to take these experiments to the next level.

Ingenious bacteria have found ways to make themselves multiresistant to various antibiotics. But now, the stakes have been raised in this race against Earth's oldest living creatures.



Order Out of Chaos

Uncovering the Laws of Cell Function



Albert-László Barabási,
the Emil T. Hofman Professor of Physics

Is there a basic recurring code hidden within the complexities of the human cell and awaiting discovery by a modern-day Isaac Newton?

Ever since Watson and Crick revealed the three-dimensional structure of DNA, scientists have been trying to establish some sense of order out of complex and seemingly random cellular processes in the same way that Newton boiled down the motion of the planets in the heavens into a few simple laws of gravitation.

Five decades have passed since Watson and Crick's seminal announcement, yet the search for some topological order, connectivity, and mapped network still has yet to produce a coherent body of laws that would simplify the tangle of molecular interactions in the cell in the same way that Newton codified the laws of gravity some 400 years ago.

"This is a huge challenge that will probably be around for the next 20 years," remarked **Albert-László Barabási**, the Emil T. Hofman Professor of Physics at Notre Dame, who is taking up biology's ultimate quest.

Having already achieved fame for his book *Linked: The New Science of Networks* and his study of scale-free networks as the underlying patterns of the Internet, Barabási has taken aim at revealing the same type of network operating within the cell.

To a great extent, the chemical inventory of the cell was already laid out, piece by piece, through the completion of the Human Genome Project. But, the day that molecular biologists completed the long-sought task of identifying all of our 30,000 or so genes was also the day that they entered a much more complicated phase of making sense out of the myriad interactions of genes, their protein progeny, and all of the molecules, nucleic acids, and metabolites that work in harmony to keep the body's machinery working smoothly. Thus, we have entered the era of "functional genomics" or "systems biology."

"It is as if somebody disassembled your car into tiny, tiny pieces on your front lawn. Even though you understand the basic principles of how your car operates, could you still reassemble your car and return it to its original condition?" Barabási asked. "That is where we are at right now."

Scientists are on the edge of a frontier—to make sense of the architecture of the cell and to determine how thousands of biochemical reactions function to turn many different genes on and off.

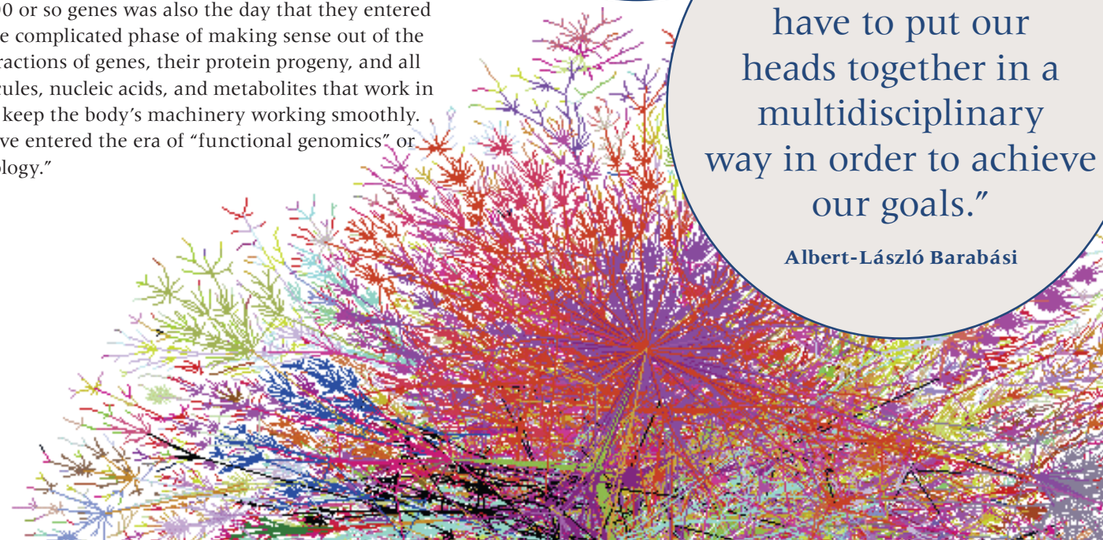
It is clear that the cell is more than the sum of its pieces. The branch of physics that Barabási and his colleagues are working on, called "emerging phenomena," does not look at individual pieces in some central design but at a sum of events that, taken at face value, are seemingly unconnected.

One analogy to this approach is the direction of human society as a whole at any given moment. "Everyone makes decisions based on what is best for him or her. Nobody cares about the whole structure of human society. But when

"It's very clear that this is not just a biologist's or a physicist's dream.

We realize that we have to put our heads together in a multidisciplinary way in order to achieve our goals."

Albert-László Barabási



> "This is a huge challenge that will probably be around for the next 20 years."
>
> **Albert-László Barabási**

all of these distributed decisions are taken together, we have created something bigger than ourselves," Barabási remarked.

In many respects, the cell is very much like the nation's electric power grid. The failure of the grid, as exemplified by the "Great Northeastern Blackout of 2003," parallels what can take place in the cell when its own network of checks and balances goes awry. "If the Internet is overloaded, it can avoid this kind of cascading failure by simply dropping messages," Barabási said. But, when electric power is produced, it must flow out. If there is too much flow in the system, a series of failures is bound to happen.

The same is true for the cell when something goes wrong inside. Cells will overgenerate one chemical. This in turn starts to affect other chemicals. "When one cell overmultiplies itself, it creates havoc. We have genes, like the p53 gene, that are supposed to be monitoring the genome all the time and making sure that all the copying is taking place in order. If something is wrong, the p53 gene is supposed to kill the cell. When there is a cascading failure in the body's chemistry, the result is cancer," Barabási said.

After having studied the topology of cellular networks—or how chemicals and genes react with other chemicals—Barabási and his crew of researchers are ready to tackle the enormous question of how these seemingly incomprehensible processes within the cell might be interpreted as patterns that could become the 21st-century equivalent of Newton's laws of motion.

The Barabási group has already uncovered some intriguing commonalities that indicate they might be on the right track in finding the cell's structural network.

Suppose Chicago O'Hare Airport shuts down even for one day. Closing O'Hare would disrupt the entire network of airlines. On the other hand, shutting down South Bend Regional Airport would not produce anything resembling such a cascading effect.

Genes behave this way too. Those that interact very frequently, like p53, are crucial for the survival of the cell, while the cell might dispense with those that sporadically interact.

Consider again the Internet. The comparatively low number of highly connected network nodes is a crucial point for the stability of the Internet. Even if servers and routers worldwide shut down due to complications, the Internet would not completely collapse. "Everybody can rest assured that e-mails will not get lost," Barabási said.

In the same manner, many genes in the cells undergo mutations without killing the organism. In fact, the huge amount of genes that are just loosely connected serve as a buffer for the consequences of mutations and help to circumvent local disruption by providing alternative routes—just like finding an alternative route in the Internet if some servers go down.

The worldwide infection of computers triggered by the launch of the "I-Love-You" virus in 2002 offered another chance to see networks at work. Targeting the address books of e-mail programs, viruses replicated by sending themselves to all entries in the address books. Thus, a very voluminous address book (a hub) was the perfect conduit for flooding the networks with viruses.

While viruses create havoc, scientists like Barabási seize these moments to study a virus spreading in social networks and search for strategies that might help contain future epidemics.

Complex organizations like the cell don't reveal their secrets easily. Some functions within the cell are convoluted, even unexpected. For example, the thousands of molecules within a cell are held together by only a few, highly connected chemicals and genes. It is a perilous state, because any malfunction in these key chemicals would most certainly kill the organism.

It is as if evolution has produced an inelegant structure of mutations and changes patched together over the eons. Can we make sense of this? Or rather, can we learn how a whole cell works from incomplete information?

Thus, systems biology is poised to become mainstream biology. It is an emerging field that aims to understand organisms as a whole. "It's very clear that this is not just a biologist's or a physicist's dream," says Barabási. "We realize that we have to put our heads together in a multidisciplinary way in order to achieve our goals."

"Uncovering quantitative correlations has led to the development of computational methods for predicting the phenotypic effect of a gene's function," said **Alexei Vazquez**, a postdoctoral researcher and a member of the Barabási group at Notre Dame.

"Determining protein functions is, however, one of the most challenging problems of the postgenomic era," he said. Great success has been achieved, in particular, with protein function-assignment methods, based on how network proteins interact with each other.

"In human social networks, people tend to socialize within their circles," noted **Stephan Wuchty**, also a postdoctoral researcher in the group. "In like manner, unclassified proteins can be assigned their functions from the interaction patterns of their immediate neighbors in the network."

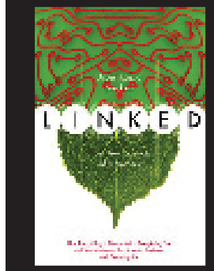
A more immediate and practical use of cellular network research is to expedite the way in which drugs are designed to treat human diseases.

"Ninety-nine percent of the medicines developed by the pharmaceutical companies are thrown out because of unintended side effects," Barabási said. "We are designing chemicals to cure certain problems. But these drugs are acting on many of the body's chemicals simultaneously. These chemicals become toxic because they affect some other aspect of the cell structure that may be essential for life. So, in order to design drugs efficiently, we have to have a good understanding of what the networks behind the cell look like."

The topological organization of cellular networks is increasingly well understood. Recent breakthroughs in the understanding of the functional utilization of metabolic networks have given the Notre Dame team much more analytical and quantitative security that what they have been seeing in the cell is not a fluke of small data sets, but may be part of a set of general principles underlying a network, according to Notre Dame graduate student **Erzsebet Ravasz**.

The group's latest paper, just accepted for publication in the prestigious journal *Nature*, describes how the bacterium *Escherichia coli* utilizes the metabolic flow network in a surprisingly uneven fashion. A few routes behave like well-traveled "highways," while most routes carry a mere trickle of flow, explained **Eivind Almass**, a postdoctoral researcher. Furthermore, this bacterial cell responds to changes in the environment by reorganizing the flow rates of a few select highways. This behavior likely represents a universal feature of metabolic activity in all cells, with potentially important biotechnological implications.

But are they on the right track? That's a question that won't be answered any time soon. "Who has the right vision of the cell?" Barabási posed. "Who has the right perspective on the data that are already out there? And are we going to be lucky enough to figure out the right principle underlying the cell?"



Since it was published in 2002, Albert-László Barabási's book, *Linked: The New Science of Networks*, sold over 25,000 copies in hardcover, and close to 20,000 in paperback.

He and his colleagues at Notre Dame have since broadened their study of networks, like the Internet, to discover similar structures in our genome.

"To secure ourselves against defeat lies in our own hands, but the opportunity of defeating the enemy is provided by the enemy himself."

—Sun Tzu, *The Art of War*

Marvin J. Miller, the George and Winifred Clark Professor of Chemistry and Biochemistry

TB UNDER SIEGE

Every enemy stronghold has a weakness, no matter how thick its fortress walls.

When the enemy is infectious tuberculosis (TB), clever strategies are required to pierce its formidable defense barriers.

One-third of the human race, nearly two billion people, test positive for TB. Between now and 2020, 200 million people will become infected with TB and 71 million of those infected will die of it.

Microbes become resistant to drugs after developing an outer membrane that is impermeable to them. As part of his laboratory's overall program of infectious disease research, Notre Dame organic chemist **Marvin J. Miller**, the George and Winifred Clark Professor of Chemistry and Biochemistry at Notre Dame, has probed the outer membrane of the tuberculosis cell looking for potential cracks and weaknesses medical science can exploit.

Recent studies that focus on the distinct way tuberculosis allows iron to pass through its cell walls have encouraged the chemists in Miller's group. They may have discovered an opportunity to defeat tuberculosis from within.

Every cell needs an agent to carry iron through its membrane and into its interior in order to live.

"Tuberculosis has a very specific iron-transport agent," said Miller, who is chair of the Notre Dame Department of Chemistry and Biochemistry. Miller's group embarked on a project to synthesize these iron-carrying agents, called siderophores, and make them unwitting accomplices by carrying not only iron in but also drugs that are toxic to tuberculosis.

Preliminary evidence shows that the mechanism developed by Miller and his group of chemists and biochemists are breaching the tuberculosis barriers. "It looks like we can kill tuberculosis from the inside out," said Miller.

To combat other bacteria, they have focused on the special role of iron-transporting siderophores that allows them to be actively transported into the cell even when normal openings in the cell wall, called porins, are closed. Similarly, they are now analyzing the receptor on the tuberculosis membrane that acts like a sentry, allowing the iron-carrying agent inside.

Organisms, such as microbes, require siderophores to carry iron through the cell walls in its plus 3 oxidation state. Once inside, the organism reduces the iron to a plus 2 oxidation state.

Early research focused on preventing siderophores from carrying iron in its plus 3 oxidation state—in effect starving the tuberculosis microbe of iron to stop its growth.

"Tuberculosis has been very difficult to treat because it has an especially greasy outer membrane. So it was hard to get drugs inside of it," Miller said.

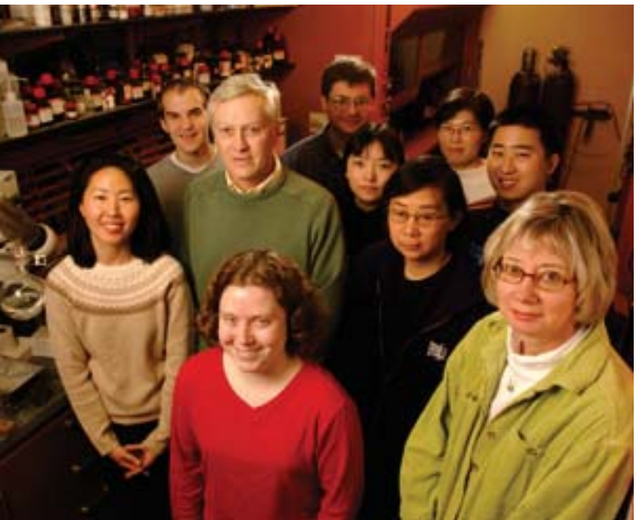
But, the Notre Dame research group did its homework—reconnaissance, if you will—on TB's iron-carrying siderophore. First, they turned to work done in the 1970s in Britain by George Snow, who isolated the natural iron-transporting siderophore for tuberculosis.

Snow recognized that this could be an exciting lead into anti-tuberculosis therapy by controlling the iron assimilation process, but he gave up in frustration, saying the molecules were hopelessly complex and beyond human capability to manipulate at the time.

The Notre Dame group went to work to synthesize this siderophore. They made some subtle molecular changes to the agent. Snow's agent and the Notre Dame synthetic version look almost identical, except for one key change in the chemical bonding.

"We find now that the molecules still bind the iron, but they inhibit the growth of tuberculosis," Miller said. "So somehow they are binding iron but interrupting the transport of iron into the cell. They may be blocking a receptor that is normally used for recognition and transport into the cell." In essence, this slight change turned the agent from a growth promoter to a growth inhibitor.

Professor Marvin J. Miller and his team of students carrying out the battle against tuberculosis.



"Now we know how to make them quite easily and in reasonable quantities," Miller said. "We made additional changes and have found we can make a quite potent antituberculosis drug," he continued.

The group is also focusing on the specific enzyme, or reductase, that reduces Iron(III) to Iron(II). "If we can inhibit that reduction process, then organisms won't get the right form of iron," he said. To do this, they took the TB iron transporter and attached it to an antimalarial agent that has no anti-TB activity.

"The reason we attached this particular antimalarial agent is that it has a peroxide linkage that is very susceptible to reduction. If there is a reduction that happens near this antimalarial agent and it breaks free, it should produce very reactive free radicals," he said.

After attaching this peroxide/antimalarial agent to the TB growth-promoting agent that carries iron into tuberculosis cells, the iron is reduced. "When that happens, the enzyme would not only have to reduce the iron, but the iron that is reduced would then release the peroxide bond and make free radicals inside the tuberculosis cell. Our hope is that the free radicals will destroy the reductase enzyme."

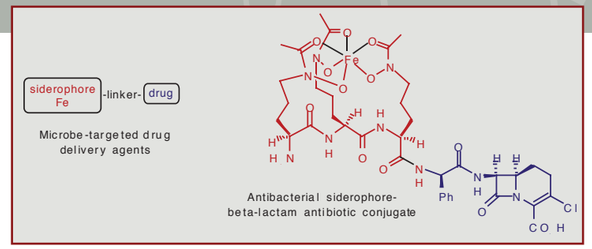
The success of this approach would in effect offer a new type of antibiotic against tuberculosis. They are using a secondary aspect of iron assimilation and iron reduction as yet another tool to help create havoc inside the cell.

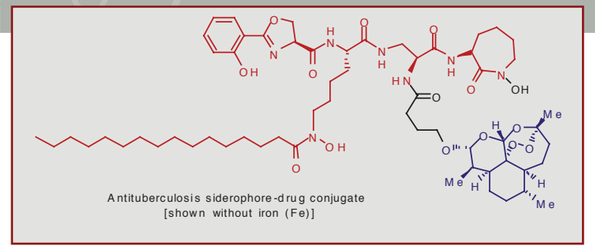
Miller's group has produced one version of this compound "and it indeed has very potent activity," Miller said. They have established a new collaboration with tuberculosis experts at the University of Illinois at Chicago to test the action of their novel approach.

Lately, the Miller group has turned its attention to fungi that are lethal to AIDS patients or transplant candidates whose immune systems have been weakened. Using their knowledge of iron-transport mechanisms, these Notre Dame chemists have joined a worldwide collaboration to bring deadly fungi under control.

"We identified the types of siderophores that are involved in the iron transport in yeast, so we will attempt to synthesize these siderophores," said Miller.

"We need to learn a new molecular trick: how to get an antifungal drug released inside the fungal cell," Miller said. "With bacteria it seemed that the antibiotics we attached to





siderophores would work even if they remained attached. But in some of these fungal cases targets are different and the drug must release from the siderophore to be effective."

Because the fungi must trigger the release of the drug, Miller's group is developing a microbe-triggering release mechanism as well as microbe recognition. "We have learned to attach the carrier and the drug so that they are covalently linked," Miller said.

Only inside the cell would the cell break that covalent link and release the drug. It is essential that this technique not prematurely release a drug that may be toxic to our own cells. "Combined with the carrier it would be recognized by the microbe and not by us," Miller said. His long-term plan is to attach a toxic drug to these carriers so that only the targeted organism takes it up and only the targeted organism releases the drug and kills itself.

For most of his career Miller has been designing and synthesizing new antibiotics to wipe out infectious diseases. Twenty-five years ago his lab received worldwide attention when it developed a new form of antibiotic whose unique structure made it as effective as penicillin.

Their development of a novel synthesis of the β-Lactam ring in the late 1970s allowed his chemists to put a variety of other groups around that ring in a way that was far more versatile than ever before. "We were able to make a very simple β-Lactam that had activity that was as good as penicillin," Miller said. "Eventually we formed a relationship with Eli Lilly and Company that has lasted to this day." Eli Lilly has helped the university protect patents in Notre Dame's name.

At the same time, Bristol-Myers Squibb Company developed a new antibiotic called Aztreonam that is held on reserve by hospitals to combat postsurgical infections. Bristol-Myers Squibb became interested in the ability of Miller's chemists to synthesize drugs and began a relationship that enabled them to mass-produce these new antibiotics.

Over the years Aztreonam has become a $250-million a-year drug for the company. That was Notre Dame's first impact on the drug development industry. Using its expertise in drug synthesis, the Notre Dame group has worked with Eli Lilly to develop an antibiotic called Lorabid, a relative and successor to Ceclor, whose patent has expired.

Synthesis of these new molecules falls on Miller's students, who are challenged to do synthesis design work. Over the years, those students have produced 54 doctoral and master's theses. More than 60 postdoctoral fellows have been part of Miller's group. "They have made a tremendous effort," Miller said. "Those kids have been in the lab days, nights, and weekends."

The financial support of Notre Dame, Eli Lilly, and the National Institutes of Health means that Miller's laboratory will be able to expand its work in designing novel antibiotics and new anti-inflammatory, anticancer, and antifungal agents.

TOO MUCH OF A GOOD THING?

Green Tea's Effect on Cancer

Chinese legend has it that it was the wise man Sheng Nong who discovered the medicinal properties of green tea. As he was boiling water under a tea tree, several still green leaves fell into his pot. Green tea would soon become renowned for its miraculous powers to stave off the ravages of cancer.

Over the course of 5,000 years, green tea has protected countless Asian men and women from cancer of the prostate, breast, lung, and stomach as well as from heart disease. It is now known that green tea is loaded with the cancer-fighting antioxidant EGCG (for *epigallocatechin gallate*), which delays the onset of disease.

EGCG dietary supplements are available at any health food store. "There is no doubt that green tea and EGCG have a very strong protective effect against prostate cancer," said **Martin P. R. Tenniswood**, the Coleman Professor of Biological Sciences, who focuses on the hormonal control of cell growth and death in prostate and breast cancer.

Professor Martin P. R. Tenniswood and colleague Professor JoEllen Welsh.

Tenniswood is equally upbeat about the effectiveness of medications, like Casodex, that are used to treat men with prostate cancer. These anti-androgens have been used to treat both localized and metastatic disease for a number of years. Casodex (also known as bicalutamide) has been used in Europe for the treatment of localized prostate cancer with considerable success and is becoming very popular in this country.

The evidence is beginning to mount, however, that Chinese medicine and Western medicines may be clashing under certain circumstances and that drinking green tea or taking over-the-counter EGCG supplements may interfere with the effectiveness of Casodex and other anti-androgens. In other words, patients may be taking too much of two good things.

So far, no research has been conducted on the interaction of EGCG and Casodex in humans. But, starting this year, a team of University of Notre Dame researchers and graduate students will begin a three-year study to attempt to determine whether Chinese medicine and Western medicine are at odds with each other if used concurrently.

"ECGC appears to alter the effectiveness of Casodex in cell culture and to have effects on the metabolic clearance rate of Casodex in animal studies," Tenniswood said. "But, we need to figure out if this is really the case in humans." If this upcoming study proves the connection, then oncologists will need to be careful to ask cancer patients about the herbal medications they are taking.

Tenniswood's team is modeling the biology of localized prostate cancer using orthotopic xenograft models. Cell lines derived from human tumors are injected into the prostate glands of immuno-compromised mice. These so-called "nude" mice are unable to reject the human tumor cells, and this allows the tumors to grow.

The animals can then be treated with Casodex and EGCG or other developmental drugs to see whether the human tumors respond to the treatment. Anti-androgens such as Casodex are designed to interfere with the action of testosterone in normal prostate cells and in tumors, which causes the cells to die by a process called apoptosis.

Edmund Lee, a graduate student in the laboratory, and several undergraduates have treated "nude" mice carrying the orthotopic tumors with Casodex to monitor changes in tumor size. They have shown that the drug significantly reduces the number of cells in the tumor that are dividing and causes a large number of cells to undergo apoptosis.

Unfortunately for humans, the drugs can stop working after several years and the tumor will start to grow again. "This is the issue we are particularly interested in. We are trying to find out what happens when the tumor stops being responsive to the drug and whether taking EGCG or other herbal supplements changes the natural history of the disease," Tenniswood said. "We know that a significant proportion of the patients treated for a long time with Casodex or other anti-androgens stop responding to the drug and the tumor starts growing again. And, when they grow again, they are much nastier tumors than they were in the first place."

For the past 20 years Tenniswood has been studying the role of hormones like testosterone in the progression of prostate cancer in men as well as the role of estrogen in breast cancer in women. "I have been particularly interested in how hormone ablation, or removal of the hormone, induces tumor regression, and whether there is a relationship between the genetic events that occur in the cells that die and the development of metastasis," he said. "We have cloned and characterized

Professor Martin P. R. Tenniswood and undergraduate students who have been engineering cells.

a number of genes that are involved in this process."

In 1987 Tenniswood showed that clusterin is one of the genes that is induced when cells in the prostate or mammary gland die. "We have also been looking at the connection between clusterin and tumor progression, mainly in breast cancer model systems, using an orthotopic model of breast cancer in which a human breast cancer cell line called MCF-7 is injected into the mammary gland of a female 'nude' mouse. A large tumor will grow but it won't metastasize," Tenniswood said.

"What **Louise Flanagan** and **Lorna Whyte** and their team of undergraduates have done is to engineer the MCF-7 cells to express high levels of clusterin. When these cells are injected into the mammary gland, they not only form primary tumors, but the tumors metastasize to other organs such as the lung. Their data show that the expression of clusterin in cells that don't die leads to metastatic progression."

Establishing whether clusterin plays the same role in prostate cancer is important because science has yet to understand why, in 7 out of 10 men, early-stage prostate cancer will probably remain dormant throughout their lifetimes. These men will normally receive treatment at some point. In the remaining 3 out of 10 men, the tumor progresses and metastasizes, and must be treated early.

"How do we distinguish between the ones that need to be treated and the ones that don't? Right now there is no way of telling whose tumor will progress, so all men diagnosed with localized disease have to be treated," Tenniswood said. "If we can figure out what it is about those individuals whose tumors will not advance versus those that need to be treated and then develop a diagnosis technique for that, we can save thousands of men a year from unnecessary treatment. It is possible that we will be able to use the level of clusterin in tumor biopsies as an indicator of the likelihood that a tumor will eventually progress."

In recent years, researchers looking for clues have also focused on normal stroma, the connective tissue around the organ or gland. It appears that the normal stroma surrounding the tumor stops the tumor from progressing. However, over several years, the stroma appears to change and becomes "reactive stroma," which allows the tumors to progress and become metastatic.

"We know that when most hormone-dependent tumors start to progress, a group of proteins called the metalloproteases become active," Tenniswood said. "These genes have been shown to be associated with the start of metastatic progression in other tumor systems."

Thus, while Casodex and other anti-androgens are killing most of the prostate tumor cells, some of the tumor cells manage to survive and start to express the metalloproteases as a result of the treatment. "We have shown that this is the case in cell culture in a paper that was published in the beginning of 2003, and we think that the reason why those cells survive and eventually metastasize is due to their interaction with the reactive stroma," Tenniswood said. "We are now trying to develop orthotopic models that will allow us to study the interaction between the tumor cells and reactive stroma so that we can test this hypothesis."

Truly Thankful

Coleman Professor of Biological Sciences Martin Tenniswood raised the concept of student involvement to new heights just before Thanksgiving 2003.

Just prior to the break, Tenniswood challenged his 300 undergraduate students to perform an explicit act of kindness on behalf of those people who, by misfortune, need to seek shelter at the South Bend Center for the Homeless.

"Find a shoebox and go to a store like Target or Meijer's and fill the box with toiletries," went Tenniswood's exhortation.

"Some of my students had never even heard of the Center for the Homeless, even though Notre Dame is deeply involved in helping the center," Tenniswood remarked.

The undergraduates went into action in a big way. Over 280 students responded to Tenniswood's challenge to participate in the center's "Welcome Shoebox" program.

In short order, stacks of toiletry-laden shoeboxes commandeered much of the available airspace in Tenniswood's office in the Galvin Life Science Building.

The center's administrators were visibly overwhelmed when students carried armloads of shoeboxes through the center's front doors on South Michigan Street.

By late January 2004, the project was still paying off. "Our people at the front desk are still handing out the gifts to new residents," said Felicia Moodie, Director of Volunteer Services and Community Education.

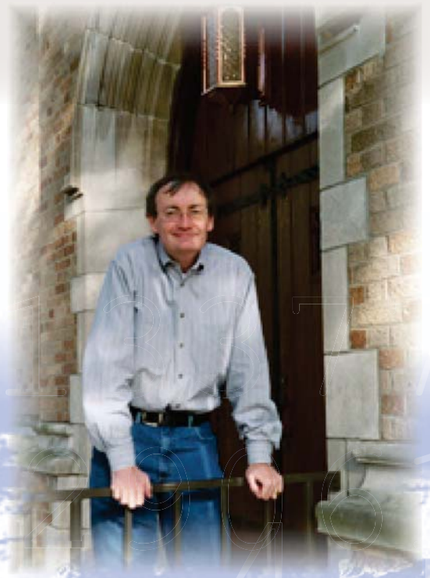
Some Notre Dame students have now gotten their dorms involved in the center's Welcome Shoebox program.

In light of the overwhelming response, Tenniswood plans to repeat the challenge for Thanksgiving 2004.

Pursuing Mathematics' Mount Everests

At the age of 11, I began Euclid, with my brother as my tutor. This was one of the great events of my life, as dazzling as first love. I had not imagined that there was anything so delicious in the world.

—Bertrand Russell (1883)



William G. Dwyer, the William J. Hank Family Professor of Mathematics

Mathematicians see the world in a way no one, except another mathematician, can imagine.

For Bertrand Russell, his love of mathematics became a sensory experience, replete with intriguing flavors. His never-ending search for mathematical truth was by itself a grand pursuit, pure and magical.

We can only imagine the exhilaration, followed by resolve, that might have swept over Sir Edmund Hillary had he scaled Mount Everest only to see yet taller mountains stretching out into infinity.

The study of higher dimensional shapes, or topology, is a pure pursuit of the beautiful mind. **William G. Dwyer** describes mathematicians as being "always confused" over something so abstract that the numbers have a ghostly quality about them. "Then you set out to try to find ways to resolve this confusion," he said.

Dwyer, the William J. Hank Family Professor of Mathematics, is pulled by that urge to understand the nature of homotopy theory, which amounts to studying three-dimensional shapes to figure out how to extract algebraic or numerical data from them and measure their properties.

"We look at problems and try to capture some aspect of the problem by devising a geometric object that corresponds to it," he said. By means of clever construction, chaotic data can be pulled from the vastness of a ghostly netherworld and transformed into a living structure.

"We study a geometric object and examine its shape in hopes that its structure will reveal some information about the problem that otherwise would have been hard to extract," he described.

> "With pure mathematics, you never come to a final conclusion; there's always another question."
>
> *William Dwyer*

Mathematicians are driven by their love of symmetry and of the beauty of order. They are like projectionists who fine-tune the lens to bring an image into sharp focus.

A solution is a source of satisfaction and pride. Yet applause may come from only a small group of like-minded colleagues who also toil along the same pathway. And the exhilaration is both lonely and fleeting. "With pure mathematics, you never come to a final conclusion; there's always another question," he said.

In the same way Sir Edmund Hillary would see higher peaks to be scaled, pure mathematicians see their work as fractals crystallizing before their eyes to the horizon. Some people have their own personal Holy Grail. But what happens once they have the blessed vessel in hand?

Topologists will read a paper that confuses them. "It may fly in the face of something that you believe is true," Dwyer said. "Part of learning topology is developing your own viewpoint. One way to get inspiration is to read something and suddenly realize that what you know doesn't fit. That makes you think harder. You realize that something is missing, so you try to sort it out. It's aggravating, but it's also fun."

His world of pure mathematics is one enormous tangent "and then it splits off more and more," he said.

Every once in a while, a mathematician publishes a paper that proves to be wrong. But, unlike other branches of science, mathematics is a social profession where fierce debates are rare. "Whether a solution is accepted or not depends largely on whether other people can understand it and whether it fits into what they know," Dwyer said.

So, in a sense, the community of mathematicians ends up verifying a proof "because, among us, there is a common idea of what a correct proof is," he said.

Dwyer teaches undergraduates. He translates his excitement to students, many of whom might be taking a calculus course just to fulfill a premed requirement. For the past quarter century, Dwyer has inspired Notre Dame freshmen and sophomores with the artistry of mathematics. "I enjoy teaching them. The students are hard working and motivated. They know what they have to do to get to where they are going, and they are willing to do it," he said.

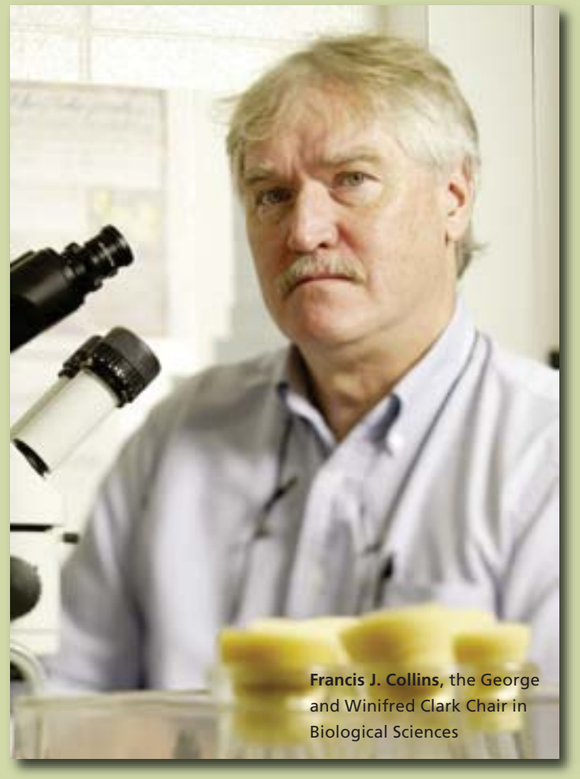
Cold numbers? Hardly. The intellectual descendants of Euclid have a secret life in which fulfillment is never abstract.

Of Mosquitoes and Men

Scientists have gathered extensive intelligence on the primary mosquito that carries malaria, *Anopheles gambiae*. They also now understand the inner machinery of the malaria parasite, *Plasmodium falciparum*, in the most intimate detail.

Now that genomic sequencing has laid bare the insides of both creatures, the time has arrived to launch what **Francis J. Collins** hopes will be a final assault on one of mankind's deadliest enemies. After having a big hand in sequencing the *A. gambiae* genome, Collins, the George and Winifred Clark Chair in Biological Sciences at Notre Dame, is marshalling key investigators from all over the world to locate genetic soft spots of both species in an effort to finally cut the link between pathogen, mosquito, and man.

"Each of the scientists in this network will bring their particular expertise, skills, and abilities to develop two integrated programs that would tackle both malaria and dengue fever," said Collins, who is also the director of the Center for Tropical Disease Research and Training at Notre Dame.



Francis J. Collins, the George and Winifred Clark Chair in Biological Sciences

Jim Gathany, CDC Scientific Photo Services

Just as the Allied invasion of Normandy required painstaking analysis of the long line of German defenses along the French coast, these scientists have had to uncover everything that can be known about these two enemies responsible for death and misery worldwide.

The *Anopheles* genome was sequenced by a collaboration between Celera Genomics, the French National Sequencing Centre (Genoscope), and The Institute for Genomics Research (TIGR), in association with several universities, including Notre Dame. No fewer than half a dozen Notre Dame scientists were featured in the October 4, 2002, issue of *Science*, which hailed the breakthrough.

Now the next phase is underway to neutralize *A. gambiae* as well as the dengue vector, *Aedes aegypti*. "My colleagues and I have been thinking about this for quite a while," said Collins, in his third floor office at the Galvin Life Science Building. "These two genome efforts are in large measure possible because a number of us have been motivated by the idea of developing genetic approaches to control malaria and dengue." Notre Dame Biology Professor **David W. Severson** is leading another project to sequence the genome of the *A. aegypti*.

In the past year, laboratory tests—pre-invasion probes if you will—have already shown that tweaking the genetics of both the mosquito and the pathogen is supremely possible. Teams of scientists are now seeking the support of The Bill & Melinda Gates Foundation to secure funds to probe deeper into the genomes of both species in search of exploitable weaknesses.

Collins has his own notion of what strategy he might employ. "I think we can introduce into the *A. gambiae* population in Africa a small genetic modification that results in the inability of this mosquito to support development of the malaria pathogen," he said. "But what that modification might be is open to a number of possibilities."

"Scientists have already made genetic changes in the mosquito in the laboratory to make them harmless," he noted. So, at the very minimum, scientists have already established a proof of principle. What Collins has in mind is hijacking

Maureen Hillenmeyer, a 2002 Notre Dame graduate, now at Stanford, takes a moment with some of the children in Mali (2003).

the mosquito's own defense system to deal with foreign pathogens in the same way that our bodies have certain immunities and defenses to attack and destroy many invaders.

"The malaria parasite has been able to get past the defense system of the mosquito. But it has not totally bypassed the mosquito's immune system," Collins noted. It has been clearly demonstrated in other research that the *A. gambiae's* defenses readily recognize that it has been invaded by *P. falciparum*. It is quite possible that the mosquito may reduce its own infection to some relatively modest level. "If we can figure out how to tweak the mosquito's own molecular protection so that it will wipe out *P. falciparum* totally, then we'll take that route," he said.

Scientists are on the track of other genetic tricks they might perform to short-circuit the molecular interactions between these two species. Their pas de deux begins when the *Anopheles* mosquito draws human blood already infected with the *Plasmodium* parasite. "When the parasites invade the mosquito, they undergo a very complicated process of development that takes 10 days to 2 weeks," Collins explained. "There is a whole set of parasite-mosquito molecular interactions that are very specific."

It is in this critical period that the parasite crosses two mosquito cell layers that enclose the insect's mid-gut and salivary glands. "If we can figure out a way to interfere with one of these highly specific interactions, then that might lead to a useful genetic trick," Collins said.

Snipping that evolutionary link would almost certainly require that scientists locate the molecules within the mosquito that the parasites recognize and exploit to their advantage. Once geneticists locate their precise target they might conceivably need only to perform a minor restructuring of the mosquito's genetic code to make it an inefficient host for the parasite.

Collins appeared to invoke some sympathy for the devil. "This genetic tinkering might even be good for the mosquito. It can't be very healthy for a mosquito to harbor this parasite," he said with a wry grin. He hopes that within five years the network of scientists with whom he collaborates will have identified at least one genetic weak spot, allowing them to do actual cage-based field testing.

On another front, biomedical researchers using the data from the *Plasmodium* genome project have made considerable progress toward the development of a human vaccine for malaria. Many people feel that, after 40 years of effort, such a vaccine is within sight.

"We still need more time to finish our business," Collins said. The "we" that he refers to are the members of a relatively small field of researchers who work with mosquito vectors.

Professor Severson would use similar methods to try to snap the mosquito–pathogen cycle that causes dengue fever, a debilitating illness that can often lead to permanent neurological damage, even death.

The genetic approach to resolving these diseases is what motivated the research of George B. Craig, the famed Notre Dame entomologist who died of a heart attack in 1995 at age 65. Craig's research was instrumental in identifying the broad means to attack these vector–pathogen relationships. But, without having had the luxury of knowing the precise genomic sequences, the work was often slow and laborious.

Now, as then, scientists simply want to gum up the works and break the cycle between the two species, not to eliminate the species from the planet. "We can't imagine having an effective worldwide mosquito eradication program for these two diseases. It's not possible to have our feet on the ground in every little tropical village where malaria and dengue thrive. You can't even get to those villages in many cases," Collins said.

The *A. gambiae* and *P. falciparum* cycle is hardly unique in the insect world. Biology can point to numerous examples of infectious agents that can move through a population.

Wolbachia is a bacterium that infects over 20 percent of all insect species. So pervasive is *Wolbachia* that in some species, the infection rate of this tiny parasite approaches 100 percent.

Wolbachia has the very unusual ability to manipulate its host in such a way that it gains an evolutionary advantage. "The net effect is that *Wolbachia* causes itself to spread through a population," Collins said.

Unlike *P. falciparum*, *Wolbachia* adds an evolutionary twist to the way it infects insects. As a means of propagating, this parasite alters the sperm of its male host, rendering it infertile when paired with an uninfected female. In this way, *Wolbachia* actually tries to remove non-infected insects by stopping them from reproducing.

Like *P. falciparum*, *Wolbachia* gets its way. The way it orchestrates the biology of the insects it infects involves some yet-to-be-discovered genetic trick. Scientists think they can learn from *P. falciparum* and *A. gambiae* and devise a gene that inhibits this interaction. From *Wolbachia*, they hope to discover the tricks that enable this bacterium to drive itself into insect populations.

"I believe," Collins said, "that we can hitch our malaria-parasite- or dengue-virus-inhibiting gene to these 'drive systems' and effectively and genetically change entire populations of mosquitoes."

With the genome projects as their guide, today's scientists

can employ far more refined strategies than the blunderbuss techniques molecular biologists used in the 1970s and 1980s in their attempts to genetically manipulate harmful species like the screwworm. Thirty years ago biologists did not have sufficient understanding of the ecology, molecular biology, epidemiology, and behavior of the insect of interest to launch an effective campaign.

"But we also have to make sure that what we are doing is safe and effective," Collins said. Scientists recognize that they will be under intense scrutiny, particularly by those who think that genetic manipulation is by definition bad. "No scientist wants to accidentally produce a new mosquito that can transmit HIV, for instance," Collins said. "Even though the likelihood of that happening is vanishingly small, we must test very carefully for possible consequences like HIV transmission."

The collaboration that Collins envisions may stumble upon something quite unexpected—say a technique that is fatal to both pathogens. The trick, he said, is not to stand in the way of any surprise development. "Every avenue of investigation that offers hope for significant new ways to deal with these problems should be encouraged," he said.

New Faculty in the College of Science

BIOLOGICAL SCIENCES

JESSICA HELLMANN, Assistant Professor
Ph.D., Stanford University
Postdoctoral, Stanford University & University of British Columbia

Jessica Hellmann brings field studies, laboratory research, and mathematical modeling to bear on such questions as: How does global change alter the risk of species and population extinction? How do interactions among species amplify or buffer the effects of change? What steps might we take to mitigate negative impacts of change when they occur? She integrates ecology and evolution to predict the trajectory of populations and communities under change.

LEI LI, Associate Professor
Ph.D., Georgia State University
Postdoctoral, Harvard University

Lei Li's primary research interest is to understand the mechanisms of molecular genetics underlying retinal degeneration and other age-related retinal diseases that affect man. In particular, he is interested in searching for gene mutations that cause progressive retinal neural degeneration. He mutates sperm precursors of zebrafish, his study model, and screens their progeny for individuals that show abnormal visual behaviors, for example, night blindness. His research is supported by two NIH grants.

JEANNE ROMERO-SEVERSON, Associate Professor
Ph.D., University of Wisconsin, Madison
Postdoctoral, Agrigenetics, USDA-APHIS

Jeanne Romero-Severson researches population genetics and genome evolution of natural populations. This work complements her collaborations with programs involved in QTL mapping and introgression in natural populations. Her most recent work involves a detailed study of genetic diversity and speciation in red oaks, the dominant tree in North American hardwood forests.

CHEMISTRY AND BIOCHEMISTRY

MAYLAND CHANG, Professional Specialist
Ph.D., University of Chicago
Postdoctoral, Columbia University

Mayland Chang is the Assistant Directorof the Walther Cancer Research Center. She is establishing the infrastructure forthe Walther Clinical Oncology Center. She will also organize and coordinate efforts in the College of Science with program projects and training grants. Chang was the Chief Operating Officer at University Research Network, Inc., in Detroit. Previously, she was a senior scientist at Upjohn Company/Pharmacia, Dow Elanco, Dow Chemical, and Columbia University.

M. KEN KUNO, Assistant Professor
Ph.D., Massachusetts Institute of Technology
Postdoctoral, JILA/NIST/University of Colorado.

M. Ken Kuno, a physical chemist, is an expert in the area of single-molecule spectroscopy. He received his B.A. in 1993 from Washington University in St. Louis and his Ph.D. at MIT. His doctoral research centered on the band edge spectroscopy of colloidal CdSe quantumdots. Following his Ph.D., he worked on single-molecule microscopy as a postdoctoral researcher at JILA/NIST/University of Colorado. He has also done research at the Naval Research Laboratory synthesizing mercurychalcogenide quantum dots and clusters.

SHAHRIAR MOBASHERY, Navari Family Professor in Life Sciences
Ph.D., University of Chicago
Postdoctoral, Rockefeller University

Shahriar Mobashery, a bio-organic chemist, is an expert in antibiotic resistance and enzyme inhibitors. He is a widely regarded expert in bio-organic chemistry, organic synthesis, protein chemistry, enzymology, and computational sciences. He has served on numerous governmental and industrial panels, and belongs to the editorial boards of eight scientific journals. His research is supported by four NIH grants.

JEFFREY W. PENG, Assistant Professor
Ph.D., University of Michigan
Postdoctoral, ETH-Zürich

Jeffrey W. Peng is a biophysical chemist specializing in protein dynamics, receptor-ligand interactions, and the development and application of NMR methods to enhance rational drug design. He obtained a Ph.D. in biophysics from the University of Michigan in 1993 for his work on novel NMR approaches for studying protein dynamics. In his postdoctoral research at the ETH-Zürich, he examined the effects of solvents and hydration on small-molecule conformational dynamics.

MATHEMATICS

FRANÇOIS LEDRAPPIER, John and Margaret McAndrews Professor in Mathematics
Ph.D., University of Paris

François Ledrappier is interested in asymptotic properties of group actions and in the relations between objects associated to them. The precise setting might include such diverse areas as: dynamical systems theory, geometry of compact negatively curved manifolds, and abelian covers, linear actions of linear groups, random walks on linear groups, zero entropy algebraic actions of free abelian groups,or geometric measure theory.

ISRAEL MICHAEL SIGAL, Professor and Rev. Howard J. Kenna, C.S.C., Memorial Chair of Mathematics
Ph.D., Tel-Aviv University

Israel Michael Sigal's research interests are in the areas of mathematical physics and applied mathematics. He works on mathematical problems arising in scattering theory, quantum field theory, statistical mechanics, and nonlinear systems. He is now working on the construction of a rigorous theory of radiation for quantum systems, the problem of return to equilibrium in quantum statistical mechanics, the problem of motion of solitons (optical, topological, describing Bose-Einstein condensates), the problem of interaction of magnetic vortices, and the problem of blow up (self-focusing) or collapse of solutions for the nonlinear Schroedinger and Yang-Mills equations.

PHYSICS

PHILIPPE A. COLLON, Assistant Professor
Ph.D., University of Wien, Vienna, Austria
Postdoctoral, Lamont–Doherty Earth Observatory, Columbia University

Philippe A. Collon is an experimental nuclear physicist whose research demonstrates how the detection of rare isotopes or of nuclei with extremelylow abundances plays an important role not only in nuclear physics, but also in many other fields of contemporary science. The detection of products of specific nuclear reactions, the properties of certain radionuclides, as well as the abundance of specific nuclides provide crucial information on important processes that occur or have occurred not only on Earth but also in the cosmos. Among these are nucleosynthesis and other galactic processes, and issues related to the determination of the age of the solar system.

MORTEN RING ESKILDSEN, Assistant Professor
Ph.D., Riso National Laboratory and the University of Copenhagen
Postdoctoral, University of Geneva, Switzerland

Morten Ring Eskildsen is an assistant professor of experimental condensed matter physics. His research presently centers around the studies of vortices in superconductors. In relation to this, the interaction of superconductivity and magnetism will also continue to be a strong interest. These investigationsare being carried out using two different experimental techniques: scanning tunneling microscopy and spectroscopy (STM/STS) and small-angle neutron scattering (SANS).

ANNA GOUSSIOU, Assistant Professor
Ph.D., University of Wisconsin, Madison
Postdoctoral, State University of New York, Stony Brook

Anna Goussiou, an experimental particle physicist, is a member of the D-Zero experiment at Fermilab. She is the co-convener of the Jet Energy Scale group. The group is responsible for the determination of jet energy scale and the measurement and optimization of the jet energy resolutions. This work is crucial for studies of particles, such as the top quark and the Higgs boson.

COLIN P. JESSOP, Associate Professor
Ph.D., Harvard University
Postdoctoral, Stanford Linear Accelerator Center (SLAC), Stanford University Panofsky Fellow, SLAC

Colin Jessop, an experimental particle physicist, is a member of the B aBar experiment at the Stanford Linear Accelerator Center, where he searched for new physics in rare decays of B mesons. He is a convener of the B working group which searches for subtle effects that can reveal the presence of new particles so massive that they are beyond the reach of current accelerators.

Standing Ovations

Physics Department Chair **Ani Aprahamian** has been appointed to the Nuclear Science Advisory Committee of the Department of Energy and the National Science Foundation. The Committee provides official advice to the DOE and the NSF on the national program for basic nuclear science research.

Two members of the Physics Department were recently honored with election as Fellows of the American Physical Society this year. They are **Albert-László Barabási**, Emil T. Hofman Professor of Physics, and **Stefan G. Frauendorf**, Professor of Physics.

Barabási was cited for "his discovery of scale-free networks and for his theories of surface roughening and strained surfaces." He was nominated by the APS Division of Condensed Matter Physics.

Frauendorf was cited for "his seminal contributions to the physics of rotating nuclei via mean-field symmetries." He was nominated by the APS Division of Nuclear Physics.

They join 13 current APS fellows in the Department: Ani Aprahamian, H. Gordon Berry, Jacek Furdyna, Umesh Garg, James Kolata, Walter Johnson, A. Eugene Livingston, Grant Mathews, James Merz, Randal Ruchti, Jonathan Sapirstein, Carol Tanner, and Michael Wiescher.

The APS Fellowship Program was created to recognize members who may have made advances in knowledge through original research and publication or made significant and innovative contributions in the application of physics to science and technology.

Ikaros Bigi, professor of physics, is a co-recipient of the American Physical Society's (APS) 2004 J.J. Sakurai Prize in theoretical particle physics for his contributions to the understanding of CP violations in B meson decay modes. In 1981, Bigi and Anthony Ichiro Sanda of Nagoya University in Japan published an influential paper, "Notes on the Observability of CP Violations in B decays,'' that contained insights into the problem of broken symmetry, or CP violation, originally discovered in 1964. The 1981 paper helped physicists account for the preponderance of matter over antimatter shortly after the Big Bang.

The J.J. Sakurai Prize was endowed in 1984 by the family and friends of Jun John Sakurai as a memorial and in recognition of the accomplishments of the renowned theoretical physicist. His theories encouraged particle physicists to examine major ideas in diverse ways and to seek out new theories that crossed distinct genres of physics research.

Bigi's research is directed mainly toward developing theoretical ideas that will suggest novel methods for uncovering new physics beyond the standard model of high-energy physics.

A member of the Notre Dame faculty since 1988, Bigi received his master's and doctoral degrees from the Max-Planck Institute.

Mario Borelli, associate professor of mathematics, is a recipient of the Council for Opportunity in Education's 2003 Walter O. Mason Award. This award was established in 1988 to honor outstanding professionals in educational opportunity programs who exemplify the life and ideals of Walter O. Mason, Jr.

Thomas P. Fehlner, the Grace-Rupley Professor of Chemistry, is on sabbatical leave from Notre Dame this spring semester to occupy the post of Leverhulme Visiting Professor at the University of Bath, United Kingdom. Fehlner will present a number of Leverhulme Lectures on his research in inorganometallic chemistry focusing on the synthesis, characterization, and utilization of unusual main group-transition element cluster systems. He will also lecture at Oxford, Cambridge, Durham, Bristol, Cardiff, Strathclyde, Herriot-Watt, and Leeds.

Michael D. Hildreth, assistant professor of physics, has been named a 2003 Cottrell Scholar, one of 12 people in the nation to receive the honor.

Offered by Research Corporation, a Tucson-based foundation for the advancement of science, Cottrell Scholar Awards fund original research that has the potential for undergraduate participation. Awards in the amount of $75,000 are made to further the teaching and research of junior faculty members in astronomy, chemistry and physics at U.S. and Canadian doctorate-granting institutions. A panel of scientists drawn from across the disciplines makes final recommendations for the awards, which are open only to faculty members in the third year of a first tenure-track appointment.

A Notre Dame faculty member since 2000, Hildreth studies the mechanism or mechanisms responsible for Electroweak Symmetry Breaking, which explains the existence of mass. He participates in the DØ (Dzero) Experiment at the Fermi National Accelerator Laboratory, which is a worldwide collaboration of scientists conducting research on the fundamental nature of matter. The research is focused on the interaction of protons and antiprotons at the highest possible energies in order to reveal the character of mass.

Hildreth is coordinator of the Central Fiber Tracking Algorithms Group, which creates the tracking algorithms used in the offline reconstruction of the DØ Trigger. Hildreth also was named an Outstanding Junior Investigator by the U.S. Department of Energy in 2002.

Dennis C. Jacobs, professor of chemistry, has been named U.S. Doctoral and Research Universities Professor of the Year by the Carnegie Foundation for the Advancement of Teaching and the Council for Advancement and Support of Education.

Professor Jacobs received B.S. degrees in chemistry and physics in 1982 from the University of California at Irvine and a Ph.D. in physical chemistry in 1988 from

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Wayne.Falda.1@nd.edu

Standing Ovations

Stanford University. In 1988 he joined the faculty at Notre Dame. He was awarded an Alfred P. Sloan Foundation research fellowship in 1993 and was named a Carnegie Scholar in 1999.

Boldizsár Jankó, assistant professor of physics, has been named an Alfred P. Sloan Research Fellow by the Sloan Foundation. The Sloan Research Fellowship, an extremely competitive award, is given to top scientists at research universities early in their careers in the fields of physics, chemistry, economics, mathematics, and neuroscience. The Foundation usually reviews some 400 nominations per year before selecting 104 Fellows.

The Sloan Research Fellowship carries a grant of $40,000 to be used in a flexible and largely unrestricted manner so as to provide the most constructive possible support of the Fellow's research.

Jankó's research focuses on a wide variety of phenomena associated with highly-correlated electron systems. Problems include high-Tc superconductivity, mesoscopic and nanoscopic physics, magnetic systems, vortex motion in superconductors, and electronic properties of carbon nanotubes.

Julia F. Knight, Charles L. Huisking Professor of Mathematics, was elected a foreign member (honorary doctor) of the Siberian Branch of the Russian Academy of Sciences.

Donovan McFeron ('03), undergraduate in the Department of Mathematics, won Honorable Mention in the NSF Graduate Fellowship Competition last March.

Steven T. Ruggiero, associate professor of physics, and **Tony Williams,** a graduate student in physics, are part of a research team that has made a breakthrough in low-temperature refrigeration. The work, which was detailed in the cover feature of the January 26, 2004, edition of *Applied Physics Letters*, involves the use of superconducting tunnel junctions to produce cooling at temperatures within one degree of absolute zero.

The principle involved is the separation of electrons statistically higher in temperature within the cooling device using an electric current, in a process akin to Peltier cooling. Cooling to very low temperatures is required for a variety of fundamental scientific investigations and for a new class of highly sensitive bolometric X-ray detectors, some of which are destined for astronomical space missions circa 2010. While mechanical and other cooling schemes can be used at very low temperatures, tunnel junction coolers will be much lighter in weight, easier to integrate with detectors, and very rugged.

Physics Professor **Michael C. F. Wiescher** was awarded the Hans A. Bethe Prize by the American Physical Society for 2003. The prize recognizes outstanding work in theory, experiment, or observation in the aåreas of astrophysics, nuclear physics, nuclear astrophysics, or a closely related field.

Standing Ovations

Michael Wiescher is the director of the Joint Institute of Nuclear Astrophysics (JINA) and the Frank M. Freimann Professor of Physics. In giving the award, the APS cited Wiescher for his "contributions to the experimental foundation of nuclear astrophysics, especially the delineation of the processes involved in explosive hydrogen burning in novae and X-ray bursters; and for providing an intellectual bridge between experimental nuclear astrophysicists and their theoretical colleagues."

This just in…

Jan. K. Labanowski was hired on Jan. 12, 2004 as director of the Science Computing Facility, located at 204 Nieuwland Science Hall.

Labanowski had been employed by the Ohio Supercomputer Center (OSC) at Ohio State University, Columbus for 15 years.

As the new director of the Science Computing Facility, he will support educational and research needs of the faculty by facilitating the continued development of the Notre Dame College of Science computing capabilities.

Dean Joseph P. Marino said he development of a high performance computing center was one of his top priorities for the College of Science.

Labanowski holds master's degrees in Chemistry and Biochemistry, and a doctorate in Cell Biology.

His background includes computational and theoretical chemistry, bio- and cheminformatics, drug design, computational materials science, chemical kinetics, laboratory automation, and data analysis and statistics.

He will lead a group that includes assistant professional specialists Mathew A. Chrystal and Jean-Christophe Ducom, and professional technician Stephen D'Ambrosia. "They are already well known to the people in the College for their amazing skills in bringing computers back to life and keeping the software running," Labanowski said.

OF DREAMING SPIRES AND GOLDEN DOMES

A One-Month Impression of Oxford

Andrew C. Serazin, Notre Dame's 14th Rhodes Scholar, has settled into academic life at Oxford University, having found that Oxfordians "are as ready to talk politics and use four-syllable words as easily as they talk of football (more recently, rugby)."

The following is a reprint from the Winter 2003 edition of ***Pathways,*** *the magazine of the Department of Biological Sciences.*

Nearly 30 days ago, the newest vintage of the United States' Rhodes Scholars (I among them) was unleashed upon this university and this university unleashed itself upon the individuals in it.

So it has been for nearly 800 years at Oxford, where each October ebullient young people from all corners of the globe come to add their names to the ancient register. Adam Smith's name is in the register and so are the names of Bill Clinton, Tony Blair, John Locke, Cardinal Newman, Robert Boyle, C.S. Lewis, Stephen Hawking, and now… Andrew Serazin.

In looking at my ever-so-brief listing of Oxford graduates, a critical reader might be tempted to play a kind of "Which one of these is not like the other?" One might ask, "What does this young punk have in common with these venerable figures?" To think this is to miss the very spirit of this university. Each day the history of Oxford presses upon you, sometimes literally, as the occasional stone veranda crumbles as you pass it.

And its effect is that one feels a participant in history, a small author in the chronicle of human events linked to other small authors via this at-once-ancient and ever-growing list of names. As any self-proclaimed participant in the history, I have made a point to tramp all over both back alleys and gilded staircases during my first month in England.

I sat on the stone bench where Bill Clinton allegedly "did not inhale" in the late 1960s. I also drank a pint of Old Hooky ale in the crusty, low-ceilinged Eagle and Child, where J.R.R. Tolkien met every week with C.S. Lewis and the rest of the Inklings literary group.

But in contrast to these dimly lit venues of the night, I have wandered the glowing halls of Buckingham Palace, invited to a reception held by Her Majesty Queen Elizabeth II with Nelson Mandela as the guest of honor.

The purpose of the event was to celebrate both the 100th anniversary of the Rhodes Scholarship and the inauguration of the Mandela Rhodes Foundation, which seeks to build leadership excellence in Africa through scholarship, mentoring, and partnership programs.

Much to my childish disappointment, the Rhodes Scholars did not travel by horse and carriage into London, rather by hackneyed buses drawn by the internal combustion engine. My spirits lifted, however, when I saw the guards at the Palace Gate and the red carpet rolled out upon arrival.

The event was held in the main Picture Gallery, a long, slender room shining with the golden lions and unicorns and the "Dieu et mon Droit" of the Royal Seal. This room gets its obvious name from the hundreds of paintings hung on the walls. It was a truly regal experience, as each of these paintings was not only a priceless masterpiece and the culmination of a man's lifework but also a family portrait!

It was under the enormous Realist depiction of Victoria in the gardens that I shook the Queen's hand, bowed my head like any good liege, and said, "Good evening, your Royal Highness. It is a pleasure to be in your home." Later on I got the chance to speak with the Queen in more depth. She asked me what it is that motivates me in my studies. I told the Queen that "I am deeply fascinated by malaria," and she gave me the strangest look ever to grace the Royal Countenance.

We chatted for a few moments about the potential for a global ban on DDT, speaking as just two human beings, not as one Defender of the Faith, Monarch of the Commonwealth, and one science nerd who likes little parasites in the bloodstream.

This same connective feeling was evident to me again as I spoke with Nelson Mandela about the process of reconciliation in post-apartheid South Africa. Mandela spoke of reconciliation as "the unthinkable irrational act, an act that makes no sense to us. But, in South Africa it has occurred, and it must occur in the future. In all places where suffering has happened, the process of forgiving the unforgiveable must also happen." With these words, Nelson Mandela demonstrated an extreme humanity.

The idea of radical empathy that he developed is, I believe, the currency by which human beings communicate across vast distances of space, time, and culture. So in light of Mandela's words, my earlier experience with the Queen made sense. Through the conduit of extreme humanity, it was possible for me to speak of the microscopic bugs that I work on and to have an impact on the Queen of England (or at least the expression on the Queen's face).

I came to England by the virtue of Cecil Rhodes for the express purpose of international understanding.

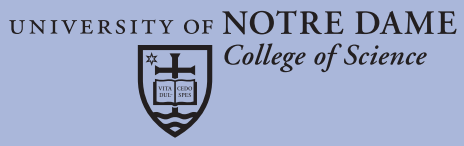
I was always skeptical of this diplomat's phrase, "international understanding." It reminded me of some "kumbaya" campfire sing-a-long that has no place in the world of pragmatism.

The lessons learned at Buckingham Palace were the first clear indication to me that such a thing as "international understanding" exists and is possible.

I can only hope that by whatever grace I came to Oxford, I will continue to strive toward that end.

I hope you enjoy this three-dimensional, animated DVD of the new Jordan Hall of Science, now under construction on the University of Notre Dame campus.

Joseph P. Marino, Dean of the College of Science, University of Notre Dame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