MIT'S MAGAZINE OF INNOVATION
TECHNOLOGY REVIEW
FEBRUARY 2003

In labs around the world, researchers are busy creating technologies that will change the way we conduct business and live our lives. These are not the latest crop of gadgets and gizmos: they are completely new technologies that could soon transform computing, medicine, manufacturing, transportation, and our energy infrastructure. Nurturing the people and the culture needed to make the birth of such technological ideas possible is a messy endeavor, as MIT Media Lab cofounder Nicholas Negroponte explains on page 34. But in this special issue, *Technology Review*'s editors have identified 10 emerging technologies that we predict will have a tremendous influence in the near future. For each, we've chosen a researcher or research team whose work and vision is driving the field. The profiles, which begin on page 36, offer a sneak preview of the technology world in the years and decades to come.

10 EMERGING TECHNOLOGIES THAT WILL CHANGE THE WORLD

IBM, which is a primary partner in the TeraGrid and several other grid projects, is beginning to market an enhanced commercial version of the Globus Toolkit.

Out of Foster and Kesselman's work on protocols and standards, which began in 1995, "this entire grid movement emerged," says Larry Smarr, director of the California Institute for Telecommunications and Information Technology. What's more, Smarr and others say, Foster and Kesselman have been instrumental in building a community around grid computing and in advocating its integration with two related approaches: peer-to-peer computing, which brings to bear the power of idle desktop computers on big problems in the manner made famous by SETI@home, and Web services, in which access to far-flung computational resources is provided through enhancements to the Web's hypertext protocol. By helping to merge these three powerful movements, Foster and Kesselman are bringing the grid revolution much closer to reality. And that could mean seamless and ubiquitous access to unfathomable computer power. —*M. Mitchell Waldrop*

UMAR MAHMOOD

Molecular Imaging

At Massachusetts General Hospital's Center for Molecular Imaging Research—a bustling facility nestled next to an old Navy shipyard—Umar Mahmood uses a digital camera to peer through the skin of a living mouse into a growing tumor. Using fluorescent tags and calibrated filters, the radiologist actually *sees* the effects of the cancer on a molecular scale: destructive enzymes secreted by the tumor show up on Mahmood's computer screen as splotches of red, yellow, and green. In the future, he says, such "molecular imaging" may lead to earlier detection of human disease, as well as more effective therapies.

Molecular imaging—shorthand for a number of techniques that let researchers watch genes, proteins, and other molecules at work in the body—has exploded, thanks to advances in cell biology, biochemical agents, and computer analysis. Research groups around the world are joining the effort to use magnetic, nuclear, and optical imaging techniques to study the molecular interactions that underlie biological processes. Unlike x-ray, ultrasound, and other conventional techniques that give doctors only such anatomical clues as the size of a tumor, molecular imaging could help track the underlying *causes* of disease. The appearance of an unusual protein in a cluster of cells, say, might signal the onset of cancer. Mahmood is helping to lead the effort to put the technology into medical practice.

It is challenging, though, to detect a particular molecule in the midst of cellular activity. When researchers inject a tag that binds to the molecule, they face the problem of distinguishing the bound tags from the extra, unbound tags. So Mahmood has worked with chemists to develop "smart probes" that change their brightness or their magnetic properties when they meet their target. "This is a big deal," says David Piwnica-Worms, director of the Molecular Imaging Center at Washington University in St. Louis. The method, he explains, "allows you to see selected proteins and enzymes that you might miss with standard tracer techniques."

In a series of groundbreaking experiments, Mahmood's team treated cancerous mice with a drug meant to block the production of an enzyme that promotes tumor growth. The researchers then injected fluorescent probes designed to light up in the presence of that enzyme. Under an optical scanner, treated tumors showed up as less fluorescent than untreated tumors, demonstrating the potential of molecular imaging to monitor treatments in real time—rather than waiting months to see whether a tumor shrinks. "The big goal is to select the optimum therapy for a patient and then to check that, say, a drug is hitting a particular receptor," says John Hoffman, director of the Molecular Imaging Program at the National Cancer Institute. What's more, molecular imaging could be used to detect cancer signals that precede anatomical changes by months or years, eliminating the need for surgeons to cut out a piece of tissue to make a diagnosis. "At the end of the day, we may replace a number of biopsies with imaging," Mahmood says.

In Mahmood's lab, clinical trials are under way for magnetic resonance imaging of blood vessel growth—an early indicator of tumor growth and other changes. For more advanced techniques such as those used in the mouse cancer study, clinical trials are two years away. The big picture: 10 years down the road, molecular imaging may take the place of mammograms, biopsies, and other diagnostic techniques. Although it won't replace conventional imaging entirely, says Mahmood, molecular imaging will have a profound effect both on basic medical research and on high-end patient care. Indeed, as his work next door to the shipyard makes clear, an important new field of biotechnology has set sail. —*Gregory T. Huang*

OTHERS IN MOLECULAR IMAGING

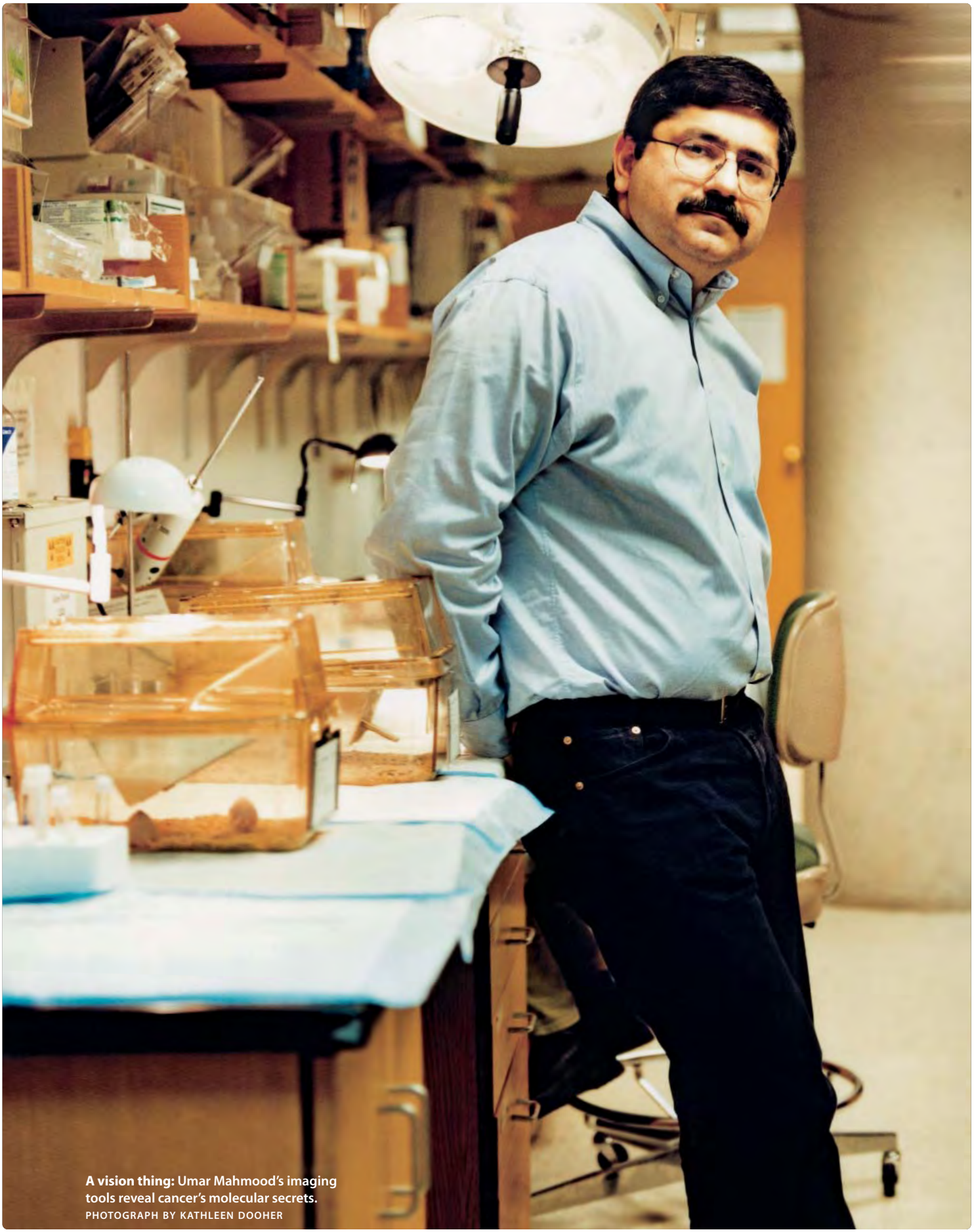
RESEARCHER	PROJECT
Ronald Blasberg Memorial Sloan-Kettering Cancer Center	Imaging of gene expression
Harvey Herschman U. California, Los Angeles	Tracking of gene therapy, gene activities
David Piwnica-Worms Washington U.	Protein interactions, imaging tools
Patricia Price U. Manchester	Clinical oncology, imaging drug targets
Ralph Weissleder Harvard Medical School	Cell tracking, molecular targets, drug discovery

STEPHEN CHOU

Nanoimprint Lithography

A world of Lilliputian sensors, transistors, and lasers is in development at nanotechnology labs worldwide. These devices point to a future of ultrafast and cheap electronics and communications. But making nanotechnology relevant beyond the lab is difficult because of the lack of suitable manufacturing techniques. The tools used to mass-produce silicon microchips are far too blunt for nanofabrication, and specialized lab methods are far too expensive and time-consuming to be practical. "Right now everybody is talking about nanotechnology, but the commercialization of nanotechnology critically depends upon our ability to manufacture," says Princeton University electrical engineer Stephen Chou.

A mechanism just slightly more sophisticated than a printing press could be the answer, Chou believes. Simply by stamping a hard mold into a soft material, he can faithfully imprint features smaller



A vision thing: Umar Mahmood's imaging tools reveal cancer's molecular secrets.
PHOTOGRAPH BY KATHLEEN DOOHER

than 10 nanometers across. Last summer, in a dramatic demonstration of the potential of the technique, Chou showed that he could make nano features directly in silicon and metal. By flashing the solid with a powerful laser, he melted the surface just long enough to press in the mold and imprint the desired features.

Although Chou was not the first researcher to employ the imprinting technique, which some call soft lithography, his demonstrations have set the bar for nanofabrication, says John Rogers, a chemist at Lucent Technologies' Bell Labs. "The kind of revolution that he has achieved is quite remarkable in terms of speed, area of patterning, and the smallest-size features that are possible. It's leading edge," says Rogers. Ultimately, nanoimprinting could become the method of choice for cheap and easy fabrication of nano features in such products as optical components for communications and gene chips for diagnostic screening. Indeed, NanoOpto, Chou's startup in Somerset, NJ, is already shipping nanoimprinted optical-networking components. And Chou has fashioned gene chips that rely on nano channels imprinted in glass to straighten flowing DNA molecules, thereby speeding genetic tests.

Chou is also working to show that nanoimprinting can tackle lithography's grand challenge: how to etch nano patterns into silicon for future generations of high-performance microchips. Chou says he can already squeeze at least 36 times as many transistors onto a silicon wafer as the most advanced commercial lithography tools. But to make complex chips, which have many layers, perfect alignment must be maintained through as many as 30 stamping steps. For Chou's process, in which heat could distort the mold and the wafer, that means each round of heating and imprinting must be quick. With his recent laser-heating innovations, Chou has cut imprinting time from 10 seconds to less than a microsecond. As a result, he has demonstrated the ability to make basic multilayered chips, and he says complex processors and memory chips are next. Chou's other startup, Nanonex in Princeton, NJ, is busy negotiating alliances with lithography tool manufacturers.

Chou's results come at a time when the chipmaking industry has been spending billions of dollars developing exotic fabrication techniques that use everything from extreme ultraviolet light to electron beams. But, says Stanford University nanofabrication expert R. Fabian Pease, "If you look at what the extreme ultraviolet and the electron projection lithography techniques have actually accomplished, [imprint lithography], which has had a tiny fraction of the investment, is looking awfully good." This is sweet vindication for Chou, who began working on nanofabrication in the 1980s, before most of his colleagues recognized that nano devices would be worth manufacturing. "Nobody questions the manufacturing ability of nanoimprint anymore," says Chou. "Suddenly the doubt is gone." —*Peter Fairley*

OTHERS IN NANOIMPRINT LITHOGRAPHY

RESEARCHER	PROJECT
Yong Chen Hewlett-Packard	High-density molecular electronic memory
John Rogers Bell Labs	Patterning polymer electronics
George Whitesides Harvard U.	Contact printing on flexible substrates
Grant Willson U. Texas; Molecular Imprints	High-density microchip fabrication

NANCY LYNCH & STEPHEN GARLAND

Software Assurance

Computers crash. That's a fact of life. And when they do, it's usually because of a software bug. Generally, the consequences are minimal—a muttered curse and a reboot. But when the software is running complex distributed systems such as those that support air traffic control or medical equipment, a bug can be very expensive, and even cost lives. To help avoid such disasters, Nancy Lynch and Stephen Garland are creating tools they hope will yield nearly error-free software.

Working together at MIT's Laboratory for Computer Science, Lynch and Garland have developed a computer language and programming tools for making software development more rigorous, or as Garland puts it, to "make software engineering more like an engineering discipline." Civil engineers, Lynch points out, build and test a model of a bridge before anyone constructs the bridge itself. Programmers,

Nano's Gutenberg: With the ease of a printing press, Stephen Chou makes tiny devices.
PHOTOGRAPH BY FLYNN LARSEN