Office of the Vice President for Research *Fall 2006*

SEARCH & DISCOVERY

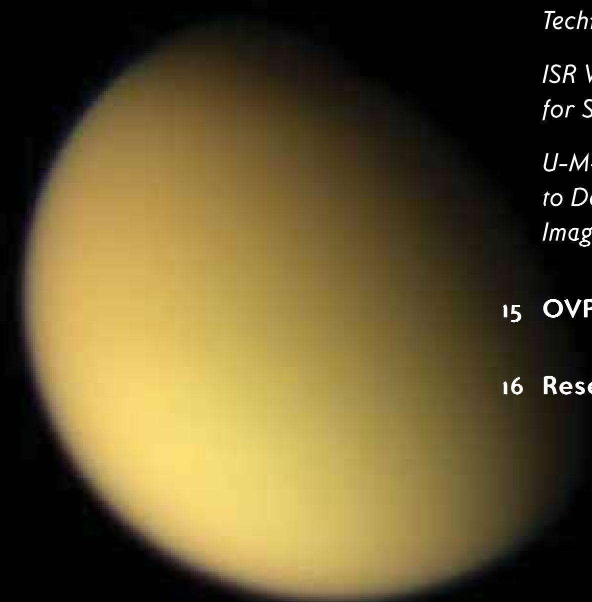
R E S E A R C H A T M I C H I G A N

College Researchers Play Roles in Space Explorations

UNIVERSITY OF MICHIGAN

ON THE COVER

On January 14, 2005, the Huygens probe, launched about three weeks earlier from the Cassini spacecraft, parachuted to the surface of Titan, a moon of Saturn, shown on the cover. Scientists expected its life expectancy to be minutes, but Huygens kept sending data to Earth for three hours. Part of its success was due to the hardiness of the gas chromatograph mass spectrometer, an instrument built in part by engineers at Michigan Engineering's Space Physics Research Laboratory. When Huygens finally went silent after sending an unexpected abundance of data, AOSS Professor Sushil Atreya and Emeritus Professor George Carignan—integral members of the Huygens research team—set to work on one of their main tasks in the mission: deciphering what all the data means. Photo courtesy of NASA/JPL/Space Science Institute.



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VICE PRESIDENT FOR RESEARCH

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SUZANNE TAINTER
SARAH WALKLING

RESEARCH PERSPECTIVES

I have now been at the University of Michigan for nine months. The time has been one of transition as I move my own research effort to U-M, and as I learn about the University and its impact on the region and the nation. The learning experience has been, in a word, intense. Two things that stand out about U-M are its size and its quality. Compared to many other academic institutions, U-M is extraordinarily decentralized. This gives it considerable strength, but it also presents challenges when you want to "get something done." The strength lies in putting the power for change and innovation directly in the hands of the researcher, allowing good ideas to "bubble from the ground up." But decentralization also creates barriers between units that can impede interdisciplinary enquiry. This is where OVPR can lend a hand. By taking the long view, OVPR can help forge ties between research activities in widely disparate areas. Our success in doing this ultimately determines whether OVPR is fulfilling its mission of maximizing U-M's research potential.

It has also become apparent that my office must enable communication throughout our large and excellent research community, and, just as importantly, to communicate with our industry and government partners. For this reason, we are launching this quarterly, called *Search & Discovery.* In addition, I have already started to hold meetings with many faculty groups from the schools and colleges to spread the word about OVPR's funding programs, oversight role in research compliance, and duties related to research units and new initiatives.

Of special interest to many within our institution is to improve and energize the University's relationships with the outside world. This includes our interactions with traditional research sponsors, such as the federal government and foundations. But of even greater importance to the nation's strategic position, the economic development of our region, and the encouragement of our most entrepreneurial faculty, we must also strengthen our connections to the private sector through sponsored research and technology transfer. Michigan has engaged in many productive partnerships with industry over the years, but we can and must do much more. This is not simply an option, but has become a necessity. With the regional economy struggling to overcome what appear to be structural and permanent shifts from our traditional heavy manufacturing base to a knowledge-based economy, U-M has a responsibility to contribute its vast wealth of intellectual depth and productivity to help smooth this disruptive and long-term economic transition. Over the summer, I have seen the potential for Michigan's interactions with the private sector, from the highly publicized announcement that Google will set up shop in the Ann Arbor area to the financing of the U-M startup NanoBio. I believe that in the coming years, these kinds of announcements will become commonplace, heralding our essential contributions to the regional and national economies.

OVPR also takes seriously its role as facilitator and catalyst of promising research areas that, if properly nourished and incubated at an early stage, may bring us into a leadership position as an intellectual risk-taker and visionary institution. To be the best in the highly competitive academic world, we must anticipate opportunities and act on them in a timely and credible manner. OVPR has the mission of seizing such opportunities once it is determined that our research community has the interest and commitment to take a leadership role in a particular area. One such opportunity that was recently initiated is the nanotechnology and science initiative. Currently, a joint committee of faculty from the College of Engineering and LSA is conducting a search for new leading faculty in this critical research area.

I have also found extraordinary enthusiasm at U-M for the fields of energy science, technology, and policy. Following the recommendations of a faculty committee, the Michigan Energy Research Council, my office has committed significant resources with the help of the Office of the President, the Provost and others to support the many faculty who expect U-M to play an international leadership role in developing new energy strategies to solve the world's problems associated with this essential resource. To this end, the Michigan Memorial Phoenix Energy Institute has been established at the site of the decommissioned Ford Nuclear Reactor on North Campus as the "home base" for the many efforts on campus focused on the energy challenges facing us. It will also act as liaison to government and our emerging energy industry in southern Michigan.

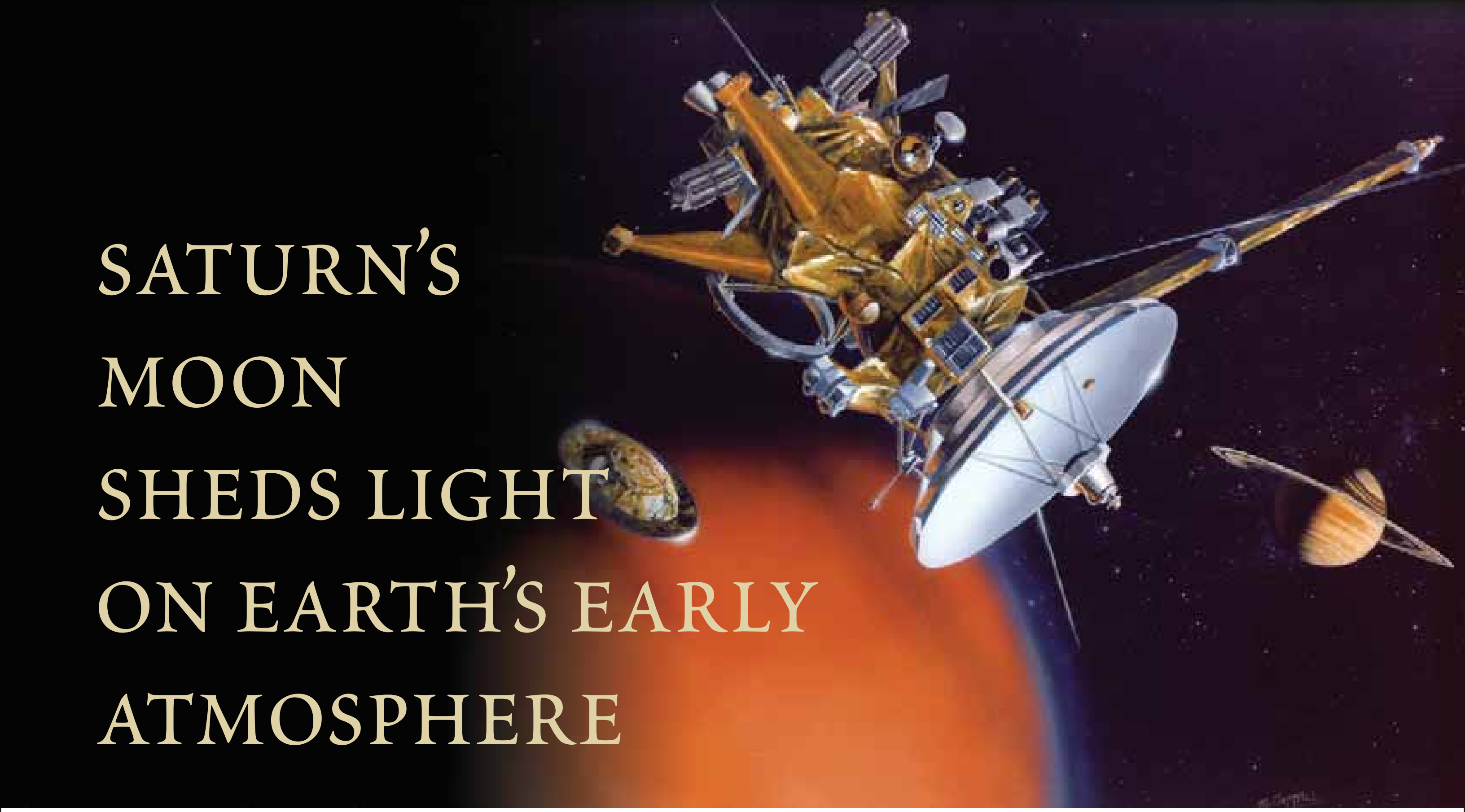
Finally, I want to remind you that OVPR has several staff dedicated to advocate and promote U-M's research agenda. Two faculty members serve as associate vice presidents — Jim Shayman, who focuses on research in the health sciences, and Steve Ceccio who concentrates on the other sciences and engineering. We will be adding a third faculty AVP to specialize on the humanities and social sciences. Two other associate vice presidents are Marvin Parnes and Judith Nowack. Marvin, among many other duties, oversees research administration and our faculty grants and awards program, while Judy is our expert on compliance issues.

I hope you find this and subsequent issues of *Search & Discovery* helpful in connecting you to the broad U-M research community. I welcome your thoughts about this publication and other topics of concern regarding our research enterprise at U-M.

Best regards,

Stephen R. Forrest

SATURN'S MOON SHEDS LIGHT ON EARTH'S EARLY ATMOSPHERE



AN ARTIST'S CONCEPT OF THE HUYGENS PROBE EN ROUTE TO TITAN AFTER RELEASE FROM THE CASSINI ORBITER. COURTESY OF NASA/JPL.

Methane is to Titan as water is to Earth. It sounds like an analogy question from a college test, but in fact describes the role of methane in the weather and geological processes of Titan. And it sums up some recent research results from the Cassini-Huygens exploration of Titan.

The largest moon of Saturn and the only moon in our solar system with a thick atmosphere, Titan has long intrigued scientists, including University of Michigan planetary scientist Sushil Atreya. He is part of an international team of researchers investigating Titan with data from the Huygens probe carried into space on the Cassini orbiter and parachuted to the Titan surface in January, 2005 for the first close-up analysis of this mystery-shrouded moon.

Thick smog obscured the surface of Titan from the Voyager spacecraft that flew by in the 1980s. Now some twenty-five years later, the Huygens probe has helped cut through the smog to reveal much about that moon. Atreya is one of several authors on a report in *Nature,* on July 27, 2006, that proposes a constant drizzle of methane rain on Titan. The source of the drizzle is the thick haze or clouds of methane, first reported in the December 8, 2005 issue of *Nature* by the Huygens Gas Chromatograph Mass Spectrometer (GCMS) Team that includes Atreya and U-M Emeritus Professor George Carignan.

Atreya has been analyzing data sent back through space from the probe to help solve the puzzle of where Titan's atmosphere came from and how it is maintained, and what role atmospheric aerosol deposits play in the surface features that appear in the radar scans of the moon taken by Cassini flybys.

Clues to planet origins

What scientists learn about Titan may help them understand what Earth was like before life evolved on our planet, and, by extension, the composition and formation of other terrestrial bodies in our solar system and elsewhere in the universe.

The Huygens probe, named for the 17th century Dutch astronomer who discovered Titan, carried six sophisticated instruments—including the GCMS built in part by U-M engineers. It touched down on the Titan surface on January 14, 2005, the culmination of a seven-year, 2.2 billion-mile ride from Earth on the Cassini orbiter that continues to survey Saturn and its rings and moons with its own instruments.

The recent report in *Nature* is based on temperature, pressure and methane concentration profiles as the Huygens probe descended through the Titan atmosphere. The scientists suggest the Titan atmosphere has an upper layer of clouds containing methane ice and a lower layer of drizzle-producing methane-nitrogen clouds.

Atreya has been around his "home" globe—recently in Beijing, for example — to present findings from the Huygens and Cassini investigations at scientific meetings. He and GCMS colleagues, including U-M's Carignan, reported on Titan's atmospheric composition measurements made from Huygens in the December 2005 issue of *Nature.* Carignan played a key role in conceiving the GCMS instrument and other U-M space engineers built many of its components.

The GCMS, a versatile chemical analyzer of gases, identified and measured the relative amounts of the chemical constituents of Titan's atmosphere. During descent, the GCMS also analyzed aerosol samples that were collected, heated and vaporized by the Aerosol Collector Pyrolyzer (ACP), another instrument on Huygens on which Atreya also is an investigator. Finally, at landing, the GCMS measured the composition of Titan's surface. Scientists were surprised when the probe landed in slush of methane "mud." The methane drizzle would account for the wet surface.

A nitrogen-rich atmosphere

Direct atmospheric measurements from the GCMS, which included profiles of the constituents, isotopic ratios and trace chemicals, confirmed that the Titan atmosphere is 95 percent nitrogen and 4 percent methane.

The GCMS provided data on the make-up and abundance of heavy noble gases, including primordial and radiogenic argon. From that information, the scientists have been able to begin to better understand the processes that formed Titan and its atmosphere.

The evidence suggests that Titan acquired some of its atmospheric components in ways similar to Earth. For instance, its gaseous nitrogen most likely occurs as the result of the conversion of ammonia, as on primordial Earth, through a reaction with the solar ultraviolet light early in Titan's formation history.

"The big question for Titan is how the methane gets replenished," Atreya says, since it is destroyed by the Sun's ultraviolet light which would, in turn, lead to a gradual collapse of Titan's nitrogen atmosphere. "The GCMS measurements, together with supporting data from other Huygens instruments, is beginning to provide some important clues to the source and recycling of methane on Titan."

In an upcoming special issue of the journal *Planetary and Space Science,* Atreya and co-authors (including U-M graduate student Elena Adams) suggest that processes in the interior of the Titan produce and replenish the gas lost to photolysis in the atmosphere. One, called *serpentinization,* occurs in an interaction between water and rock. In this process hydrogen is produced, which in turn reacts with Titan's original carbon-containing molecules such as carbon dioxide and carbon monoxide to produce methane. Methane is then stored in clathrate hydrates—cages of water molecules—in which the gas is trapped for later release to the atmosphere.

Direct evidence of outgassing from the interior comes from the detection of radiogenic argon by the GCMS in the atmosphere. Such argon is produced in the radioactive decay of potassium, which is a component of the rocks in the core of Titan. Cassini radar and visual infrared mapping spectrometer images provide evidence of cryovolcanism, which allows material from the interior, including methane, to be upwelled to the surface. Impacts of objects from space onto Titan may also release the methane from the clathrate hydrates.

A glimpse at a "young" Earth

Space scientists think of Titan as a time vault. Its thick atmosphere may resemble that of Earth some several billion years ago, before Earth's life forms began creating oxygen for our atmosphere. "When we look at Titan, the possibility is that we might be looking at Earth before life began," Atreya says.

There are limits to what Titan can tell us about early Earth or the origins of life on our planet. For one, there is the intense cold on Titan. Titan's surface temperature drops to -179 degrees Celsius (-290 F). Consequently, there is no water in the liquid state, and thus no readily available reservoir of oxygen on the surface. On the other hand, the interior of Titan is believed to contain an ocean of liquid water-ammonia brine, an environment some scientists believe may be conducive to the formation of prebiotic molecules or even life. Although exploration of the interior of Titan is beyond the

THE HUYGENS PROBE IS INSTALLED IN THE CASSINI ORBITER AT THE KENNEDY SPACE CENTER. COURTESY OF NASA.

A TITAN TIMELINE

1655	TITAN DISCOVERED BY CHRISTIAAN HUYGENS
1903	JOSE COMAS SOLÁ SUGGESTS TITAN HAS AN ATMOSPHERE
1980	VOYAGER 1 FLYBY, TITAN'S DENSE SMOG OBSCURES THE SURFACE
OCT. 15, 1997	CASSINI-HUYGENS LAUNCHED
JULY 1, 2004	CASSINI-HUYGENS ENTERS ORBIT AROUND SATURN
DEC. 25, 2004	HUYGENS PROBE SEPARATES FROM CASSINI
JAN. 14, 2005	HUYGENS PROBE TAKES A TWO-HOUR DESCENT THROUGH THE TITAN ATMOSPHERE, LANDS DOWN ON SURFACE
THROUGH 2008	CASSINI ORBITER FLYBYS CONTINUE

scope of Cassini-Huygens, there is some hope that analysis of surface material measurements made by the GCMS upon landing might provide some clues to the types of molecules produced in the interior ocean, says Atreya.

The long development times of planetary instruments and their long journeys after launch mean that scientists become masters of "delayed gratification." The development of the science objectives began decades before the Cassini spacecraft was launched.

IN THIS DRAMATIC CASSINI MURAL, THE MYTHOLOGICAL ROMAN GOD SATURN IS REPRESENTED AS THE SYMBOL OF TIME, DRAWING BACK A VEIL TO ALLOW THE CASSINI SPACECRAFT TO REVEAL THE MYSTERIES OF THE VAST SATURNIAN SYSTEM. THE MURAL ALSO SHOWS THE CASSINI SPACECRAFT FIRING ITS MAIN ENGINE TO BRAKE INTO ORBIT ABOUT THE PLANET SATURN ON JULY 1, 2004. BENEATH THE SPACECRAFT LIES THE VAST SHEET OF ORBITING ICEBERGS AND PARTICLES THAT MAKE UP THE MAGNIFICENT RINGS OF SATURN. THE CASSINI MURAL EMBODIES A CULTURAL BLEND OF ART AND SCIENCE MADE POSSIBLE BY A JOINT UNDERTAKING BETWEEN CASSINI PERSONNEL AND THE ACADEMIA DE ARTE YEPES IN LOS ANGELES.

Atreya and Carignan were at European Space Agency's Huygens mission at Darmstadt, Germany as the 700-pound probe made its final descent to Titan's surface. "There is a great deal of euphoria when the data are finally in hand," says Atreya. "However, that feeling is very short-lived, as the real task of figuring out what it all means begins. The final gratification will come when we can really crack the code—how did the solar system come about, how did it evolve, why is the earth so unique in our solar system, what can we learn about billions of other solar systems expected to be present in the universe, etc. etc. We are not there yet in our quest, but planetary exploration missions, such as Voyager, Galileo, Cassini-Huygens, Juno, Mars Rovers, Mars Science Laboratory, etc., are paving the way. Those of us who are part of this adventure feel some gratification in being able to contribute to the advancement of humanity in some small way."

NASA, the European Space Agency, and Italian Space Agency joined forces to create the Cassini-Huygens mission launched from Earth in 1997 to explore Saturn and its moons.

And while NASA budget priorities for manned missions may imperil future unmanned probes, such as Cassini-Huygens, Atreya is undeterred. "This makes our job only so much more challenging!" he says. "Nevertheless, the planetary community is solidly behind robotic exploration of the solar system, which we hope will see us through these difficult times. We are also working harder at engaging our international partners in Europe and Asia in joint planetary exploration, and Cassini-Huygens is an excellent success story that speaks for itself."

More information on Atreya's work can be found at http://www.umich.edu/~atreya S&D

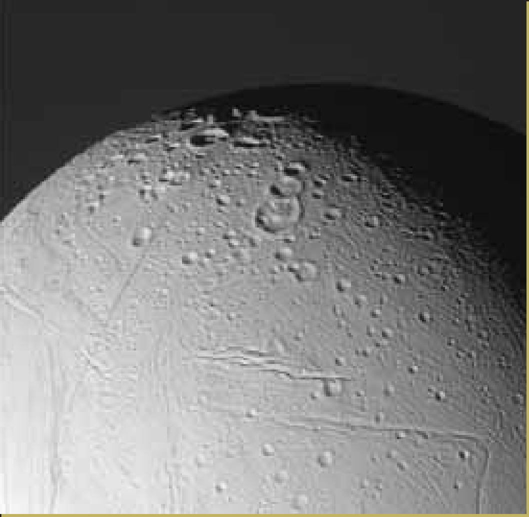


IMAGE OF ENCELADUS TAKEN DURING THE CASSINI ORBITER'S CLOSEST-EVER APPROACH ON MARCH 9, 2005. COURTESY OF NASA/JPL/SPACE SCIENCE INSTITUTE

A TALE OF TWO MOONS

One moon is second largest in the entire solar system, larger than Pluto and almost as large as Mercury. The other, no wider than Arizona, is but a bright speck among Saturn's 35 named moons. One tantalizes with a thick atmosphere that shrouds its surface. The other dazzles with bright sunlight reflected from its ice crust.

Over the last year, both moons have been "stars" of special magazine treatment—one in *Nature* in December 2005 and the other in *Science* in March 2006—as they have offered up bits of their stories to instruments on the Cassini-Huygens mission to Saturn and its rings and moons.

The data the instruments have been able to send back to Earth are keeping University of Michigan space scientists, who have leading roles in the Cassini-Huygens mission, busy thinking about how atmospheres are developed and maintained and what it may reveal about the formation of the solar system and our own planet.

Titan, Saturn's mega-moon, is the largest moon of Saturn. Because scientists were unable to see through its thick atmosphere, they sent a probe loaded with six instruments parachuting to its surface.

After a seven-year-long journey to upper reaches of the Titan atmosphere, the Huygens probe collected data for more than two hours on the 400-mile-long descent through the atmosphere and another hour after touching down on the Titan surface on January 14, 2005. (See "Saturn's Moon Sheds Light on Earth's Early Atmosphere" for more on what U-M space scientists have learned about Titan.)

Six months after the Huygens probe touched down on Titan, another moon drew attention as the Cassini spacecraft made its closest approach to Enceladus on July 14, 2005, flying only about 109 miles above the moon surface. In a special issue of *Science* published on March 10, 2006, scientists reported what they have learned about this intriguing moon from that flyby and two earlier ones.

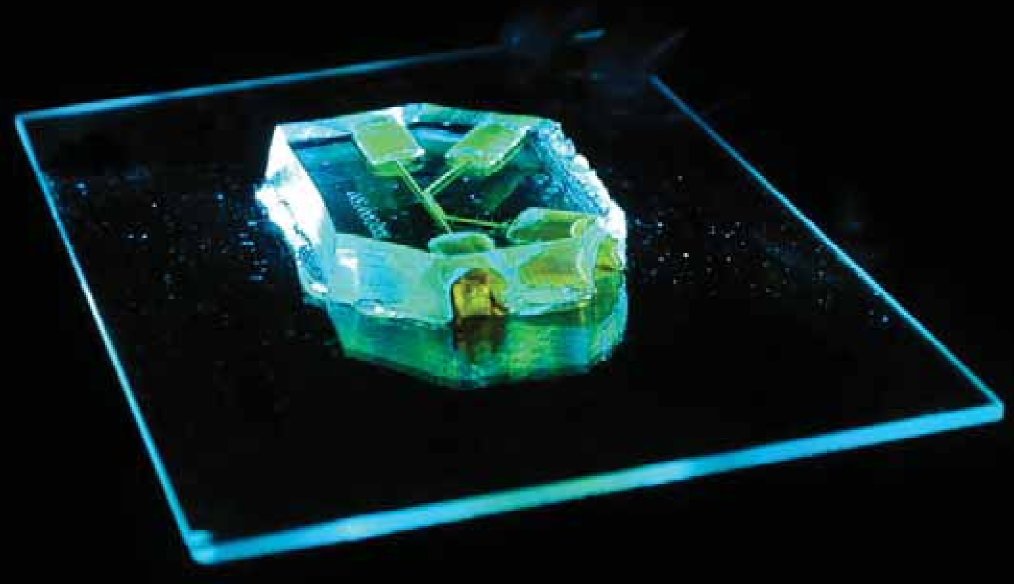
U-M Atmospheric Science Professor J. Hunter Waite, Jr. is the team leader for the Ion and Neutral Mass Spectrometer Subsystem (INMS), which is gathering data to study the neutral gases and positive ions in the atmospheres of Saturn and Titan and gases in and near the rings and other Saturn satellites. From the Enceladus flyby, the INMS data reveal that the moon's atmosphere is about 65 percent water vapor, with significant amounts of carbon dioxide, methane, and either carbon monoxide or molecular nitrogen. The variation of water vapor density with altitude suggests the water vapor may come from a source near Enceladus's south polar ice caps, which some scientists compare to a Yellowstone-like geyser of water vapor, ice, and dust particles.

That the atmosphere persists on this low-gravity world, instead of instantly escaping into space, suggests the moon is geologically active enough to replenish the water vapor at a slow, continuous rate, according to the scientists.

While Titan's large size was consistent with a geologically active moon, Enceladus's active geology was a surprise to space scientists. The Cassini flyby also confirmed that Enceladus seems to be the source of the particles that form the largest of Saturn's famous rings.

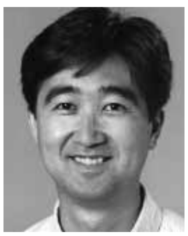
The Cassini mission continues until at least 2008 and may be extended to 2010. S&D

THIS ARTIST'S RENDERING SHOWS THE NOTABLE BRIGHT SURFACE OF ICY ENCELADUS. IN THE FOREGROUND, AN ICE GEYSER CAN BE SEEN PROJECTING A JET OF VAPOR INTO SPACE. BY DAVID SEAL



BIG PLANS FOR TINY MICROCHANNELS

GARY SMITH



SHU TAKAYAMA

A small clear block, easily mistaken for a large ice cube, sits on the desk. On closer examination—holding it a few inches from your eye—you can see a little detail inside the cube. Something like an elongated letter "U" seems to have been scratched through the middle of the block. And the block, though clear like ice or glass, is rubbery, not hard.

This unassuming little device supports a large field—the remarkable world of microfluidics. The "block" is called a "chip" and the details inside are "microchannels," about the size of a single human hair. These chips can be designed to mix extremely small quantities of liquids for chemical and biochemical tests and an increasing array of other uses. This particular microfluidics chip has been developed by University of Michigan researchers as an "embryo culture chip" to aid *in vitro* fertilization (IVF) techniques. So far, the U-M researchers have published in academic journals, developed several inventions, and established a new company to bring these emerging technologies to broader use.

This research, says U-M reproductive biologist Gary Smith, "shows how interdisciplinary collaborations can attain great things. We have a biomedical engineer, a reproductive biologist, and an entrepreneur coming together to create a company that has the potential to turn our research into something really useful."

Smith is associate professor of obstetrics and gynecology, urology, and physiology at the U-M Medical School. Other team members are Shu Takayama, associate professor of biomedical engineering and of macromolecular science and engineering at the U-M College of Engineering, and Michael Crowley, a 2005 MBA graduate of the U-M Ross School of Business. The three have formed Incept Biosystems to move their infertility technology from the lab to the market. (For the Incept Biosystems story, see page 11.)

"From a gamete or embryo biologist point of view, there were certain conditions within the body that we would like to replicate in culture, but we could not with technology and methods previously available," says Smith. For instance, various efforts have gone into perfecting the nutrient solution and ways to change it over time for growing embryos, or to monitor the development of embryos. But Smith says there remains much room for improvement in these and other areas of clinical laboratory practices for treating infertility.

Chance Meeting

In the fall of 2001 Takayama presented a seminar at the Medical School on "Microtechnologies for Cell and Developmental Biology" that piqued Smith's interest. "At the time, I knew nothing about microfluidics," recalls Smith. "After the seminar, I approached Shu, we began to talk, organized joint lab meetings, and it just started to come together."

Takayama notes that when he and Smith first met, microfluidics was primarily being used for chemical analyses, such as detecting or identifying proteins or DNA fragments—dubbed "lab-on-a-chip" applications. Few researchers were working with whole cells, such as embryos. "I had done work with cells and microfluidics as a postdoc and was focusing effort in this burgeoning area as an assistant professor, so I was intrigued by the questions Gary raised about sorting sperm or determining embryo development as part of the IVF process," says Takayama.

In vitro fertilization to assist human reproduction is a mature technology in use for more than 20 years. Hundreds of clinics in the U.S. and around the world perform the procedure each year, which involves removing eggs from a woman's body and combining them with sperm in a Petri dish. After a few days, fertilized eggs or embryos are returned to the woman's body where it's hoped that the embryo will develop into a healthy pregnancy.

But IVF doesn't meet the needs of all couples. In some, the sperm count is too low or have inadequate motility to successfully fertilize an egg when combined in a Petri dish. A method to overcome this problem is a technique called intracytoplasmic sperm injection (ICSI) where a single sperm is injected into an egg. If fertilization occurs, resulting embryos are transferred to the woman.

Smith and Takayama's collaboration, performed in conjunction U-M assistant professor Timothy Schuster and graduate student Brenda Cho, led to the application of microfluidics as a potentially advantageous means of sperm isolation for some couples where the man's sperm count or motility is poor. Thus far experiments look very promising.

No Turbulence

There are several ways that microfluidics may make a difference to IVF success. One is to improve the sperm sample used to fertilize the egg. Takayama and Smith developed a "sperm sorter" that separates motile sperm from inactive sperm in a semen sample. Two narrow channels enter the sorter from different starting points, then flow alongside each other in parallel fashion. Because the channels are so small, there is no turbulence in the streams and the two can flow side-by-side without mixing.

To "sort" sperm, a semen sample flows into one channel, while a solution that supports cell culture enters the other channel. When the two meet to flow side-by-side, some of the active sperm swim from the stream of semen to the other stream. The streams then separate with the cell culture stream having a highly enriched population of motile sperm, which can be directed to a waiting oocyte, or egg cell.

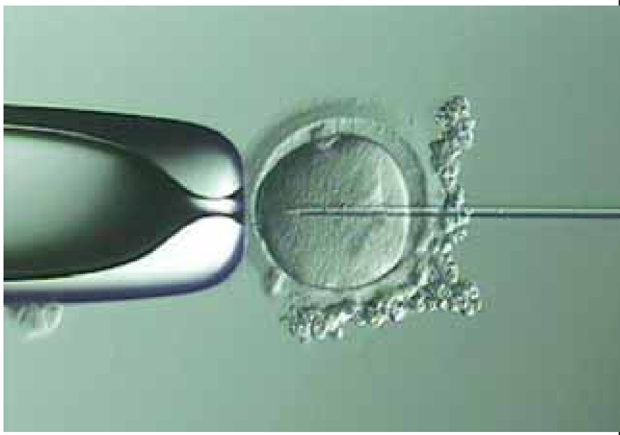
"The sperm sorter allows us to isolate active, motile sperm," explains Smith. And since it relies on the sperm's activity to cross from one fluid stream to the other, and not centrifugal forces as currently used today, there is less potential of physical sperm damage.

A second microfluidics chip has been developed to facilitate fertilization. This chip is designed to permit cell culture solution containing sperm to flow to a waiting egg. The channel provides a space large enough for the egg, with very small outlets so that the cell media can exit. The researchers point out that this set-up has features more like the fallopian tube, and constrains the area of egg and sperm interaction, thus removing the randomness present in current practices of *in vitro* fertilization within the Petri dish.

Smith, Takayama and Ronald Suh, a former resident in the U-M Department of Urology, published the results of experiments using their

"From a gamete or embryo biologist point of view, there were certain conditions within the body that we would like to replicate in culture, but we could not with technology and methods previously available."

MICROFLUIDIC TECHNIQUES BEING DEVELOPED AT THE U-M OFFER AN ALTERNATIVE, LESS-INVASIVE FERTILIZATION METHOD COMPARED TO THE DIRECT INJECTION OF A SPERM INTO AN OOCYTE SHOWN HERE.

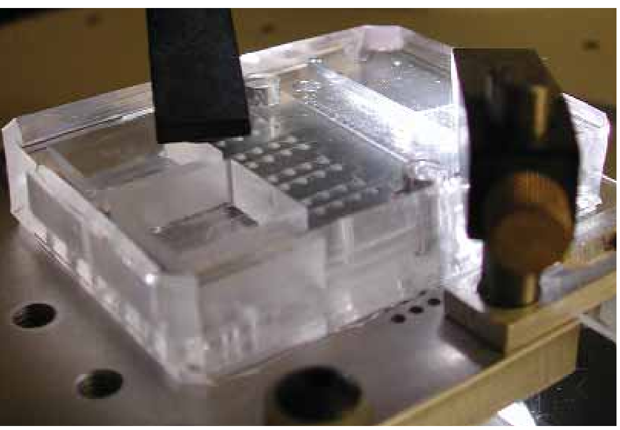


microfluidics chip to conduct IVF using mice sperm and eggs. The report appeared in the February 2006 issue of the journal *Human Reproduction*. They conducted trials at several low levels of sperm. They found that at normal sperm counts of 500,000 mouse sperm per milliliter, their microfluidic method was less successful than the standard Petri dish method. However, when the sperm count was dropped to extremely low level of 20,000 sperm per milliliter, significantly better fertilization rates were obtained with microfluidic insemination compared to the standard Petri dish.

Mimicking Nature

"We're not sure yet why the microfluidic system is sub-optimal when high concentration sperm samples are introduced," says Smith. One hypothesis is that the microfluidic system, which contains a grating to capture the egg also increases the local sperm concentration around the egg so that the sperm depletes the energy supply and their motility drops off significantly over time. But when the initial sperm count is low, then the concentrating effect of the grating and closer proximity of sperm and egg in the microfluidic system enhances fertilization compared to the Petri dish method.

THIS "CHIP" HAS BEEN ADAPTED TO ALLOW FLOW CONTROLS THROUGH ITS MICROCHANNELS, ALL CONTROLLED BY A MODIFIED BRAILLE PRINTER.



Their current efforts to more closely mimic actual biological systems have the U-M scientists working on other ways to use microfluidics to improve IVF success rates. "Research shows that the environments in the oviduct and in the uterus are chemically different," says Smith. Thus, IVF clinics often place embryos during the first few days of development in one variety of cell media, then a few days later, move developing embryos into a new Petri dish with a slightly different cell culture solution.

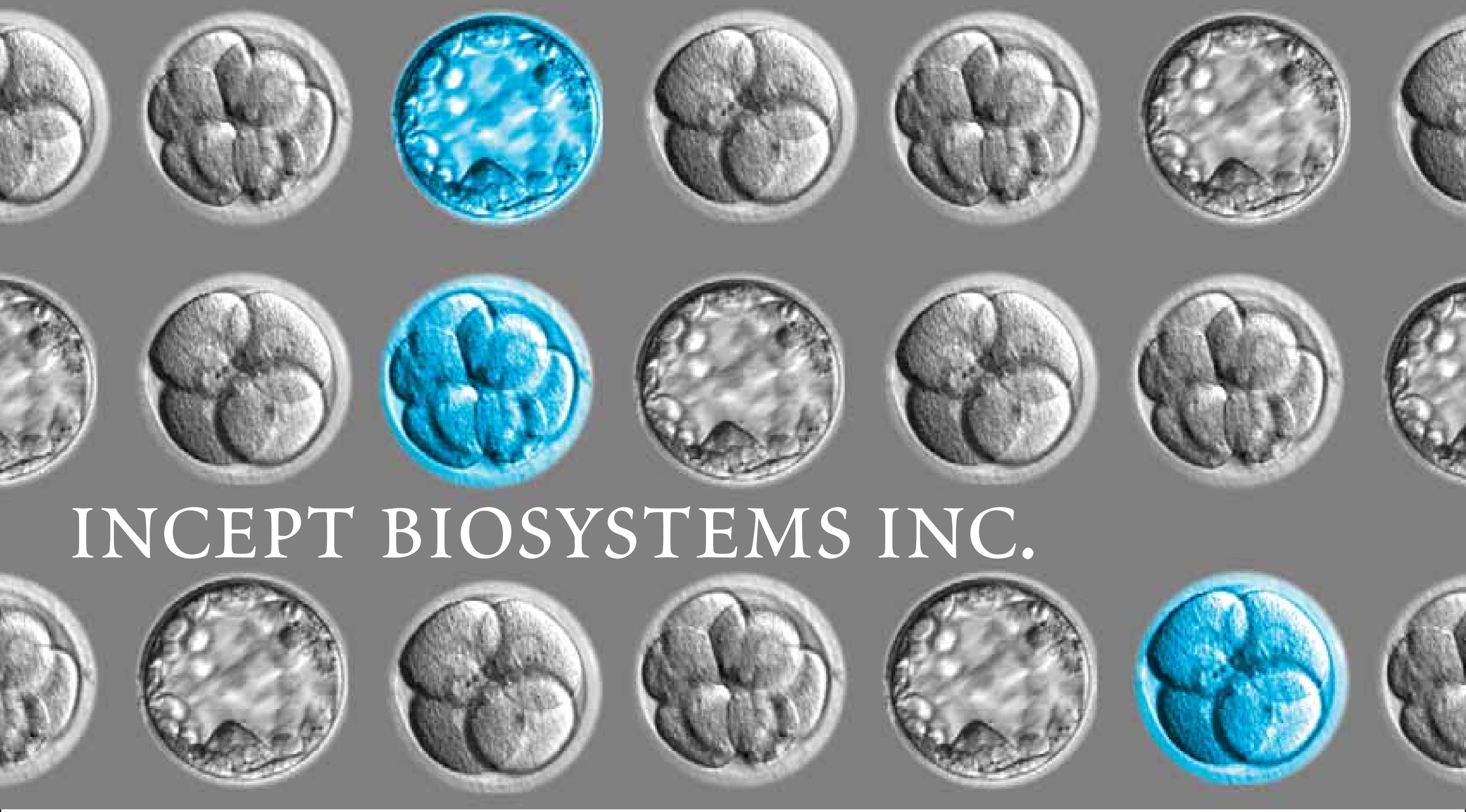
"In the body, however, the change in chemical composition is gradual," says Smith. "We think a microfluidics system might be able to better duplicate this simply by making it possible to change the cell medium more gradually over time."

This gradual shift in solutions requires a way to start and stop the flow, something that has proven difficult on the miniscule scale of microfluidics. A common method has involved moving extremely small cubes of material into and out of a microchannel opening using pumps that, compared to the size of microfluidics circuits, are big and bulky.

Takayama, with help of undergraduate student Wei Gu and postdoctoral research associate Nobuyuki Futai, has come up with a remarkable new approach by adapting a device originally built to enable the visually impaired to read computer text as Braille characters using their fingertips. The Braille displays use a grid of eight pins, which can be raised in various patterns to represent letters and other symbols. In their adaptation, the pins push against the outside of the silicone rubber chip. The pressure applied deforms the channel and stops or pumps the fluid flow.

"The great thing about this development is that it eliminates the need to add more tubes and external pumps to the system," says Smith. Also, because the Braille pin movement is electronic and computer regulated, it can run by computer-controlled software originating from a remote controller outside an incubator, where cells and fluids can be kept under the proper conditions.

"The ability to use valves and precisely move cell media is key," adds Smith. "It's something we've never done previously in gamete-embryo research or laboratory clinical procedures." S&D



INCEPT BIOSYSTEMS INC.

Incept Biosystems Inc. has come a long way in the last three years. In 2003, the technology that drives the company was in the mid to late stages of research — one of many promising projects underway at the University of Michigan. In this case, Associate Professor of Biomedical Engineering Shuichi Takayama and Associate Professor of Obstetrics and Gynecology Gary Smith, who also directs a U-M Health Systems fertility treatment laboratory, were making significant enhancements to an ingenious microfluidic device developed by engineering undergraduate student Wei Gu and postdoctoral researcher Nobuyuki Futai.

With the adaptation of off-the-shelf Braille technology to act as a heart for fluidic micro-channels, the two scientists were able to create a device that housed an array of tiny valves and pumps ideally suited for evaluating, culturing, and sorting cells. Although the science was progressing well, the two had reached an impasse. Was their product commercially viable? If so, what market niche should they be pursuing? And where could they find the market research expertise they needed at this crucial juncture?

The answer to those and other key questions arrived in the form of TechStart volunteer researcher and Michigan MBA student Mike Crowley. Crowley had arrived at the Stephen M. Ross School of Business with a specific goal in mind. "Having presided over three other start-up ventures," he says, "I knew I wanted to do another technology start-up."

So when the time came to shop around for MBA programs, Crowley didn't contact business schools directly. Not at first, anyway.

Instead, in the spring of 2003, he made a short list of leading universities and called their technology transfer offices. "I definitely wanted an MBA degree," Crowley says. "But I knew that in order to spin something out properly, I would have to immerse myself in the campus research environment. I'd have to find a network of resources. And that meant going through technology transfer."

Of all the contacts he made at various schools, the group that impressed him most was the University of Michigan Office of Technology Transfer. "They were by far the most welcoming and enthusiastic. In particular, their TechStart program was a real point of interest for me. I liked the way it brought together graduate student consultants with faculty scientists and inventors."

Following a series of discussions with U-M Tech Transfer staff members, Crowley enrolled in the Ross School of Business. To jump-start his quest, he co-founded the Nanotech Commercialization Group (NCG), a team of business student

"I can't think of another university that offers entrepreneurs and scientists such a synergistic combination of resources and technology."

consultants. It was through NCG that he began doing volunteer research projects for Tech Transfer and ultimately met his future business partners—Smith and Takayama.

By the spring of 2004, after a commercial platform for the technology had been developed, the next logical step was TechStart and a multidisciplinary team of graduate student consultants. As part of that team—which included students from law, business and science—Crowley helped explore new applications for the technology. Through their research, the TechStart cohorts confirmed that the device could help infertility clinics solve their biggest single challenge: selecting the healthiest embryos for transfer.

"So," as Tech Transfer Executive Director Ken Nisbet points out, "TechStart did what it was intended to do. It accelerated the project, provided guidance on commercialization options and brought people together to, in this case, consider a new business startup."

Which is exactly what Crowley, Takayama and Smith began to do—with considerable help from Tech Transfer staff members, especially Karen Studer-Rabler. "Our tech transfer staff has the experience and resource connections to move projects forward with speed and skill," Nisbet notes. "Scouting for critical early stage funding, adding commercialization talent, and providing guidance and encouragement is a very necessary role that we're happy to fill for our inventors and partners."

By January of 2005, Crowley was president of Incept BioSystems and the company had won $75,000 from nationwide business competitions and $10,000 from the Dare to Dream Competition sponsored by the U-M Ross School of Business. It had also helped to secure an additional $102,000 grant from the Michigan University Commercialization Initiative plus $364,000 in NIH grants, approximately $400,000 from the U.S. Department of Agriculture, and $957,000 from the Michigan Tri-Corridor Fund to the U-M labs.

Today, Incept is well on its way to securing $2 million in first-round venture funding, enough to get the company to the point of meeting key development milestones.

Thanks to teamwork and collaboration, the company has generated strong data demonstrating the ability of its device to determine embryo efficacy. "This data surpassed even our most optimistic hopes," Smith explains. "It shows that we've effectively closed the gap between what happens in a Petri dish and what happens in a human body. It's a significant jump forward for the fertility industry, and it's generating a great response among investors who like our novel approach."

According to Crowley and his faculty partners, Incept is a true University of Michigan success story. "We've been able to leverage every asset the University has to offer, including Tech Transfer, TechStart and the Business School," Crowley says. "Michigan has been our partner in every sense of the word. And quite frankly, I can't think of another university that offers entrepreneurs and scientists such a synergistic combination of resources and technology." S&D

TECHSTART

Developing the Entrepreneurs of Tomorrow

TechStart alumnus Mike Crowley has nothing but praise for the summer consulting program, which brings together graduate students from business, engineering, science, law, and other disciplines and pairs them U-M faculty in search of consulting expertise. "More than anything else, TechStart has a broad view of the technology landscape," Crowley says. "It has the unique ability to teach people how to become entrepreneurs. I certainly couldn't have gotten Incept off the ground without it."

THE 2005 TECHSTART TEAM INCLUDED (PICTURED BELOW LEFT TO RIGHT) SYLVIE KHAJURIA (MASTERS OF SCIENCE IN INFORMATION), TRUSHAR NAIK (MD/MBA DUAL-DEGREE PROGRAM), ROY ESAKI (MD PROGRAM), LINDA SANCHEZ (MASTERS OF SCIENCE IN BIOMEDICAL ENGINEERING), CRAIG KOMANECKI (JD PROGRAM), JAY NG (MBA PROGRAM), WENYUN "SUNNY" SUN (MASTERS OF SCIENCE IN FINANCIAL ENGINEERING AND INFORMATION SCIENCE) AND MARK MAYNARD (U-M TECH TRANSFER).

According to TechStart Director Mark Maynard, the program serves a number of different functions. "It's a kind of business matchmaking service," he notes, "a way of introducing faculty to outstanding student talent." Unfortunately, at the end of their summer assignments, most TechStart team members don't have the luxury of continuing with their client companies. Instead, facing the specter of student loans, the majority of them move into the corporate world.

However, very soon, TechStart student consultants may have another option. As Maynard explains, "In the near future, we hope to offer TechStart participants year-long stipends. By mitigating the risk factor, and providing a measure of financial security, these stipends would serve as a bridge—giving students the option of exploring entrepreneurial opportunities and giving U-M faculty access to extraordinary talent and expertise." S&D

NOTES FROM WASHINGTON

New Director of Federal Relations for Research in DC

Sarah Walkling has been named the new director of federal relations for research and assistant director of the Washington, D.C. office. Walking will work with faculty and staff to strengthen U-M's profile in Washington. She will coordinate the University's interactions with Congress and the executive branch on research-related issues. Walkling will also advise and brief faculty and administrators on federal legislative activities, regulatory and policy developments, and she will coordinate liaison actions.

Walkling comes to the U-M from Vanderbilt University, where she served as associate director of the D.C. office for the past four years. In this role, she coordinated the annual appropriations and legislative campaigns for Vanderbilt and worked closely with deans, public affairs staff and community leaders to develop strategies on numerous topics, such as nanotechnology, energy research and export control policies.

Prior to Vanderbilt, Walkling served as the senior legislative assistant to Rep. Rosa DeLauro, D-Conn., from 1997–2002. In this capacity she advised the Congresswoman on defense appropriations and on federal policies that affect research universities and the business communities surrounding them. She also served on the staff of the Select Committee to create the Department of Homeland Security.

SARAH WALKLING

Prior to her work with the Select Committee, Walkling worked as a senior analyst with the Arms Control Association, where she focused on conventional arms control and sat on the Steering Committee for the Campaign to Ban Landmines. From 1993–1994, she was an analyst at the Science Applications International Corp., where she tracked arms control treaty implementation.

Walkling graduated from the University of Chicago with a master of arts degree in international relations and from Cornell University with a bachelor of arts in history. S&D

RESEARCH NOTES

U-M Professor's Nanotech company secures $30 million investment

NanoBio Corporation, a company founded by Dr. James R. Baker, Jr., the Ruth Dow Doan Professor of Biologic Nanotechnology at the University of Michigan, has secured $30 million in funding from Perseus, L.L.C., a leading private equity fund management company based in Washington, D.C.

The investment is one of the largest single institutional investments in a biotechnology company in the state of Michigan.

Established in Ann Arbor six years ago, NanoBio Corporation develops therapies and vaccines against infections ranging from cold sores to nail fungus and influenza using a novel nanoemulsion technology developed at Michigan.

"This is an outstanding example of the way academic research at the University of Michigan spawns new ideas that will create economic growth in the region," said U-M President Mary Sue Coleman. "Our enhanced technology transfer efforts and the support of the Michigan Economic Development Corporation have paid off handsomely in the case of NanoBio, and we are expecting many more successes to come."

"The University is proud that it could provide the environment for Dr. Baker to conduct this science and to launch this promising company," said Stephen R. Forrest, U-M vice president for research. "This groundbreaking technology is positioned to create a wide range of treatments that could dramatically improve human health in the years ahead."

NanoBio's nanoemulsion consists of very tiny droplets of oil—each just one-thousandth the diameter of a human hair—suspended in water and stabilized by detergents. The droplets in the nanoemulsion are surface active and react specifically with the outer membrane of infectious organisms. This reaction tears the pathogen membrane, which kills the organism. The technology works differently than antibiotics or traditional antiseptics, and is safe for humans, animals and the environment.

OVPR Announces New Award for Innovators

In June, Stephen Forrest, vice president for research, announced the establishment of a new award to recognize innovation related to research at the University of Michigan. Called the Distinguished University Innovator Award, this prestigious honor will recognize a faculty member or small team led by a faculty member who have demonstrated a noteworthy accomplishment through the development of a transformational innovation, movement of an innovation to market-readiness, or creation of new means for moving innovations from the University into the private sector.

The awardee or team receives a $5000 honorarium and is invited to deliver a lecture on a topic related to his or her accomplishments.

"I can envision several ways for a nominee to demonstrate the qualities called for by this award," says Forrest. "He or she may invent a new technology and then show, perhaps in partnership with others inside or outside the University, that this technology can make a significant contribution to a particular need or private sector area of business."

This award may also go to those who have successfully worked to develop and foster partnerships or other initiatives that significantly promote the strategic or economic progress of the region, state or nation, he added.

Nominations are due November 10, 2006. The first award will be announced in January, 2007.

OVPR Seeks New Associate Vice President in Humanities and Social Sciences

Stephen Forrest, vice president for research, recently opened a search for a U-M faculty member to serve as an associate vice president with special responsibilities for humanities and social sciences. "OVPR takes seriously its responsibilities to serve all faculty involved in research and scholarship," says Forrest, "We need someone who can build and maintain close links with faculty in the humanities and social sciences in order to fulfill this responsibility." To submit the names of candidates or to apply for the position, contact Marvin Parnes in OVPR.

Research Administrators Honored

The Office of the Vice President for Research (OVPR) presented awards to three staff members at a May 4 reception to recognize their noteworthy service to campus research administration. The Distinguished Research Administrator Award was presented to Violet Elder, administrative director, Center for Computational Medicine and Biology, Medical School; Ruth Freedman, administrative director, Molecular and Behavioral Neuroscience Institute, Medical School; and Jane Holland, administrative director, Department of Microbiology and Immunology, Medical School.

The Distinguished Research Administrator Award honors people from any unit at the University who have demonstrated distinguished service exemplifying the goals of professional research administration. The winners were selected by Vice President for Research Stephen Forrest with the assistance of an awards advisory committee: Kelly Cormier, College of Engineering (CoE); Betty Cummings, CoE; Julie Feldkamp, Division of Research, Development and Administration; Francine Hume, Medical School; and Dennis Martin, Medical School.

Ford School Program to Explore Policy, Technology Nexus

A new program at the University will enable graduates to better affect science and technology policymaking that runs through so much public debate.

The Gerald R. Ford School of Public Policy will offer a graduate certificate in science, technology and public policy, including courses about how science and technology are influenced by politics and policymaking, through the new Science, Technology, and Public Policy Program.

Starting in the 2006-2007 academic year, the graduate certificate program will be available to all master's and doctoral students. The program also will sponsor seminars and conferences featuring leading scholars and policymakers involved in science and technology policy issues.

"We believe this certificate program will be a perfect complement to existing educational initiatives at the University," says Rebecca Blank, Ford School dean. "It should help to position the University of Michigan as a leader in science and technology policy matters at both the national and international level."

Former U-M President James Duderstadt, professor of science and engineering, and Shobita Parthasarathy, assistant professor of public policy, will direct the program. The program is the result of work over several years by an OVPR-sponsored committee that Duderstadt chaired.

Only a handful of educational programs at the graduate level in the United States focus on science and technology policy issues. Duderstadt says the new U-M program will offer a variety of courses to bridge the instructional gap between science, technology and public policy.

ISR Wins $70M Grant for Study on Aging

In June, the National Institute of Aging announced that it will renew the project grant for the University of Michigan Health and Retirement Study (HRS) providing the Institute for Social Research (ISR) $70 million over the next six years to study the health and economic well-being of older Americans.

"Since it began in 1992, the Health and Retirement Study has provided a vast amount of information about the health and economic status of the aging U.S. population," Dr. Richard Hodes, director of the National Institute on Aging, told Booth News Service.

The HRS paints a detailed portrait over time of older Americans' physical and mental health, insurance coverage, financial well-being, labor market status, retirement planning, social support systems, intergenerational transfers of time and money, and living arrangements. "It makes a powerful tool for understanding societal aging," said James Jackson, ISR director.

At a briefing in Washington, D.C. in June, Michigan Congressman John Dingell announced the new award, calling the project a "great opportunity" for the state of Michigan and the nation. "We're talking here about information that is going to be valuable," he said.

The study, started in 1990, surveys more than 20,000 people every other year to provide data on people from pre-retirement to advanced age. The HRS is co-directed by David Wier, ISR economist, and Robert Willis, LSA professor of economics. About 40 researchers participate in the project in Ann Arbor, and another 150 interviewers work for HRS around the country.

New to the project this year is the collection of detailed medical information as well as DNA samples from some respondents. Wier said the samples will give scientists the opportunity to examine the influences of both genetics and social factors on seniors health and well-being.

U-M-led Team Funded to Develop "Perfect" Imaging Materials

A U-M research team led by Physics Professor Roberto Merlin, will receive a combined total of $5 million over the next five years to support an interdisciplinary research project on negative refraction. The group of physicists, electrical engineers, materials scientists, chemists and biologists from five universities will explore methods to produce new synthetic materials that can refract, or bend, light waves "backwards." The other Michigan team members are Vice President for Research and Physics Professor Stephen Forrest, and Materials Science & Engineering Professors Rachel Goldman and Jinsang Kim.

One goal of this research is to create materials that can perform as a lens without needing the curved surfaces found in traditional lenses. It has been predicted that materials with negative refraction can image objects that are significantly smaller than the wavelength of light. Although this is an impossible task for common materials, this may be achieved by the development of negative refraction media.

The negative refraction project is one of 30 in the nation to be funded by the Department of Defense (DoD) in fiscal year 2006 under the Multidisciplinary University Research Initiative (MURI) program. David Martin, U-M professor of materials science and engineering and of biomedical engineering, is involved in another new MURI project aimed at improving the control of prosthetics directly linked to the nervous system.

The MURI program is designed to address large multidisciplinary topic areas representing exceptional opportunities for future DoD applications and technology options. The awards provide long-term support for research, graduate students and instrumentation development to support science and engineering research themes vital to national defense. S&D

OVPR INITIATIVES

One of the key roles served by the Office of the Vice President for Research is the development and promotion of research initiatives. These initiatives aim to enhance existing areas of expertise as well as create new strengths in areas of special interest to the faculty. But these initiatives are not just the "property" of OVPR. In all cases, the office works with the schools and colleges and interested faculty to make sure that these activities have the greatest impact possible. Two on-going examples of OVPR-supported initiatives are the Nano-Science and Engineering Initiative, and the Initiative on Energy Science, Technology, and Policy.

Nanoscience and Engineering Initiative (NSEI)

Nanoscience involves understanding physical processes of matter at the nanoscale (10-9 m), and nanotechnology involves the creation of materials and processes that are engineered at this scale. The University of Michigan is a leader in this important area of discovery, but continuing investment in faculty and infrastructure are needed to keep pace in this rapidly changing field. Hence, OVPR launched the Nanoscience and Engineering Initiative in the spring of 2005 in collaboration with several schools and colleges. The initiative has focused on providing support for teams of researchers seeking major external research awards, and providing strategic seed funding. Lastly, NSEI will support the schools and colleges as they recruit leading faculty in nanoscience and engineering to Michigan.

Energy Science, Technology and Policy Initiative

The nation has recently re-awoken to the importance of energy generation and consumption to our economy, lifestyle, and environment. Michigan has a long tradition in energy related research, and the goal of OVPR is to support and strengthen Michigan's expertise in energy science, technology, policy, and education. In the fall of 2003, then-Vice President Fawwaz Ulaby asked President Emeritus James Duderstadt and a group of interested faculty to explore how Michigan could strengthen its research activity in hydrogen generation, storage, and use as a source of energy. Over the ensuing 18 months, the group's scope of discussion expanded beyond hydrogen, as did its membership, until the committee was officially transformed last fall into the Michigan Energy Research Council (MERC). MERC was charged with developing recommendations for how the University could support a broad range of existing energy-related research activity and develop strengths in critical and emerging research areas. In June, MERC submitted a draft of its recommendations to Vice President for Research Stephen Forrest. A key recommendation of MERC is the development of a University-wide enabling organization to facilitate multidisciplinary research, seed the growth of emerging research areas, and advocate for Michigan's energy-related activities both within and outside the University. The Council recommended that the Michigan Memorial Phoenix Project (our WW II memorial originally dedicated to the peaceful use of nuclear energy) be transformed into the Michigan Memorial Phoenix Energy Institute (MMPEI) and serve as the University's energy research "enabling organization."

In parallel with MERC's development of the energy institute proposal, OVPR has been formulating an Initiative on Energy Science, Technology, and Policy that would provide resources to the campus community and empower the MMPEI. OVPR will provide support for faculty to encourage campus-wide emphasis on research, and to assist with hiring new faculty members in areas of energy research that are currently underserved at the U-M. The creation of the Phoenix Energy Institute will strongly enhance and support OVPR's efforts, and it will ultimately become the focus of our University-wide energy initiative. Also, MMPEI will be a fitting complement to the newly established Graham Environmental Sustainability Institute. OVPR will be working with the University community to formulate and implement the energy initiative in the coming months. S&D

OFFICE OF
THE VICE PRESIDENT
FOR RESEARCH

4080 Fleming Building
503 Thompson Street
Ann Arbor, MI 48109-1340

UNIVERSITY OF MICHIGAN

CONTACTS

Stephen R. Forrest
Vice President for Research
734/764-1185, stevefor@umich.edu

James A. Shayman
Associate Vice President
734/936-2680, jshayman@umich.edu

Steven L. Ceccio
Associate Vice President
734/936-3933, ceccio@umich.edu

Marvin G. Parnes
Associate Vice President
and Executive Director
for Research Administration
734/936-3933, mgparnes@umich.edu

Judith A. Nowack
Associate Vice President
734/763-1289, jnowack@umich.edu

Sarah K. Walkling
Director of Federal Relations
for Research & Assistant Director,
U-M Washington Office
734/764-1185; 202/554-0578,

Curt W. Smitka
Director, Budget & Administration
734/936-2681, cwsmitka@umich.edu

RESEARCH UNITS

Biophysics Research Division (BRD)
Open
734/764-5258

Center for Human Growth
and Development (CHGD)
Daniel P. Keating, Director
734/764-2443, keatingd@umich.edu

Institute for Research
on Women and Gender (IRWG)
Carol J. Boyd, Director
734/614-6468, caroboyd@umich.edu

Magnetic Resonance
Imaging Facility (fMRI)
John Jonides, Co-Director,
734/764-0192, jjonides@umich.edu
Douglas C. Noll, Co-Director,
734/764-9194, dnoll@umich.edu

U-M Transportation
Research Institute (UMTRI)
Peter F. Sweatman, Director
734/764-6505, sweatman@umich.edu

ADMINISTRATIVE/ SERVICE UNITS

Business and Industrial
Assistance Division (BIAD)
Marian J. Krzyzowski, Director
734/998-6201, mjsk@umich.edu

Center for Statistical Consultation
and Research (CSCAR)
Edward D. Rothman, Director
734/763-2052, erothman@umich.edu

Division of Research Development
and Administration (DRDA)
Marvin G. Parnes, Executive Director
734/936-3933, mgparnes@umich.edu

Institutional Review Boards (IRBs)—
Behav-Sci and Health
James A. Shayman, Director
734/936-2680, jshayman@umich.edu
IRB office: 734/936-0933,
irbhsbs@umich.edu

Office of Human Research
Compliance Review (OHRCR)
Ronald F. Maio, Director
734/ 647-0489, ronmaio@umich.edu

Office of Technology Transfer (OTT)
Kenneth J. Nisbet, Executive Director
734/763-0614, knisbet@umich.edu

Unit for Laboratory
Animal Medicine (ULAM)
Howard G. Rush, Director
734/764-0277, hgrush@umich.edu

Women in Science
and Engineering (WISE)
Cinda-Sue Davis, Director
734/647-7012, 734/615-4455,
csdavis@umich.edu

INCUBATOR UNITS

Core Technology Alliance (CTA)
of the Michigan Life Sciences Corridor
M. Walid Qoronfleh, Executive
Director
734/763-2948, walid.qoronfleh@vai.org

Hydrogen Energy
Technology Lab (HETL)
Levi Thompson, Director
734/936-2015, ltt@umich.edu

Imagining America
Julie Ellison, Director
734/615-8370,
imaginingamerica@umich.edu

U-M Substance Abuse
Research Center (UMSARC)
Margaret E. Gnegy, Director
734/998-6500, pgnegy@umich.edu