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ANNOUNCEMENTS

Faculty Position: Department of Engineering Science and Mechanics and Department of Mechanical Engineering

Virginia Tech's Department of Engineering Science and Mechanics and Department of Mechanical Engineering are jointly seeking a colleague in the area of multiscale simulations for a tenure track faculty position (or tenured at any rank). These simulations, based on high performance computing, should address issues from the nano- and microscales to the macroscale, and focus on materials performance and functions or transport phenomena. Scientific applications of interest to our programs include smart structures, biomedical engineering, manufacturing, and energy systems. The ideal applicant is an individual with exceptional promise for research accomplishments or a proven record of the same, who will excel in teaching our undergraduate and graduate students, and has a strong interest in collaborating with faculty from both departments. The Departments of Mechanical Engineering and Engineering Science and Mechanics have combined numbers of roughly 70 faculty and 1210 students, with annual research expenditures of 11 million dollars. Applicants must have a doctorate, be committed to educational leadership, and are expected to develop a highly visible externally-funded research program. Further information about these two vibrant departments can be found at http://www.esm.vt.edu and http://www.me.vt.edu.

The committee will begin screening applicants on December 15, 2004, and will continue receiving applications until the position is filled. Applicants should submit a curriculum vita, the names of five references, and a cover letter summarizing their research and teaching interests. These items must be submitted electronically at http://www.jobs.vt/edu with Posting Number 041583. Questions may be directed to Search Committee Chair: Prof. Dan Inman at 540-231-4709 or dinman@vt.edu

Virginia Tech, the land-grand university of the Commonwealth, is located in Blacksburg, adjacent to the scenic Blue Ridge Mountains. The University has a total student enrollment of 25,000, with approximately 6,500 students in the College of Engineering. Additional information about Blacksburg, Virginia, can be found at http://www.bev.net**.**

Virginia Tech has a strong commitment to the principle of diversity and, in that spirit, seeks a broad spectrum of candidates. Women, minorities, and people with disabilities are encouraged to apply. Virginia Tech aggressively participates in the NSF ADVANCE Program: http://www.advance.vt.edu. Individuals with disabilities desiring accommodations in the application process or needing this material in an alternate format should notify Ms. Vanessa McCoy, (540) 231-6505, vamccoy@vt.edu, by the application deadline.

COBEM 2005

18th International Congress of Mechanical Engineering

The International Conference of Mechanical Engineering – COBEM is the most important Brazilian congress in the area of mechanical engineering. Its objective is to bring together professionals from industries, universities and research centers in order to share experiences and to discuss the main advances and trends of Mechanical Engineering and related fields. It is held every two years since 1971, under the patronage of the Brazilian Society of Engineering and Mechanical Sciences (ABCM).

We are pleased to announce the upcoming 18th COBEM, which will be held from 6 to 11 November, 2005, in Ouro Preto, MG, Brazil, jointly organized by the Technological Institute of Aeronautics – ITA and the Federal University of Minas Gerais – UFMG.

Ouro Preto is one of the most important historical cities in Brazil, exhibiting, in its narrow, strongly sloped and winding streets, a large number of well-preserved civil and religious buildings, recognized as magnificent examples of the 17th century baroque architecture. In April 21 1981, Ouro Preto was declared by UNESCO as part of the World Heritage

You are invited to submit electronically a short abstract (about 300 words) through the conference website (http://www.abcm.org.br/cobem2005) no later than February 11, 2005, addressing the theoretical aspects and/or practical applications related to one or more of the following symposia:

Aerospace Engineering
Automotive Engineering
Bioengineering
Combustion and Environmental Engineering
Dynamics, Solid Mechanics and Optimization
Engineering Education
Energy and Transport Phenomena
Manufacturing Processes
Materials
Mechatronics
Off-shore and Petroleum Engineering

Complete information about each symposium, including submission guidelines, is available in the Cobem2005 website.

2004-5 Founders Prize and Grant Awarded

The winnder is **Charlotte Barbier**, graduate student at **The University of Virginia**, the Prize awarded for her excellent essay: “Progress through Mechanics: the Quantum Computer”. The Prize check for one thousand dollars will be awarded by President Ted Belytschko at the ASME Applied Mechanics Dinner. The recipient is also entitled to expenditure for equipment of up to nine thousand dollars to support her research program. The Founder Prize and Grant is sponsored by The Robert M. & Mary haythornthwaite Foundation: (www.Haythornthwaiteorg).

Progress through Mechanics: The Quantum Computer

2004-5 Founders Prize Winning Essay

Charlotte Barbier
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Charlottesville, VA
barbier@virginia.edu

Since their conception, computers have inexorably increased their speed and storage capacity. If these trends continue to follow Moore's law, whereby the size of a transistor is predicted to be halved every eighteen months, electronic circuits on a microprocessor may be on an atomic scale in twenty years. The concept of a quantum computer, a computer able to perform memory and process tasks at the atomic level, is already a major driver for many research efforts worldwide, both in academia and industry. If rendered practicable, computing at the atomic scale will revolutionize the information technology industry and thus transform society: the beneficial impacts in the fields of health and medicine, energy, transportation, safety and security and the environment are potentially enormous.

A quantum computer differs from its classical counterpart mainly by the information that it can express. Today's computers work by manipulating bits, which represent one of two states identified by 0 and 1. In contrast, quantum information is encoded with quantum bits (or *qubits*) that can process more than two states: 1, 0 and superposition of these states. Thus, a quantum computer is not limited to linear processes and, consequently, can perform tasks beyond those of current computers.
The existence of superposition states in the qubit provides a new dimension to the concept of computing. For instance, a quantum computer – in contrast to a classical computer – is capable of generating a real random bit. It is also clear that a quantum computer does not strictly follow binary logic. Not only can a quantum computer emulate classical logical gates, but it can possibly implement new logic gates. This expanded range of logic gates can be used to notably improve the information processing power during computing. Nevertheless, the most interesting feature of a quantum computer is quantum parallelism. Because of superposition states in qubits, a quantum processor can perform calculations using all possible input values simultaneously. So, with only one calculation, all the possible outputs can be computed. Because of this, a quantum computer has the potential to be 10^6 times more powerful than current supercomputers and, as a consequence, could simulate complex mechanical behaviors ranging from quantum systems to models describing the movements of electrons within crystals. Because of its potential economic and social impact, governments, universities, national research labs and industries worldwide are investing heavily in quantum computation research.

To realize the full potential of quantum computers, new algorithms must be designed that will exploit quantum parallelism fully. Such algorithms have already been expressed mathematically and are considerably more efficient than those used for digital computers. For example, Peter Shor of Bell Labs [1][2] has demonstrated the capacity of a quantum computer to quickly factor a large number, a very challenging problem for current supercomputers. With Shors' algorithm, a quantum computer can, in principle, factor a 1,000 digit number in about 20 minutes, whereas the same exercise on a current computer would take 10^{24} years. This is of great interest for cryptography since the codes used for encryption are based on the inability of today's computer to decipher encrypted information. Similarly, Lov Grover [3] has written an algorithm that will speed up any kind of database search, particularly for unsorted data. In order to find a specific item in an unsorted database of N entries, typically, N/2 queries on average are needed to find it, whereas Grover's algorithm, using quantum parallelism, requires only $N^{1/2}$. Thus, the effect of the speedup is especially drastic as N becomes large.

Presently, the main obstacle to implementing a quantum computer is the degradation of superposition states with time (decoherence), which essentially leads to loss of stored information and causes a failure in the computation. In addition, the environment can interact with a qubit and cause collapse of the wave-function, destroying the quantum information stored in the superposition. To avoid decoherence, research has been directed mainly in two directions: a) Develop systems with minimal interaction or entanglement with the environment. (Trapped ions, Nuclear Magnetic Resonance (NMR), quantum dots, and cavity quantum electrodynamics (QED) are currently the main technologies being used to build quantum computers.); b) Develop algorithms for reducing errors due to decoherence. Shor and Steane [4][5] have shown that error-correcting routines – or quantum stabilizer codes – based on quantum logic, could effectively reduce decoherence and errors in a quantum computer.

Although quantum computers with seven qubits have already been built [6], many more qubits are necessary to simulate multidimensional and complex physical-chemical problems. However, recent advances give hope that quantum computers will emerge earlier than expected. Lately, Duke and Purdue university researchers [7] have managed to incorporate “quantum dots” (a small device containing free electrons inside a semiconductor) on a transistor. This new kind of transistor is not only very small, but also capable of quantum computing. Another great advancement has been made by Blinov *et al*. [8] at the University of Michigan with the observation of a “flying qubit”. The information on the state of a single trapped ion was read by measuring the polarization of the photon that the ion emits spontaneously. This system could possibly be used as a communication link inside a quantum network.

With current computers approaching physical performance limits, quantum computers promise a new and unprecedented level of computing power. Because of the limitations on speed and memory in current computers, it is impractical to calculate in any detail multivariable, multidimensional, highly non-linear problems such as arise in relation to, for example, turbulent fluid motions, the folding and unfolding of large protein molecules, and the molecular dynamics of chemically reacting systems. Even if quantum computing is still in its infancy, it very much heralds a new era in computing.

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SELECTION OF THE EDITOR

Experiences in Teaching Multi-scale Material Modeling: From Nano- to Macro-scale

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Modules for teaching multi-scale modeling of materials behavior were developed and distributed on our "Wave-Java" Web-server.[1] This project used existing Web-based commercial software and created a new user-friendly *Web-based Java interface* that allowed simulations to be submitted to remote computers which were better suited to handle the larger simulation models.

Students used this *Web-based Java interface* to: 1) enter information required by the simulation, 2) compile that information into a data file, 3) submit the file as a batch job to a remote computer, and finally to 4) send raw data of simulation back to server where images of data were generated for viewing on the client's remote Web browser. Unique to this project was the level of industrial participation by SUN and VNI in the creation of the *Java Web-based interface*. Modules discussed here were largely motivated initially by a student project, "Educational Atomic Models Using PV-Wave and Java" by Arturo Falck, as a class project for ESM4714: *Scientific Visual Data Analysis and Multimedia*, spring semester 1996.[2] Early Java/PV-Wave applet prototypes developed at Virginia Tech have been replaced with the JWave interface developed by VNI. The Network Program Interface Builder[3] (NPIB) replaced the original *Web-based Java interface* developed by Arturo Falck. The same functionality was maintained except simulation execution was initially limited to the Web-server.

Development of the Web-server continued with funding from the NSF Combined Research and Curriculum Development (CRCD) Program[4]. With NSF funding, the Web-server was upgraded and used to execute larger simulations and generate more representative results for analysis by students. Further development extended the execution of simulations to larger remote site computers, which provided students access to more realistic simulation results.

Two courses were organized on the Web-server with hyperlinks to Web modules that were divided into lectures, assignments, and interactive modules.[4,5] The first course focused on atomistic and continuum mechanics models; the second course focused on micro-scale models that predict mechanical behavior at the scale between the atomistic and continuum. For comparison, the same micro-scale legacy code was used to develop modules that used two different *Web-based Java interfaces*: 1) module01 that used the JWave interface and 2) module02 that used NPIB interface. These two modules have been specifically documented in a previous publication as working examples that demonstrate how to setup JWave and NPIB interfaces.[6] Here we describe how CRCD modules facilitated students' efforts to parametrically study the mechanical behavior, which was based on legacy computer programs previously written by the class instructors.

For both classes, a list of lecture topics and interactive computer simulation modules contained topics in the nano-scale, mirco-scale, and macro-scale, as shown in Table 1. Most of the interactive computer modules were associated with the lectures and homework assignments.

Two nano-scale modules and one micro-scale module were designed for use in conjunction with the CAVE virtual reality visualization facility. For these modules students could open the Web URL address on the CAVE computer and directly load files into the CAVE using the DIVERSE API.[7] The students could then navigate through these complex three-dimensional (3-D) structures. A CAVE simulator is also available for use in the desktop. Figures 1 and 2 show two examples, using the desktop CAVE simulator. In Figure 1 we see an atomistic simulation of a mode-I crack propagating along a grain boundary in a NiAl intermetallic material. From this simulation students can observe dislocation emission from the crack tip which results in a crack with a larger crack tip radius, hence higher fracture strength. Figure 2, from the micros-scale modules, shows the elastic anisotropy of a special orthorhombic crystal class symmetry that results in a single connected stress wave surface glyph: longitudinal and both transverse wave surfaces connect into a single surface.[8] In both cases the fully immersive experience of the CAVE can be used to study and analyze these structures and their corresponding material properties. Several publications are referenced here that show how the CAVE was used as an effective research tool.[10-14] The two examples of topics covered shown in figures 1 and 2 represent interactive modules used to learn about

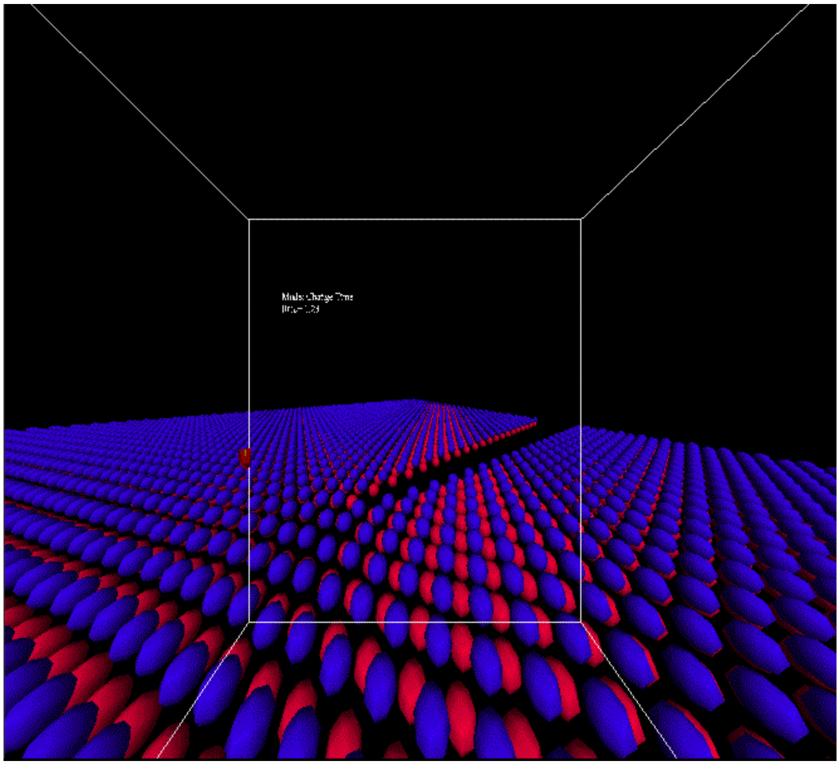

Figure 1. CAVE simulation view of a Mode-I crack propagation along NiAl grain boundary (nano-scale module01). White lines simulate the CAVE room boundaries.

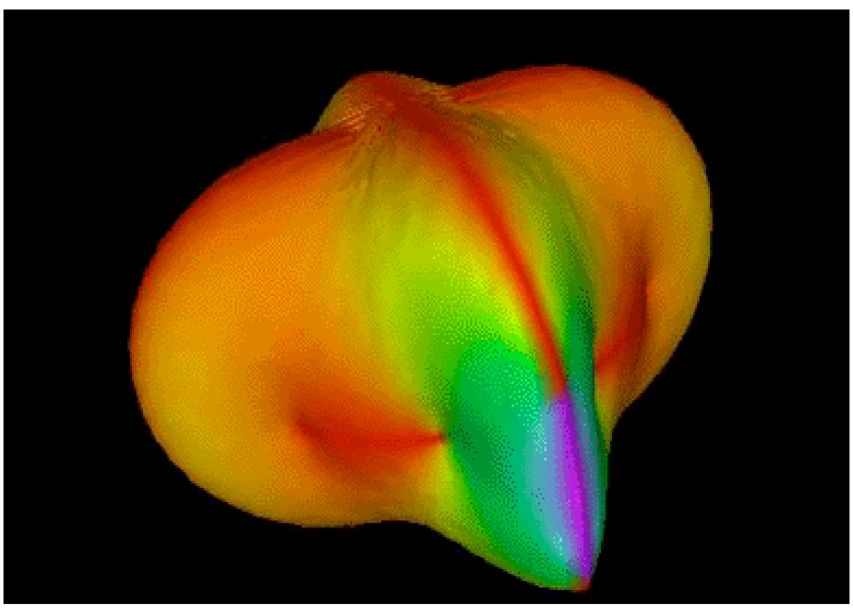

Figure 2. CAVE simulation view of a fourth-order stiffness tensor wave-surface glyph representation of a special crystal class symmetry for orthorhombic symmetry, where the longitudinal and both transverse wave surfaces are connected into a single surface.

mechanical behavior at two different scales. The first example is from a Nano-scale Module: Crack Propagation along a Grain Boundary. The second is from a Micro-scale Module: Influence of Elastic Anisotropy on Mechanical behavior.

The first senior-level course (ESM-MSE4984) was taught in the Fall semester, 1998. This is a three-credit hour class, meeting for one hour three times a week: Monday, Wednesday, and Friday. Mondays and Wednesdays were reserved for lectures. The class was team taught by professors whose research was precisely at the nano, micro and continuum levels. On Fridays students met with instructors in a special Scientific Modeling and Visualization Classroom (SMVC). For the educators and students, interactive Web-based access to simulation results allowed instructors to monitor students' progress and enhance class participation in sharing and discussing results. For researchers, similar modules can be used for collaborative development and discussion of simulation results. The simulation results span various length scales -- at the atomistic level, interactive modules use embedded atom method techniques, and at the micro- and macro-scale (continuum) interactive modules use finite element model simulations. Interactive modules attempt to stress the way in which macroscopic properties are controlled by phenomena at the atomistic and micro-structural levels. Over twenty modules were developed. Results from the undergraduate class, revealed that the most productive time spent using the CRCD modules was when students and instructors met in the SMVC on Fridays. Friday classes resembled lab sessions where students could ask questions and try out their ideas with comments from the professors who also helped interpret the simulation results. Instructors also received valuable feedback on how the JWave and NPIB forms were working and what needed to be improved. Friday sessions also built student confidence for successful completion of their homework assignments. Java interface development is a difficult, if not impossible, for most engineering professors without backgrounds in computer science. Even using javascript with HTML is beyond the abilities of most professors. These same professors are also not experienced in routine systems administration needed for configuring and maintaining Web-servers. Hence there must be a commitment from the department or college to support a courseware Web-server and to train professors how to access and use systems such as the NPIB. Because of limited resources and reluctance to accept new technology, building and supporting courseware servers has been the most difficult aspect of this project. Because of these difficulties the CRCD Web-server was maintained by the Problem Solving Environment group of the Department of Computer Science.[15] We also discovered, that programmers and system administrators need to work more closely. Typically all that was needed was to install a standard language compiler, with a user service group to answer any questions. With the advent of the network, professors and technical support staff can no longer afford to isolate themselves in the "new world" of computing where popular Web-based software applications are constantly changing.

The modules we developed are extensible to other classes taught in the Engineering Science and Mechanics (ESM) Department. We hope that this interest will grow to other ESM classes and that eventually the ESM Department will support their own JWave courseware Web-server.

Acknowledgements: We would like to thank Prof. Romesh Batra for contributions in the macro-scale modules listed in Table 1 and useful discussions in team teaching the classes mentioned here. The authors also acknowledge the NSF grant "Combined Research and Curriculum Development: Computer Simulation of Material Behavior - From Atomistic to the Continuum Level" (EEC-9700815), and the foundation grant from SUN Microsystems Inc. and Visual Numerics Inc. to create the Scientific Modeling and Visualization Classroom.

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Table 1. Course Decomposition

<table>
<tr><th>Nano-scale</th><th>Micro-scale</th><th>Macro-scale</th></tr>
<tr><td>Lecture Topics:
• Crystal bonding
• Crystal structures
• Crystal mechanical behavior
• Dislocations
• Fracture
• Fracture at Interfaces</td><td>Lecture Topics:
(56) Interface cracks
(57) Anisotropy
(58) Composite fiber-reinforce composites
(59) Stress-free laminate edge problem
(60) Laminate interface singularities
(61) Laminate ply crack singularities
(62) Cracks in homogeneous materials:
(63) Isotropic
(64) Anisotropic
(65) Wave propagation:
• Isotropic
• Anisotropic</td><td>Lecture Topics:
• Stress
• Equilibrium
• Strain
• Material characterization
• Boundary conditions
• Work external forces
• Minimum potential energy
• Uniqueness theorem
• Axial bar deformation
• Beam bending terminal couples</td></tr>
<tr><td>Atomistic modules:
• (01) Ni-Al grain boundary crack
• (02) Vacancy in Iron</td><td>Heterogenous modules:
• (01,02) Anisotropic polar plots
- (03,04) Cijkl stiffness tensor glyph
- (05,08) Linear elastic laminated plate analysis (LELPA)
• Generalized plane strain edge stress laminate Finite Element Model (FEM)
• (06) Nonwoven $[0/\pm45/90]_s$
• (07) Woven $[0/90]_s$
• Generalized plane strain interior stress laminate Finite Element Model (FEM)
• (09) Without interior ply crack
• (10) With interior ply crack
• Singularity Stroh's method
• (15a) stress free edge
• (15b) laminate ply crack
• Dynamic anisotropic mechanical behavior
• (18) 1D FEM
• (19) 2D FEM (30x60) mesh
• (20) 2D FEM (45x180) mesh</td><td>Continuum modules:
• (01) Stresses in thick walled cylinders
• (02) Brittle-Ductile transition</td></tr>
</table>

Chip Shots

By Carol Ezzell Webb

LOOK IN ANY MEDICINE CABINET and you're bound to find a veritable pharmacopeia: tablets, capsules, suppositories, syrups, inhalers, transdermal patches, and maybe even a syringe or two. In 2002 doctors wrote an average of 10.6 prescriptions for each person in the United States. As the population of the industrialized world ages, pharmaceutical companies are struggling to find compounds that ward off—or even reverse—the maladies that historically have plagued aging adults.

But for many of these scourges, the existing means of getting drugs into the body are only moderately effective and may be disruptive or downright painful. For instance, people with adult-onset diabetes—an increasingly common affliction of the middle to later years—suffer more complications if their blood sugar fluctuates widely. Popping pills and injecting insulin a few times a day can lead to peaks and troughs in blood sugar that can wreck small blood vessels, resulting, in the worst instances, in blindness or amputation of the feet or lower legs.

Some of the newer drug candidates for treating other illnesses are based on proteins discovered using information gleaned from the human genome. But they can't be taken orally or by injection because stomach acids chew them up or the liver filters them out of the bloodstream too quickly for them to be effective. And many of those wasted molecules are just the ones that aging bodies need to keep them hale and hearty.

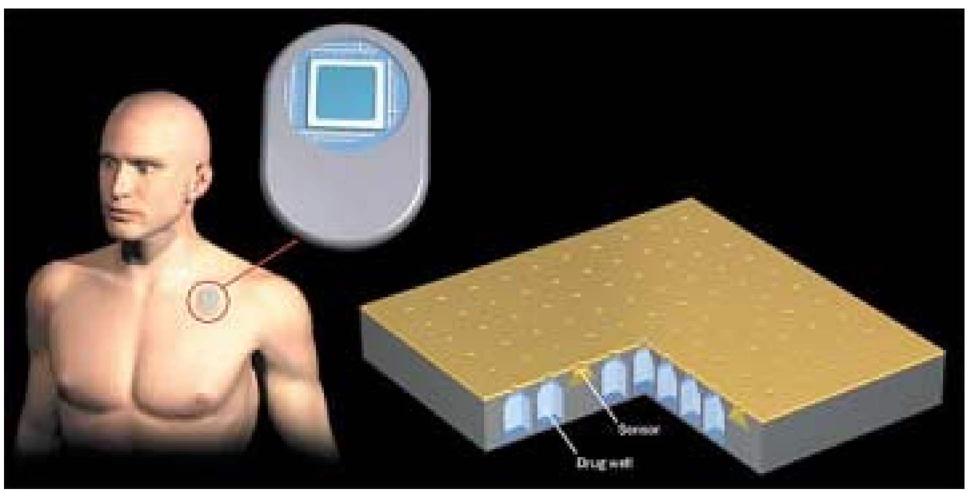
To address these problems, electrical engineers are teaming up with gene jockeys and drug developers to invent new drug-delivery systems that marry electronics and semiconductors to biotechnology. Experts agree that new drugs need a degree of intelligence to get where they must go and to arrive on time, and that's where semiconductors come in.

Two approaches are just now being tested for feasibility. One features implantable microchips dotted with tiny drug reservoirs that pop open at the touch of a wireless telemetry button. The other relies on injections of nanometer-scale beads of semiconductors, termed quantum dots, that exploit the energy of electrons to kill cancer cells selectively.

The first disorders to be treated with these "smart" drug-delivery systems will probably be chronic diseases for which patients must take one or more drugs for months or years. Like adult-onset diabetes, many of these maladies—including congestive heart failure—predominantly affect older adults. Research into microchip-based devices, called biological microelectromechanical systems, or bioMEMS, is currently much further along than studies of quantum dots, just now being tested in academic labs as a means for delivering drugs.

In the microchip approach, bioMEMS would be implanted in the body and, ideally, would serve as "closed-loop" systems, holding not only the means to administer a drug but also sensors that could tell when a patient needs another dose. So far, though, only a handful of studies describing bioMEMS-based drug-delivery systems have appeared in peer-reviewed scientific literature, and few companies have such systems in development.

ONE SUCH COMPANY is MicroChips Inc., in Bedford, Mass. At the core of its device is a 15-millimeter silicon microchip that is made using essentially the same techniques for producing integrated circuits. Instead of transistors, however, the device is dotted with 100 tiny reservoirs that are filled with a drug. Each reservoir is capped with a thin layer of platinum and titanium, all of which are fabricated into a network



SILICON PHARMACIST*: A drug-delivery device under development by MicroChips Inc. is a silicon chip with 100 or more nanoliter-size wells containing either drugs or biochemical sensors [center]. Each well is covered by a thin metal foil, which is connected to wires on the face of the chip. When current runs through a well's wire, the metal foil breaks open, releasing a drug or exposing a fresh biochemical sensor [next page]. The chip is fastened to the outside of a pocket-watch-size electronics package that is implanted beneath the skin [left]. Within the package is an antenna that receives instructions via radio and a microprocessor that controls the opening of individual wells. ILLUSTRATION: JOHN MACNEILL* of circuitry that includes patterned gold conductors. It takes just a 4-volt zap to remove an individually addressable well covering, allowing the drug to diffuse out.

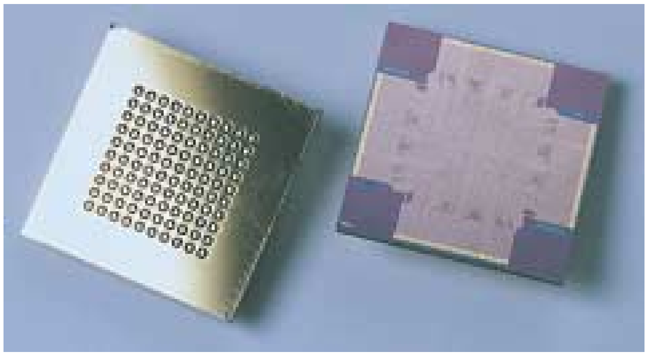
Best of all, the whole operation can be triggered by remote control. The bioMEMS unit is stuck to the outside of a sealed titanium case, roughly the size of a pocket watch, that contains a battery, a wireless telemetry chip, and a microprocessor.

MicroChips has been conducting experiments that track the performance of the chips in animals for three months or longer. The drug-dispensing chip and its associated electronics have been implanted under the skin of an animal's shoulder, where the device can be triggered wirelessly. "To administer a dose of drug, we just walk up to the animal and activate the device with a remote control," says John T. Santini Jr., president of MicroChips.

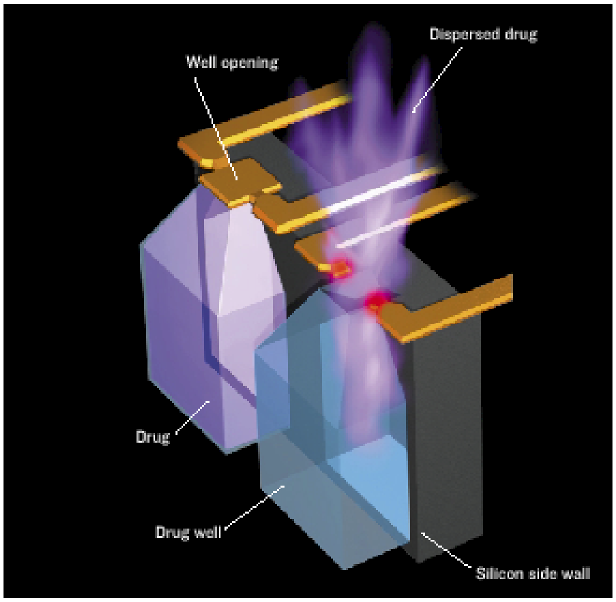
Another company, ChipRx Inc., in Lexington, Ky., has also pursued bioMEMS-based drug delivery, but development of its first product, an implantable matchstick-size drug-delivery vehicle that uses electrically activated artificial muscles to open and close drug reservoirs, is on hold for now. Marc Madou, cofounder of ChipRx and an engineering professor at the University of California at Irvine, says that for the immediate future ChipRx intends to concentrate on making genetically engineered proteins that might be dispensed as part of a closed-loop device.

WITH OR WITHOUT SENSORS, developers still don't know how long and how reliably bioMEMS will function once implanted into living systems, a factor that will determine whether doctors and their patients accept the devices. The objective is to design implants that can meter out precise doses of drugs for months or years before they must be removed or replaced. MicroChips' Santini says that his company has unpublished data from ongoing experiments in animals demonstrating that its chip has continued to release a drug for more than three months.

As with any medical implant, fouling might limit the useful lifetime of a bioMEMS device. In fouling, cells and molecules of the body's immune response stick to the



***DRUG DISPENSER**: Silicon chips containing 100 wells full of drugs are being tested by MicroChips Inc. Each well [left, bottom of chip] can be opened independently by current flowing down a set of electrodes [right, top face of chip] and melting away a thin foil covering.*



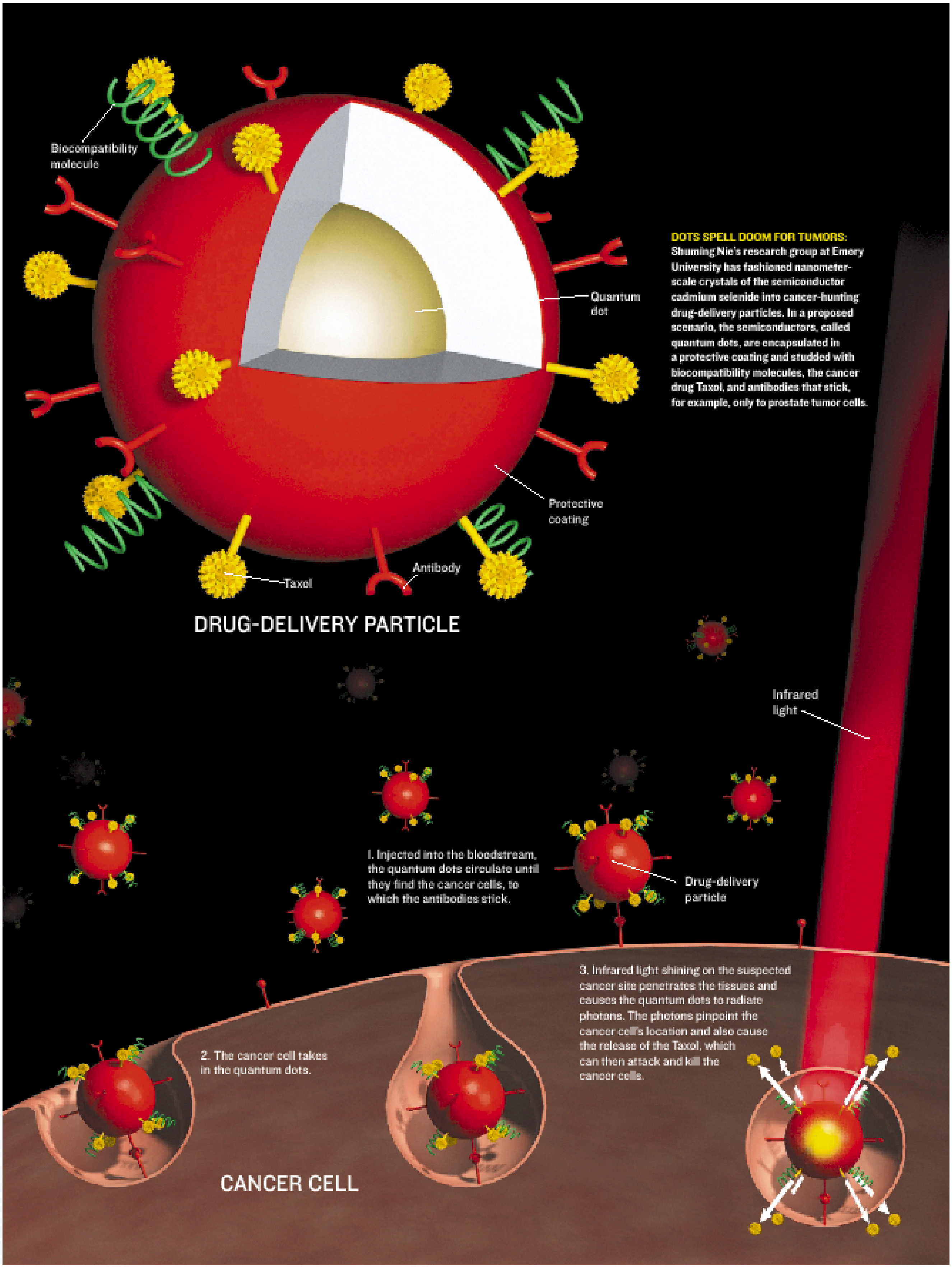
surface of an implant, preventing it from functioning properly. Many implants may also become surrounded by a thick capsule of scarlike tissue that essentially blocks them from communicating with the rest of the body. Coating the implants with anti-inflammatory drugs might prevent them from being attacked by the immune system.

"Fouling is a real biggie" among the issues confronting bioMEMS, says Burton Sage, cofounder and chief scientific officer of Therafuse Inc., in Carlsbad, Calif. His firm is developing wearable (but not implantable) pumps that exploit MEMS technology by using a tiny needle to administer precise doses of drugs, such as insulin, through the skin.

Sage adds that it is impossible to predict now whether fouling will foil the prospects of bioMEMS. The degree of fouling appears to depend on the chip's location in the body, the type of drug the device contains, and the kinetics of that particular drug's release and diffusion.

In the case of implantable sensors—a blood glucose meter, for example—bioMEMS might even be used to compensate for fouling, asserts Santini. Such sensors are now effective only for a few days or weeks, after which they become irreversibly clogged. Encasing multiple sensors in a bioMEMS device could yield an implant in which wells could be opened, one at a time, to reveal a fresh sensor when the old one has become clogged beyond use.

Therafuse's Sage wonders about another lifetime issue: how to refill the implants. "How do you put enough drug in there for the long term?" he asks. Retrieving and refilling a bioMEMS device would require outpatient surgery. To circumvent this, some scientists are designing implants with drug chambers that can be refilled from syringes without removing the devices from the body.


Biocompatibility molecule
Quantum dot
Protective coating
Antibody
Taxol
DRUG-DELIVERY PARTICLE
DOTS SPELL DOOM FOR TUMORS:
Shuming Nie's research group at Emory University has fashioned nanometer-scale crystals of the semiconductor cadmium selenide into cancer-hunting drug-delivery particles. In a proposed scenario, the semiconductors, called quantum dots, are encapsulated in a protective coating and studded with biocompatibility molecules, the cancer drug Taxol, and antibodies that stick, for example, only to prostate tumor cells.
Infrared light
1. Injected into the bloodstream, the quantum dots circulate until they find the cancer cells, to which the antibodies stick.
Drug-delivery particle
2. The cancer cell takes in the quantum dots.
3. Infrared light shining on the suspected cancer site penetrates the tissues and causes the quantum dots to radiate photons. The photons pinpoint the cancer cell's location and also cause the release of the Taxol, which can then attack and kill the cancer cells.
CANCER CELL

Among those who might be willing to undergo repeated implant placement, Sage says, are patients who have had a heart attack and are at high risk for another. In such instances, a bioMEMS could be loaded with a clot-dissolving drug or the heart stimulant epinephrine (also known as adrenaline). The patient could activate the implant at the first symptoms of a heart attack.

The ultimate goal, however, is to take the patient out of the loop by relying on microprocessors to do the regulation automatically. "The whole reason for wanting intelligent drug-delivery technologies is so you can do closed-loop sensing and drug administration," says Santini, whose company is working on precisely that challenge. Putting sensors and drug reservoirs on board the same chip could yield a device that would automatically monitor the presence of a given molecule in the blood and then administer the drug precisely when it is needed.

Such an approach would be a huge boon to people with congestive heart failure, says Nader Najafi, founder and president of Integrated Sensing Systems Inc., in Ypsilanti, Mich. In that disease, imbalances in water regulation by the body lead to fluid buildup around the heart, impeding its ability to pump blood. An automatic sensing and delivery system might detect increases in pericardial fluid and reduce the buildup by releasing a diuretic, a drug that causes the body to eliminate water. Congestive heart failure, which afflicts an estimated 15 million people worldwide, is the most frequent cause of hospitalization among those 65 and older in the United States and a major cause of death if not treated in a timely manner.

For now, Integrated Sensing Systems is conducting early research into the sensor side of things by attempting to develop a wireless, batteryless, implantable pressure sensor for use in congestive heart failure, according to Najafi. The company is still working out the details of exactly how the device would function; researchers at the company eventually intend to couple it to a mechanism for dispensing drugs to treat the disorder.

Under the company's current plans, physicians would implant a pressure-sensing bioMEMS into a patient's left heart ventricle during outpatient surgery by threading a cardiac catheter through the blood vessels and into the heart chamber. A signal from the sensor would then activate a diuretic drug-delivery system.

Right now, most researchers are working on either sensors or drug-delivery systems, but not both. "Everybody who is in this field is working toward closed-loop technology, but it's at least 10 years away," says Therafuse's Sage.

A VERY DIFFERENT KIND of semiconductor drug-delivery system, the quantum dot approach, might be just as far away. Quantum dots are crystals—often of the II-VI semiconductor cadmium selenide—which, because they are mere nanometers across, retain the quantum properties of single atoms. Critical for biomedical applications, these properties include the ability to absorb and emit photons of a very specific wavelength.

In single atoms, the wavelength depends on the type of atom involved, but with quantum dots the stimulation wavelength is related to their size. Smaller dots absorb and give off a shorter wavelength—that is, the light they absorb and emit is closer to the violet end of the spectrum—whereas larger dots produce longer wavelengths closer to the red end.

Most of the current commercial investment in quantum dots is related to their use in computing applications and lasers. The market for quantum dot-based chemicals for biomedical research—now roughly US $720 million—has also been growing, says Stefanie Lattner, portfolio executive at the publicly funded venture capital firm Innovation Works, in Pittsburgh. But at the moment, no venture capital money is chasing drug-delivery applications, she says.

That may be because studies of the therapeutic uses of quantum dots are still mainly at the academic level. Shuming Nie, adjunct professor of biomedical engineering at Emory University in Atlanta, is one of the first researchers to investigate quantum dots as drug-delivery systems. Specifically, Nie has chemically bound the breast and prostate cancer drug Taxol to quantum dots in an effort to deliver it specifically to tumor cells, leaving the rest of the body unaffected

The scheme could increase the drug's efficacy and reduce its side effects. The American Cancer Society, in Atlanta, estimates that in 2004, 15 percent of cancer deaths among U.S. women will be from breast cancer; similarly, 10 percent of cancer deaths among U.S. men will be from prostate cancer.

Nie's group started its research by studding the Taxol-bound quantum dots with a molecule that binds to folic acid receptors, which are present on tumor cells at concentrations roughly 1000 times those found on normal cells. The receptor-targeting molecule allows the nanoparticles to home in preferentially on cancer cells. In work published in August, the Emory scientists got even better results using antibodies against prostate cancer cells rather than folic acid binders.

Nie and his co-workers injected the Taxol-coated nanoparticles into mice that had been surgically implanted with human prostate tumors. After the injections, they illuminated the mice with infrared light, which penetrates into their tissues and excites the quantum dots. As the energy states of the dots fall back, they emit energy sufficient to cleave the bonds between the Taxol and the particles, releasing the drug to attack tumor cells. "We have evidence that our quantum dot conjugates can get into cancer cells and kill them," says Nie.

He acknowledges that the approach will be more difficult for human patients, whose bodies are thicker than that of the average mouse. Infrared light will penetrate only a few centimeters into living tissues. "I don't think there's any hope for this in treating cancers of the internal organs," says Nie, "but it might work for [the skin cancer] melanoma or for breast cancer."

Sangeeta Bhatia, associate professor of bioengineering at the University of California at San Diego, is taking the idea of drug targeting to an even finer level. She's investigating the use of quantum dots for steering compounds to particular compartments or organelles within a cell—such as the nucleus, where the genes are, or the energy-producing mitochondria.

Addressing cancer drugs to specific organelles could reduce side effects. But the toxicity of the quantum dot materials—especially cadmium—has made Bhatia cautious. Indeed, environmentalists have made much of the possible health effects of nanoscale particles.

Earlier this year, Bhatia and her graduate student, Austin M. Derfus, reported that quantum dots containing cadmium do indeed kill cells. But they are no more noxious than ordinary elemental cadmium, which can accumulate in the body and has been linked to kidney damage, heart disease, hypertension, cancer, and bone and joint pain.

"The bottom line is that our initial findings suggest that quantum dots are not especially toxic just because they are nanomaterials," she says. Though that is not a great endorsement for a potential drug-delivery scheme, Bhatia and Derfus also showed that the nanoparticles can be made much less poisonous by encasing them in various types of protective coatings.

DIAGNOSIS BY DOT: Injected into a mouse, quantum dots stick to a tumor in the mouse's thigh. Glowing red under infrared light, the dots help to locate the tumor.

The U.S. government also wants to determine the overall safety of nanoparticles containing quantum dots. Peter E. Barker, project leader for the National Institute of Standards and Technology-National Cancer Institute Biomarkers Validation Laboratory, in Gaithersburg, Md., says that although he is optimistic about the future of the technology, many more experiments are needed. Barker is putting together an analysis of the safety of quantum dots, among other nanotechnologies, for the U.S. Environmental Protection Agency. "How long do quantum dots last in the body, and which organs clear them?" he asks. "How they are going to affect the viability of normal cells is still pretty much up in the air."

If quantum dots prove safe, Barker suggests they might be used to tag cancer cells in the blood, which could then literally be plucked from circulation using a cell sorter, such as those now employed in clinical laboratories to count various types of white blood cells. The approach could be used not only for leukemias and lymphomas but also to remove metastatic cells from solid tumors that are spreading by circulating in the blood.

Such a scenario is still far in the future. But scientists such as Santini and Nie dream of a day when semiconductors will help us triumph, at last, over heart disease and cancer, two of the worst remaining scourges of old age.

Why So Few Women, Still?

By Jill S. Tietjen

"Why are there so few women in engineering?" queried the e-mail from a male engineering student. As I listed the reasons put forth by various experts, the thought occurred to me: "We've been working on this issue for 50 years now. If we really knew the answer, we would have solved it already." But the question still remains. Why aren't more women in the United States pursuing engineering education and careers, and what can we do about it?

In the United States, women constitute about 11 percent of the engineering workforce and earn about 20 percent of undergraduate engineering degrees. According to the Washington, D.C.-based Commission on Professionals in Science and Technology, engineering has the lowest percentage of female graduates among all the professions—lower than medicine, law, economics, dentistry, architecture, and pharmacy. While entry-level doctors and lawyers earn more than the average first-year engineer does, they also typically endure workdays that are far more grueling. Meanwhile, other professionals, such as veterinarians and architects, earn less at entry level than engineers do. So why are women choosing these fields and not engineering?

I've read lots of research on this topic and conducted many recruitment and outreach programs over the years to try to interest more women in studying engineering, and the conclusion I've reached is what I'll call "Jill's Theory": engineering in the United States suffers from a huge image problem. Until the U.S. public understands the value engineers bring to everyday life, the field will continue to see low female enrollments, not to mention declining overall enrollments.

Well over half of the U.S. public, including almost three-quarters of women, don't know what engineers are or what engineers do, according to a Harris Poll on public perceptions of engineering. Conversely, from daily experience, people regularly interact with doctors, lawyers, dentists, and veterinarians and know the value those professionals bring to their lives.

It doesn't help matters that the most famous engineer in the United States is probably the cartoon character Dilbert—a hapless, dateless white male who labors away in Cubicle Row with dysfunctional co-workers and a clueless, if not malicious, boss. Not the sort of environment to which any of us aspire or to which, absent any other information, we would guide our children.

To the average citizen, engineering accomplishments are largely invisible and taken for granted, the main exception being when the lights go out or the phone stops working. Members of the public don't know how they get clean water, what it takes to run the Internet, or the engineering wizardry behind the automobile. People grumble about flight delays without appreciating the meteorological, communications, and navigation systems that protect them and enable them to travel safely.

It wasn't always this way. Jill's Theory posits that engineering's invisibility began with the environmental movement in the 1960s and reached a crescendo with Earth Day in 1970. Underlying people's environmental concerns was the feeling that all technology must be bad because some forms of technology caused air and water pollution. Sensitive to these concerns, companies stopped touting their engineering achievements, and technology went underground. Though engineering continued to power our economy, it and its practitioners lost their visibility and allure.

About the same time as Earth Day, U.S. women began going to college in record numbers. For the first time, they were free (or at least freer) to study any profession they wanted, and the professions they chose were the ones they knew about and saw value in. They didn't choose engineering. Among the small number of women who did enter engineering in the 1970s and early 1980s, most had a family member, usually a father, uncle, or brother, who was an engineer.

The solution to the recruitment problem, according to Jill's Theory, is that engineering needs to make itself visible again. Only by casting engineering's image in a positive light and showing its value to the world will we be able to recruit higher numbers to the field, including more women. It's been demonstrated that popular movies and TV shows like "L.A. Law" and "ER" helped boost the number of lawyers and health-care professionals. I can't think of any network shows that glamorize engineering.

Companies, technical societies, and nonprofit organizations must all work together to increase the visibility and promote the value of the profession. Some organizations are already working on the image problem, to be sure. The National Society of Professional Engineers, for example, has created a state-by-state sightseeing guide to engineering-related attractions. The Girl Scouts of the USA has launched a pro-science and technology campaign with the tag line "It's her future, do the math." A number of engineering societies, including the IEEE, sponsor the annual National Engineers Week. But much more must be done.

Individual engineers also have a role to play. They can visit their children's schools to talk about what they do, and they can lend their technical abilities to the community. Engineering role models, both male and female, need to be as prominent as possible. My friend Kristy Schloss runs a company that makes water treatment equipment. She regularly speaks to students about the tremendous satisfaction she derives from helping to clean up the world's water and thus boost people's life expectancies. My friend Sandra Scanlon's company wires schools, bringing computers and the Internet to thousands of children; in her spare time she organizes engineering outreach programs for middle-school girls.

The mainstream media rarely talk about engineering's accomplishments, at least not in proportion to its impact. The group Engineers without Borders, for example, builds water conveying and filtration systems in poor communities around the world. Its efforts reduce disease and also allow village children (especially the girls) to go to school, because they no longer spend their days toting water. Now, this is engineering that makes a difference. And yet the group has received virtually no press attention.

I look forward to the day when top engineering and science prizes get the same level of coverage as the Academy Awards. Then we will know that the public has come to understand the value that engineers bring to society. I'll also bet that, by that time, the engineering field will have reached gender parity and will also be significantly ethnically diverse.