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MIT technology insider

FROM THE EDITORS OF TECHNOLOGY REVIEW

January 2007

SPINOFF SPOTLIGHT

Targeting a Network

Merrimack Pharmaceuticals identifies new drug candidates by deciphering complicated interactions in disease processes

When a group of MIT researchers founded Merrimack Pharmaceuticals in 2000 to try to discover new cancer drugs, they thought it would be five to seven years before they identified even one promising candidate. Today they already have seven anticancer drugs under development.

"The research platform has been so much more productive than we ever expected," says Robert Mulroy, president and CEO of the company, which is based in Cambridge, MA.

Merrimack calls its research platform Network Biology; the idea is to examine the dynamics of a disease process, studying how proteins interact with each other and how biological pathways influence, say, the growth and development of tumors. "A lot of molecular biology was looking at one step at a time," Mulroy says. "Biology is actually governed by dynamic interactions among components. No one really in the world was studying the systems dynamics of biology."

But in the late 1990s, as the Human Genome Project advanced, Peter Sorger, professor of biology and biological engineering at MIT, was taking a systems-oriented approach. A colleague at Harvard, associate professor of chemistry and chemical biology Gavin MacBeath, was working along similar lines. Together they developed methods of printing tiny spots of proteins onto glass. They created plates with three or four shallow wells in them, and printed an array of a couple of hundred different proteins in each well. In experiments they added a different solution containing a dozen or so more proteins to each well and measured how the various proteins interacted—for instance, how a change in one might lead to a change in another, which in turn would send out a new signal to alter what was happening. "It was sparked by a need for dynamic systems data," says Ulrik Nielsen, then a postdoc in Sorger's lab and now vice president of research at Merrimack. "The tools just weren't there at the time."

IMAGE: ISTOCKPHOTO.COM

This type of array has since become common, Nielsen says, but Merrimack, which Sorger and MacBeath helped found, takes the technology a step further. Its scientists use the quantitative data they glean about biological pathways to develop a computational model of a whole system. There can be as many as 700 or 800 biological molecules in a model, Mulroy says, all influencing one another in a complicated feedback system that's hard to visualize. "When we print out maps of our models, they look like the nastiest hairball you've ever seen," he says.

But once they have the models, the researchers can use them to predict how altering a specific pathway would produce different results. For

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MIT TECHNOLOGY INSIDER

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instance, various factors can stimulate the growth of tumors, including hormones, growth factors, and interactions among cells. Once they've identified the network of signals that causes cancer cells to grow, scientists can look for drugs that interfere with those signals and shut down the network. Unlike more traditional approaches to drug discovery, which test compounds against a single target, Merrimack's models predict ways to disrupt one or more interactions among proteins. Mulroy says that's a more focused, and therefore faster, way to find drugs.

"Part of what we're doing is getting a molecular view of what disease is," he says. "Everything after that is actually engineering."

The approach is also narrow enough to help target therapies to specific patients. There are two general approaches to personalized medicine, Nielsen says. One involves actually sequencing a patient's genome to look for individual variations. The other looks for "biomarkers," molecules that act as proxies for a particular type of disease—a person with a prostate tumor might have an elevated level of prostate-specific antigen (PSA) in his bloodstream, for instance. That approach, says Nielsen, is too generic. Rather than look for proxies, Merrimack's models allow it to discover biomarkers directly involved in the disease process, and not those that may be a mere by-product. Such biomarkers might be not just indicators of the disease but potential targets for therapy. He says the same computational models used to identify disease pathways in the first place can also identify biomarkers that reveal which patient has a particular pathway activated, so that a drug developed for that pathway could be given to that patient.

Of the seven possible anticancer drugs the company has in its labs, Mulroy hopes to get one into clinical trials each year over the next five years, starting this year. In general, getting a drug approved can take five to seven years, depending in part on how long it takes to recruit enough patients with the targeted disease into the trials.

Merrimack already has a drug for autoimmune diseases in clinical trials. Called M-093, it is being tested in patients with rheumatoid arthritis, psoriasis, multiple sclerosis, and uveitis, an inflammatory disease of the eye. It is a genetically engineered version of a natural protein called alpha fetoprotein. Women produce more of the protein during pregnancy; many doctors have anecdotally noted a corresponding decrease of symptoms in pregnant patients with autoimmune diseases such as rheumatoid arthritis and psoriasis. The drug was actually developed by Mulroy's former company, Atlantic Biopharmaceuticals, which merged with Merrimack in 2002. Although Merrimack didn't design that drug, the company used its own technology to understand how it works and to figure out which diseases it might treat.

It can take hundreds of millions of dollars to bring a drug to market, and so far Merrimack doesn't have that kind of money. It is doing fairly well, though, with $140 million in four rounds of financing, the latest a $65 million round that closed in April. It has also received more than $1 million in Small Business Innovation Research grants from the National Cancer Institute to develop its technology. Mulroy thinks Merrimack will probably develop drugs until they look likely to succeed, and then partner with a large pharmaceutical company for the marketing phase. It's still a bit early to make those decisions, though, he says.

The company is growing at a good clip, with about 55 employees and an additional 13 job openings. It moved into a new facility in September 2006.

Along with Sorger, MacBeath, and Nielsen, the company's founders were Anthony Sinskey, an MIT professor of microbiology and health sciences and technology, who now sits on the company's board of directors; associate professor of biology Michael Yaffe, who sits on the scientific advisory board; and former biology professor Michael Cardone. Douglas Lauffenburger, the Uncas and Helen Whitaker Professor of Bioengineering and director of MIT's biological-engineering division, sits on the scientific advisory board, as do Sorger and MacBeath.

Liana Moussatos, an analyst at Pacific Growth Equities, calls Merrimack's approach "insightful, unique, and cutting-edge." She says Merrimack is ahead of other companies using systems biology to search for drugs, having already started clinical trials to show that the therapies work. According to Moussatos, "It could be the platform that starts putting personalized medicine into actual practice."

IN BRIEF

COMPANY
Merrimack Pharmaceuticals

CEO
Robert Mulroy

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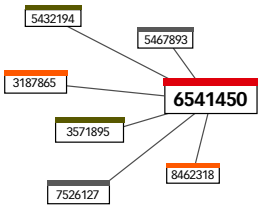
www.merrimackpharma.com

MAJOR PRODUCTS
Drug for autoimmune diseases
Anticancer drugs

FUNDING
More than $10 million

PATENT STRENGTH
Core protection

TIME TO MARKET
More than three years



PATENT MAP
For a graphical analysis of Merrimack's patent position, go to www.ipvisioninc.com/techinsider/01/07.

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We invite you to participate in a brief online survey that will help us improve the *MIT Technology Insider*.

To participate, please visit: http://www.surveymonkey.com/s.asp?u=534482837251.

Finding Yourself, Wirelessly

Researchers in the SENSEable City Laboratory have launched a new social-networking application that allows users to broadcast their physical location to an approved list of friends. Called iFind, the program computes a user's location based on signals broadcast from a Wi-Fi access point to a wireless networking card in a portable device such as a laptop. The software, which pinpoints a user's location to within a few meters and displays it as a dot on a map of the MIT campus, uses peer-to-peer networking to broadcast that information to anyone the user wants. No information goes through a central server, so an intruder cannot use it to hijack location data. Researchers placed a high emphasis on privacy and on letting users control the information. The software is currently designed to work only on the densely networked MIT campus, but the researchers hope to expand it to the outside world as wireless access points become more widespread.

A Faster Chip Recipe

Computer chips get faster because engineers keep shrinking transistors, packing more devices into the same space. But researchers fear that within 10 or 15 years, they won't be able to make the silicon-based devices any smaller. Now engineers in MIT Microsystems Technology Laboratory have used a different material to build transistors that, although similar in size to state-of-the-art silicon devices, operate at faster speeds.

At a recent conference, Dae-Hyun Kim, a postdoc in the lab of Jesus de Alamo, professor of electrical engineering and computer science, described a circuit the lab made using indium gallium arsenide (InGaAs). This compound semiconductor is used to build lasers; electrons travel much faster through it than they do through silicon. Transistors made from InGaAs include a thin layer of indium aluminum arsenide to confine the electrons, but previous versions far exceeded the 65-nanometer scale of advanced silicon chips—and engineers couldn't get smaller versions to work. The MIT team found that by making this layer even thinner—only a few nanometers thick—it could build smaller transistors with the desired electrical properties. A 60-nanometer transistor made from InGaAs carried 2.5 times as much current as a 65-nanometer silicon transistor in their tests.

More Tolerant Yeast

Scientists have long wanted to improve the ability of common yeast cells to convert cornstarch into ethanol; such a change is essential to making ethanol a practical fuel for cars. But there are significant obstacles: high ethanol levels are toxic to the microbes, and multiple genes control the process. Trying to boost efficiency and ethanol tolerance by traditional methods, tweaking one gene at a time, would be next to impossible. So Hal Alper, a postdoc in the labs of chemical-engineering professor Gregory Stephanopoulos and Whitehead Institute for Biomedical Research professor Gerald Fink, used a novel technique called global transcription machinery engineering to alter transcription factors, the proteins that control how genes are expressed.

Alper's team found that a group of three mutations in one gene created a transcription factor that led the yeast to make extra copies of the proteins encoded by at least a dozen different genes. The combined increase helped the yeast survive high concentrations of ethanol. The altered yeast also produced 50 percent more ethanol in a 21-hour period than ordinary yeast. DuPont and the U.S. Department of Energy, which are hoping to improve production processes for fuel ethanol, were among the sponsors of the research.

A New Stab at the Flu

A new antimicrobial paint that can be applied to doorknobs and other surfaces destroys the flu virus by ripping it to shreds. The paint, developed by biology professor Jianzhu Chen and chemistry and bioengineering professor Alexander Klibanov, is a thin polymer containing minuscule spikes made up of about 30 carbon atoms; these spikes rip through the membrane surrounding the influenza virus. The spikes can also destroy bacteria, including *E. coli* and staphylococcus, many strains of which have developed resistance to antibiotics.

Commercially available antibacterial products, which rely on timed release of antibiotics or heavy metals, aren't able to kill viruses. Those substances also eventually run out, ending the antibacterial effect, and they can harm the environment. The paint, on the other hand, is environmentally inert and should last about as long as regular paint, although it would require occasional cleaning to remain effective. And it doesn't appear to create antibiotic resistance. In tests, the coating killed 99 percent of bacteria that came in contact with it. Klibanov says it's difficult to imagine how bacteria could evolve resistance to having holes poked in their membranes.

NEWS LINKS

Memory experts show sleeping rats may have visual dreams
web.mit.edu/newsoffice/2006/visual-cortex.html

Parkinson's disease process may be curtailed by regenerative processes in yeast, fruit flies
web.mit.edu/newsoffice/2006/lindquist.html

Chemists shed light on solar energy storage
web.mit.edu/newsoffice/2006/solar-nocera.html

Genetic map offers new tool for malaria research
web.mit.edu/newsoffice/2006/malaria.html

MULTIMEDIA LINKS

Leadership in the Automotive Industry
mitworld.mit.edu/video/407/

Educating Engineers for 2020 and Beyond
mitworld.mit.edu/video/409/

MIT ZigZag: Episode 13
web.mit.edu/zigzag/

A New Spin on Chemistry

Troy Van Voorhis models the behavior of electrons, which could lead to better LEDs, improved solar cells, and human-controlled photosynthesis

The phrase "chemistry professor" may conjure images of beakers and Bunsen burners, but for Troy Van Voorhis the instrument of choice is a computer.

"Depending on what day you come in, we could look like computer programmers or we could look like mathematicians. It's very rare that we look like chemists," says Van Voorhis, an assistant professor of chemistry whose specialty is quantum chemistry. Rather than running experiments, his group designs algorithms and software to model how electrons behave in various molecules. With a better understanding of how charges move and change within a given molecular structure, researchers could design molecules that increase the efficiency of light-emitting diodes or enable artificial photosynthesis for energy storage.

Understanding the electronic state of molecules is a complex challenge, Van Voorhis says. It's relatively simple to describe the status of electrons when they're all in their lowest energy state. But when some are excited and are transferring excess energy from one to another—as happens in chemical reactions and electronic devices—it's much more complicated to determine what state each electron is in, which other electrons it might transfer excess energy to, and how fast that might happen. Van Voorhis and his group had to develop mathematical methods to describe the various possible states of a set of electrons and the ways they change from moment to moment.

As esoteric as this research is, it has immediate practical applications. Take organic LEDs (OLEDs), which several companies are developing for cheaper, longer-lasting lighting and thin, low-power computer displays. OLEDs consist of thin layers of organic molecules, such as those used to dye clothing. Pump electricity into them, and excited electrons with the right amount of energy combine to emit light. If the energy states are wrong, the result is waste heat. Developers want to get the most light they can for the electricity they put in.

A quantum-mechanical property called spin determines which state the electrons wind up in. If two electrons are spinning in the same direction, they are less likely to emit useful photons. If they're spinning in opposite directions, they produce a state that is more likely to yield light. Unfortunately, about 75 percent of electrons naturally combine in matching spin states; only 25 percent have opposite spins.

What Van Voorhis's model showed was that contrary to his expectations, the opposite-spin state was more energetically "comfortable" for the electrons. This means that the matched-spin majority should eventually lose energy and become opposite-spin pairs. Alas, that conversion process is slow, and the model showed that the charges would disperse before the conversion could take place. But the model also predicted that adding a few atoms of a heavy metal to the material would change how energy flowed through the system and accelerate the conversion process, producing a greater percentage of the desired electron pairs. Van Voorhis passed the information on to Marc Baldo, the Esther and Harold Edgerton Career Development Associate Professor of Electrical Engineering, who used it to produce OLEDs that had 85 percent of their electrons in opposite-spin pairs.

Now Van Voorhis is exploring whether a similar approach can improve solar cells, which take incoming photons and convert them to electricity. He's also trying to understand electronic behavior in photosynthesis, the process plants use to convert sunlight into food. A key step in photosynthesis involves breaking up water molecules; if researchers could devise an energy-efficient way to do this in the lab, they could convert solar energy into hydrogen for long-term storage.

Researchers have been trying for years to replicate the photosynthetic processes that plants have mastered over millennia of evolution. "People know that these things work, but they are so amazingly complicated that there's a huge degree of controversy about how they work and about how we could make them better," Van Voorhis says.

His work recently got a boost when he received one of 20 highly competitive David and Lucile Packard Foundation fellowships. That gives his group an unrestricted research grant of $625,000 over five years, which he says should help him demonstrate the validity of his work. It will also help to pay his six graduate students, one postdoc, and one undergraduate.

Mark Ratner, a professor of chemistry at Northwestern University, says that others have wanted to understand the electronic behavior of molecules, but Van Voorhis has succeeded where others have failed, in part because he created a whole new set of equations for his computer models. "He is trying to develop what I think is a much more sophisticated and at the same time much more physical approach to the problem," Ratner says. "He's going after interesting and important chemical effects that I think are beyond the abilities of most other people."

IN BRIEF

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Van Voorhis Group

DIRECTOR
Troy Van Voorhis

CONTACT
web.mit.edu/vanvoorhisgroup

MAJOR PROJECTS
Modeling electron dynamics
Studying electron spin

Joint Project

The first company spun off from the Cambridge-MIT Institute, a collaboration between MIT and Cambridge University, has completed a Series A funding round of £5 million (about $9.6 million). OrthoMimetics, of Cambridge, England, received the funding from Eden Financial, Schroders Investment Management, Oxford Capital Partners, and Sloane Robinson Private Equity.

The company is developing a line of porous, multilayered tissue regeneration scaffolds that support simultaneous regeneration of several tissue types to help repair damaged cartilage, ligaments, tendons, and bone. OrthoMimetics will use the funding to begin clinical trials of its first two products. It hopes to provide off-the-shelf devices that surgeons can use to treat joint damage early, allowing patients to delay or avoid joint replacement surgery.

The company was founded in 2005 by William Bonfield, a professor of medical materials at Cambridge; Andrew Lynn, who received a PhD from Cambridge and is now CEO; Lorna Gibson, the Matoula S. Salapatas Professor of Materials Science and Engineering and associate provost at MIT; Brendan Harley, who received a PhD in mechanical engineering from MIT; and Ioannis Yannas, professor of polymer science and engineering at MIT.
www.orthomimetics.com

Power Boost

A company that makes batteries based on MIT technology has received a $15 million contract to develop lithium-iron-phosphate battery technology. A123 Systems, of Watertown, MA, was awarded the 36-month contract by the U.S. Department of Energy and the U.S. Advanced Battery Consortium, which comprises DaimlerChrysler, Ford Motor, and General Motors.

The goal is to develop a cost-effective, high-power battery that is tolerant of rough environments, such as car engines. Such a battery would be used in future hybrid-electric vehicles, which use energy from braking to produce electricity that runs an electric motor. The consortium is working to develop batteries that store energy not only for hybrid cars but also for hydrogen-fuel-cell and electric vehicles.

The company was cofounded in 2001 by Yet-Ming Chiang, the Kyocera Professor of Ceramics in MIT's Department of Materials Science and Engineering; Ric Fulop, a fellow at MIT's Sloan School of Management; and Bart Riley, now vice president of research and development. It has raised $62 million in three rounds of financing.
www.a123systems.com

Green Genes

Codon Devices, a company that produces artificial DNA segments, has closed a Series B financing round of $20 million, bringing the company's total funding to $33 million. Highland Capital Partners led the round, joined by Alloy Ventures, Flagship Ventures, Khosla Ventures, and Kleiner Perkins Caufield & Byers. The company plans to use the money to improve its technologies and market itself worldwide.

Based in Cambridge, MA, the company quickly and accurately synthesizes DNA using its BioFab platform, which combines informatics, robotics, and gene sequencing technology. Last summer, Codon made what it said was the longest strand of DNA ever shipped commercially. The strand was 35,000 bases long; most previous synthetic DNAs had been 10,000 bases long. Formerly known as SynBio, the company was founded in 2004 by Drew Endy, an assistant professor of biological engineering and cofounder of the MIT Synthetic Biology Working Group; Joseph Jacobson, associate professor and head of the Molecular Machines Group at the Media Lab; George Church, professor of genetics at Harvard Medical School; and Jay Keasling, professor of chemical engineering at the University of California, Berkeley.
www.codondevices.com

Sensing a Market

A technology transfer company has signed an agreement with an MIT professor to commercialize a blood monitoring device. Competitive Technologies, of Fairfield, CT, signed the deal with Rahul Sarpeshkar, associate professor of electrical engineering and computer science.

The device the company plans to bring to market is an ultra-low-power pulse oximeter that can be used for wireless, remote monitoring. Pulse oximeters have been used for more than 20 years to measure the amount of oxygen in a patient's bloodstream; they work by shining light through a patient's fingertip and measuring how much of it is absorbed. Sarpeshkar's design uses a novel photoreceptor to make that measurement. Its compact circuit design uses an order of magnitude less power than current devices, so it can run on a battery. This makes it possible to use the device for long-term remote monitoring.

Sarpeshkar is head of the Analog Very Large Scale Integration and Biological Systems Group. The group combines research into neurology with analog electronics and is working on such bioelectronic devices as a bionic ear—a low-power cochlear implant.
www.competitivetech.net

DATEBOOK

January 8–12
3:00–4:30 P.M.
IAP Lecture Series: On Blindness—The "Seeing" Project
Building N52-390, MIT

events.mit.edu/event.html?id=7626953&date=2007/01/03

January 25
5:30–8:30 P.M.
Financial Markets: Outlook 2007
Kresge Auditorium, MIT

enterpriseforum.mit.edu/network/broadcasts/200701/index.html

January 29
6:30–9:00 P.M.
Digital Car Toys: Digital Media Takes Pimping Your Car to a Whole New Level
Building E51-376, MIT

www.mitforumcambridge.org/DigMediaSIG.html

January 31
2007 CSBi Symposium
Kresge Auditorium, MIT

csbi.mit.edu/events/annualsymposium/2007

$1K Warm-up Awards

MIT's annual $100K Entrepreneurship Competition is designed to encourage students to start companies. Since 1989, more than 80 companies, including Akamai, have been launched by teams in the competition. The contest started off in the fall semester with the $1K Warm-up. Of 138 entrants, 10 teams were chosen to move on. Each received $1,000 cash and will now compete in the $100K.

CATEGORY	COMPANY	CONTACT	PROJECT
Information technology	Borisville	Boris Iyutin iyutin@mit.edu	OpenContentMart, a forum for interactive online tutorials, questionnaires, stories, and textbooks. Authors can sell their material for online publishing or release it into the public domain and receive voluntary donations.
Biotechnology	Hemetrics Development	David Kaufman david.Kaufman@hemetrics.com	A portable, handheld device designed to help emergency responders determine quickly whether a patient is dehydrated; initially targeted to the chronically dehydrated elder population.
Tiny tech	MAD Nanolayers	Helen Chuang hchuang@mit.edu	A multilayer coating that provides timed release of active agents, such as antibiotics and growth factors applied to orthopedic implants, fragrances in consumer goods, or fertilizers applied to seeds.
Consumer products	RadioSherpa	Joshua Lifton lifton@media.mit.edu	Real-time program guide and search engine for broadcast radio; works with Internet broadcasts or specially equipped radios.
Services	RemesaTel	Jose Dominguez-Caballero jadc@mit.edu	International money transfers and payments via text messaging.
Social	Bagazo	Amy Banzaert amybanz@mit.edu	Concentrated cooking fuel made from agricultural waste products; designed to reduce the use of wood and dung fires, which cause indoor pollution in Third World countries.
Energy	AeroVortex Mills	Sandeep Beri sberi@mit.edu	New turbine technology aimed at efficiently harvesting wind power in low-wind areas.
Future technology	LightFace	Dan Walsh dwalsh@sloan.mit.edu	Customizable panels for high-end architectural lighting; made of organic LEDs printed on flexible substrates, with 10 times the lifetime of current devices.
Medical devices	Picosense	John Ho ho_2002@mit.edu	PNUT, the Personal Nut Ultra-trace Tracker, a portable sensor for those with peanut allergies. It detects trace amounts of peanut contamination in food and on surfaces.
Development	Solar Turbine Group	Sorin Grama grama@mit.edu	A turbine generator powered by solar energy to produce not only electricity but also heating and cooling for Third World countries.

ILP REPORT: TOP STORY

IT Conference Celebrates New, Agile Technologies

April's conference features Nicholas Negroponte's $100 Laptop, Rodney Brooks on AI, plus the latest on robotics, agile modeling, networking, Internet security, location-based services and more.

by Eric Brown

From the research lab to the boardroom, there is no more sought-after quality than agility. Global marketplaces and networks demand quick responses to multiplying, yet ever-shrinking, windows of opportunity. The 2007 MIT Information Technology Conference, to be held on April 25-26 at Kresge Auditorium, will show how MIT researchers are addressing this challenge with agile new technologies and business strategies. Presentations will cover both long-range projects and near-term technologies that could start disrupting industry in a few years.

The morning keynote will feature Nicholas Negroponte, Professor of Media Technology and Chairman Emeritus of the MIT Media Laboratory, discussing a project that could have a major impact on both consumer technology and the development of emerging nations. Building on the strengths of an innovative low-cost computer, One Laptop per Child (OLPC) hopes to jump-start a technological awakening in the developing world. As chairman of OLPC, Negroponte will present the $100 Laptop as an example of how ingenuity can be applied to the low-end market without sacrificing essential functionality. Tech manufacturers, claims Negroponte, are fearful of the commodity pricing brought on by Moore's Law, and therefore add features to justify higher prices. As a result, he adds, "many of us now have bloated laptops and cell phones, sometimes unreliable and slow because of all these features."

The afternoon keynote by MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL) Director, Rodney Brooks, will discuss his vision of Artificial Intelligence and establish some key goals for robotics. These include improving visual object recognition, spoken language, manual dexterity and social understanding. "Significant advances in any one of them will open wide the gates for a deluge of new applications, companies, and changes in our world," says Brooks.

Another important quality for robots, adaptability, will be discussed by CSAIL Professor Daniela L. Rus. Whether searching for survivors in a bombed building or exploring Mars, her self-reconfiguring lattice robots can change shape to adjust to changing terrain. Other presentations of near-term technology include CSAIL's William T. Freeman discussing his computational photography research, including anti-blur algorithms and a "motion microscope," and Devavrat Shah, Assistant Professor in Electrical Engineering and Computer Science (EECS), reporting on a new parametrized class of simple, distributed message-passing algorithms for resolving network contention disputes.

Jerrold Grochow, Vice President of Information Services and Technology (IS&T) at MIT, will explain how IS&T provides innovative management techniques for enterprise computing in order to supply IT services to over 20,000 demanding clients. For a longer range view, David D. Clark, CSAIL Senior Research Scientist, will look at the future of the Internet, including potential solutions for security issues expected to emerge from widespread mobile and embedded access.

While computer scientists try to make networks more robust, the MIT Media Laboratory is always there to make their jobs more challenging with new, innovative applications. Alex Paul Pentland, Toshiba Professor of Media Arts and Science at the Media Lab, will demonstrate how wireless technologies can automate and enrich the analysis of employee interactions. His Sensible Organizations project helps companies analyze productivity by using proximity-aware communications badges and other "social sensors" to identify who employees are speaking to and how gestures and other behavioral cues affect business interactions.

To adopt innovative applications like Sensible Organizations, companies need to establish considerable structural — and cultural — groundwork. The following stories from four additional conference speakers suggest that building a solid foundation is a necessity for agility and innovation.

Digitally Augmenting the City

Like Sensible Organizations, the SENSEable City Lab uses wireless communications and location tracking to analyze social patterns. Yet SENSEable City, part of MIT's Department of Urban Studies and Planning, focuses instead on public urban environments, where privacy concerns are more pressing.

At the conference, Professor Carlo Ratti, Director, will discuss his Lab's long-term Wiki City project, which is based on last year's Real Time Rome project. Here, Ratti and his collaborators used analysis of aggregate cell phone traffic to generate traffic maps. With cell-phone locations mapped anonymously at regular intervals, Roman city planners could see the pulse of the city in real time. Wiki City builds upon this idea, envisioning an interactive, digitally augmented city that would also integrate location-based services, WiFi-based wikis and environmental sensor input.

"How do we build new cities that combine digital and concrete forms?" says Ratti. "We're exploring how to capture and process time- and location-sensitive data and build a real-time control system for a city."

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One of Wiki City's applications is social networking, which is the goal of the Lab's iFIND opt-in, friend-finding service. Now available for download, iFIND is a map-based, instant messaging application that uses linked WiFi networks to determine location. iFIND answers the growing question: How do you find your friends and colleagues when they're wandering around campus?

iFIND protects privacy with a completely opt-in, encrypted system. Users decide who can view their location information, and no central authority can track an individual's location. Future plans call for adding mapping layers and location-specific wikis and scaling up for citywide networks. "We're exploring how to let users decide how much to reveal and to whom," says Ratti. "With MIT's techno-enthusiast community and pervasive wireless coverage, it could provide a highly relevant case study."

A Vote of Confidence

The issue of "how much to reveal and to whom" also challenges Ronald Rivest, the founder of RSA Security, who will report on his research and its progress towards improving the security and usability of voting systems. Rivest, the Andrew and Erna Viterbi Professor of EECS, proposes that it's still too early for all-digital voting technology. "Building secure, usable voting systems is a surprisingly hard problem," he says. "Much more research is needed."

Rivest will discuss "end-to-end auditable" voting systems that allow each voter to confirm that their vote was counted, and allow anyone to confirm the tally's correctness. Rivest's ThreeBallot system not only achieves this goal, but is the first to do so without cryptography.

A Foundation for Business Agility

After years of intensive field work, Peter Weill and the MIT Center for Information Systems Research (CISR) have concluded that business agility requires more than innovative product and customer strategies. First, one needs to establish a solid foundation.

"Most companies spend too much time and money integrating too many ways of processing the same things," says Weill, Senior Research Scientist at MIT Sloan School of Management. "Successful companies like UPS, Citibank and 7-11 Japan, have standardized and digitized their core processes, enabling them to be more agile. It's difficult to be agile on an unstable platform."

Weill holds up business agility as the prize for those companies willing to build foundations for effective enterprise architectures. Each company must first identify its core processes and operating model and then work through the stages of enterprise architecture maturity. Many companies have moved from the Business Silos stage to Standardized Technology and Optimized Core, he says, yet few have graduated to Business Modularity.

Companies are often tempted to skip a stage, such as jumping to modularity before core processes are unified, but this rarely works, says Weill. Each transition requires new approaches toward incentives, governance, training and decision-making, and companies must persuade local managers to surrender autonomy on core processes so they can focus on innovation in localized customer service. "It sometimes takes three or four years per stage," says Weill. "The good news is there are measurable business benefits to be earned at each stage."

CISR is now identifying the factors that characterize agile companies. One quality is "IT savviness," which requires that a company not only be creative with IT resources, but also know when not to be. "You don't want innovation centralized," says Weill. "There should be strong governance in the core and little variability."

Alloy: Lightweight Agile Modeling

In software, unlike business, one can innovate in the core – but very carefully. As requirements grow more complex, bugs – along with more serious gaps and flaws – have a more disastrous impact. CSAIL Professor Daniel Jackson, has addressed this issue with Alloy, one of a new class of 'lightweight formal methods' for software modeling. Alloy combines a supercharged, automated SAT analyzer with a modeling language that provides first-order logics for expressing designs and properties. It's not only adept at catching bugs, but at an early stage can reveal whether a project has major flaws that might otherwise go undetected for months.

Relatively few developers use modeling packages, says Jackson, and the pressure to produce is intense. "Productivity is typically measured by how many lines of code you deliver," he says. "There's no reward for sharing code or writing succinctly, and there's a deep reluctance to spend a month thinking about the problem. There's often a kind of fog of confusion and massive amounts of wishful thinking. Developers exhaust their attention over technical problems so they don't think clearly about fundamental design questions. Soon you have an incredibly complicated beast that's out of control."

Formal modeling methods use mathematical proofs of correctness to help spot errors, but they require considerable expertise. Another solution is agile programming, by which teams of programmers quickly develop code in stages, showing it to clients along the way. This has its advantages, says Jackson, but it can't spot all the problems. Hence, the need for lightweight "agile" modeling.

Based on the "model-checking" algorithms used in IC modeling, Alloy offers a number of innovations that make it faster and easier than traditional modeling. Yet it's a "ruthless, emotionless critic," says Jackson, forcing developers to slow down and think. "Alloy sits in the corner of the room, humbling you whenever you write something down," he says. "But it holds you to a higher standard."

April 25-26, 2007 MIT Information Technology Conference, Kresge Auditorium, MIT Campus, http://ilp-www.mit.edu/events/IT2007

PUBLICATIONS AND LECTURES

"CONTROLLING FOR THE IMPACT OF VARIABLE LIQUIDITY IN COMMERCIAL REAL ESTATE PRICE INDICES"
by J. Fisher, D. Gatzlaff, D. Geltner, D. Haurin, MIT Center for Real Estate

http://web.mit.edu/cre/research/credl/pdf/FGGH_Variable_Liq_REE.pdf

PERSPECTIVES ON FREE AND OPEN SOURCE SOFTWARE
Edited by J. Feller, B. Fitzgerald, S. Hissam, K. Lakhani, MIT Press, [Forthcoming March 2007]

http://mitpress.mit.edu/catalog/item/default.asp?ttype=2&tid=11216

"MASTER PRODUCTION SCHEDULE STABILITY UNDER CONDITIONS OF FINITE CAPACITY"
by E. W. Schuster, C. Unahabhokha, S. J. Allen, MIT Data Center

http://mitdatacenter.org/LEC20054-14-05R1.pdf

"AN INTRODUCTION TO SEMANTIC MODELING FOR LOGISTICAL SYSTEMS"
by D. L. Brock, E. W. Schuster, S. J. Allen, P. Kar, MIT Data Center

http://mitdatacenter.org/BrockSchusterAllenKar.pdf

ILP REPORT

Sustainability Conference Seeks to Make "Clean and Green" Possible and Economical

by William Manning

"Sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs."

So said the United Nation's 1987 Brundtland Commission – formally, the World Commission on Environment and Development (WCED) -- chaired by Gro Harlem Brundtland.

Twenty years later, sad to say, the need to tackle a wide range of issues relating to environmental sustainability — in such matters as energy, agricultural practices, and clean water — is as crucial as ever.

That's why anyone who wants to learn about, or help set the direction of environmental sustainability in the years ahead, should hop a flight and be in Barcelona, Spain, March 18 through 21 in 2007.

That's when the Alliance for Global Sustainability's "Pathways To Our Common Future," the title of this year's annual conference, takes a look not only at what's possible in promoting responsible energy development and use and promoting smarter agricultural methods. It also identifies the technologically and politically practical measures that can be taken in the near term to advance the cause of environmental sustainability.

The Energy to Succeed

The Alliance for Global Sustainability (AGS) is a collaboration of four universities, explains David Marks, co-director of MIT's Laboratory for Energy and the Environment (LFEE), who was present at the AGS' creation.

The AGS brings together world-class expertise from member institutions, including the Massachusetts Institute of Technology, a founding member, as well as the University of Tokyo, Sweden's Chalmers University of Technology, and the Swiss Federal Institute of Technology.

Those institutions have joined forces to develop research and education, in collaboration with government and industry, on the challenges of sustainable development.

By marshalling their intellectual resources in engineering, social sciences, and natural sciences, the AGS' members are uniquely positioned to offer not just detailed assessments of technological impacts, but also insights into the challenges associated with the successful deployment of those technologies. And in a way that is accessible by all.

"The March conference will focus on two main areas," explains Marks. " The first is related to sustainable energy production and use. That one is farthest along in its funding and research on energy use and security in both the developed and developing world."

"One of the AGS energy pathways initiatives is what we call the Wells to Wheels program that looks at the issue of mobility and greener automobiles, an area where a lot of work is being done at MIT by John Heywood and others." Marks reports. "We're looking into hydrogen-powered cars, for example, but believe they are still a long way off. In the near-term, we have to evaluate an evolving mix of technologies, such as more efficient internal combustion engines and hybrid cars, as well as alternate fuels like ethanol.

"Another initiative addresses 'clean coal' legislation in Europe and how to put existing and future technologies in place to create more sustainable low carbon power generation in the next 10 or 15 years using coal. That's important. Because a ton of CO2 sent into the atmosphere stays there for a long time and contributes to climate change."

So far the AGS' energy initiatives have raised $20 million from foundations, the auto companies, governments and other sources to fund its work over the next five years.

Clean-Room Chicken in KFC's Future?

The second AGS initiative is food and water. The organization's funding efforts and research in the area of sustainable food and water is just beginning, says Stephen Connors, LFEE's Director of the Analysis Group for Regional Energy Alternatives, and head of the energy initiative. The Food and Water program holds much promise for creating better methods of production and more secure sources for each.

"In the food and water area, we're looking at both human needs and demand on one side, and the technology and social systems around growing food on the other side of the equation so we can see how that whole ecosystem works," Connors points out.

"With all the instances of mad cow disease and bird flu possibly tainting the food supply and affecting human health, for example, research activities in this area are more important than ever," Connors notes. "For instance, at last year's AGS annual meeting in Bangkok I saw an interesting talk by a major Thai poultry producer who spoke of essentially raising chickens in clean room environments to prevent the start or spread of disease."

While raising funds, technological breakthroughs, and coordination of international efforts can be a challenge, perhaps the biggest obstacle to creating sustainable and secure energy and food sources may be human nature.

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PROJECTS, LABS AND CENTERS

MIT CREATES 3D SCAFFOLD FOR GROWING STEM CELLS

Stem cells grew, multiplied and differentiated into brain cells on a new three-dimensional scaffold of tiny protein fragments designed to be more like a living body than any other cell culture system. [MIT News Office, December 27, 2006].

http://web.mit.edu/newsoffice/2006/scaffold.html
http://web.mit.edu/lms/www/

FLU VACCINE SHORTAGES CAN BE AVOIDED, MIT ENGINEERS SAY

With the annual flu season upon us, vaccines remain the primary weapons for fighting influenza outbreaks. Yet, there frequently aren't enough doses to go around.

One major reason is that the contracts between governments and manufacturers do not provide vaccine makers with enough of a financial incentive to produce sufficient doses. Now, MIT researchers and colleagues have come up with a new model for contracts they hope will benefit both parties and prevent vaccine shortages. [MIT News Office, December 27, 2006].

http://web.mit.edu/newsoffice/2006/influenza.html
http://cee.mit.edu/index.pl?id=2375

"It's a real problem changing people's behavior when it comes to conservation and other matters – it's something we don't understand well yet," Marks observes.

"For example, in the United States there is a great fear of regulation, as it relates to the environment and other areas, and especially a distrust of international regulation, which conjures up black helicopters and other images. There's a lot of push-back on CO2 regulation here and a distrust of techniques like cap-and-trade to control emissions even though work at MIT's Department of Economics and elsewhere shows them to be effective. In some minds, those kinds of government-sanctioned controls suggest the risk of more and bigger government interference in the future."

The other and more compelling behavior consideration, says Marks, is an economic one. It revolves around the question of making the appropriate investments necessary to become carbon-neutral without it affecting an industry or nation's international competitiveness. To solve that problem means building institutions that plan and educate societies at all levels in order to build a consensus on values, goals, and methodologies. There is a concern that being more energy efficient will be more costly but there are ample evidence that it need not be. The are plenty of "win-win" examples at which to point.

While the AGS goals are ambitious, and the resources never enough, the organization's researchers continue to look for that sweet spot where the recognition of the economic and social value of being "clean and green" is not only obvious but possible. That will come as an environmental sustainability sensibility is cultivated in people and brought to bear on the design of everything that's made or grown, by using greener forms of production and more recyclable materials

"And that's why the role of education and universities is so important in solving multigenerational problems like these," notes Marks. "It starts in grade school with helping a student decide whether to take that science course in the first place and continues on into higher education. These students are our leaders for the future and we must nurture and encourage them now.

"The issues the AGS is addressing are interdisciplinary problems. And MIT is doing well in creating scientists, in the traditional hard sciences and social sciences, to create literate graduates, not just narrowly focused majors. They'll be the ones who can think more broadly and creatively to discover the sustainability solutions on which our future depends."

Conference information and registration: http://congress.cimne.upc.es/ags_am07

CONFERENCES

JANUARY 19, 2007
2007 MIT in Japan Conference
Tokyo, Japan

http://ilp-www.mit.edu/events/JPN2007

MARCH 29-30, 2007
2007 Achieving Growth through Strategic Innovation Conference
Brussels, Belgium

http://ilp-www.mit.edu/events/EURO-2007

APRIL 25-26, 2006
2007 MIT Information Technology Conference
Kresge Auditorium, MIT Campus

http://ilp-www.mit.edu/events/IT2007

MAY 9-10, 2007
2007 MIT Healthcare Industries Conference
Wong Auditorium, MIT Campus

http://ilp-www.mit.edu/events/HLTHCR