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FRONTIERS OF ENGINEERING

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LINKING ENGINEERING AND SOCIETY

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The BRIDGE

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Editor's Note

Julia M. Phillips

Highlights of the 2008 U.S. Frontiers of Engineering Symposium

Every year NAE sponsors a U.S. symposium on the Frontiers of Engineering (US FOE). For three days, about 100 outstanding young engineers (ages 30 to 45) from academia, industry, and government laboratories come together to share ideas and learn about cutting-edge research on a variety of engineering topics. These competitively selected emerging engineering leaders come from a wide range of backgrounds to share their interests and talents. The symposium offers them a unique opportunity to learn about the latest research in engineering areas other than their own and to share their work and ideas with researchers in other fields.

Six papers based on this year's presentations are included in this issue of *The Bridge* (summaries of all of the papers delivered at the symposium will be published in February 2009 in the annual FOE volume). The four topics for the fourteenth US FOE Symposium, held on September 18–20, 2008, at the University of New Mexico in Albuquerque, New Mexico, were: drug-delivery systems; emerging nanoelectronic devices; cognitive engineering; and understanding and countering the proliferation of weapons of mass destruction.

The session on the revolution in drug delivery was chaired by William Grieco and Efrosini Kokkoli. The first speaker, Samir Mitragotri, whose paper appears on p. 5, outlined the challenges of delivering medicines to patients in a way that is both safe and likely to encourage their compliance. He highlighted recent advances in the development of painless, patient-friendly approaches to delivering macromolecular drugs that have historically been administered by injection. The second speaker, Jeffrey Hrkach (see p. 10) focused on the development of particle-based drug delivery via encapsulation in a polymer matrix.

Daniel Pack turned his attention to the challenges of gene therapy. He described recent progress in the design of materials that could deliver genes more safely and effectively. Xiaohu Gao, the last speaker in the session, described the use of quantum dots to trace the pharmacokinetics and pharmacodynamics of drug candidates and to elucidate design principles for drug-carrier engineering.

The session on emerging nanoelectronic devices, chaired by Jia Chen and Victor Zhirnov, included presentations on how novel nanoscale materials and devices, circuit concepts, and sensor functionalities can be brought together to develop new technologies for information processing. Jeff Welser focused on the need for new technologies in response to the exponential increases in power density in semiconductor technology, which is negating the benefits of scaling to smaller devices. Nikolai Zhitenev's talk was on using short molecules and macromolecules as active materials for a new generation of switching devices.

Ali Javey and collegues, whose paper appears on p. 18, described an approach to printing inorganic materials, specifically crystalline semiconductor nanowires, for mass produced, inexpensive device and sensor integration. Mihrimah Ozkan concluded the session by outlining a tiered approach to nanomanufacturing molecular electronics that overcomes the challenges of charge-carrier transport across bio-inorganic interfaces, error-free repeatability of the synthesis of hybrid building blocks, and direct integration on Si platforms (see p. 25).

The third session, on cognitive engineering, was chaired by Barrett Caldwell and Kim Vicente. Cognitive engineering is a branch of study that analyzes and improves systems design and training to support cognitive and decision-making skills, particularly in applied, naturalistic settings. In the first presentation, Stephanie Guerlain provided something of a tutorial on cognitive engineering, which she described as a combination of the features of many different fields of study, some engineering and some not, for the purpose of understanding and designing effective, safe systems that include human operators “in the loop.” John Lee, whose paper begins on p. 32, relayed some astonishing data about the percentage of automobile accidents caused by distraction and inattention. He then described how sensor, data fusion, and control technology could potentially improve driving safety by mitigating the effects of the devices most likely to distract drivers.

Ronald Boring outlined the three process phases (identification, modeling, and quantification) historically associated with human-reliability analysis, a tool used to design and train human operators in nuclear power plants and other high-consequence occupations. He argued that a fourth phase, error prevention, should be added to the methodology. Human-reliability analysis should be part of the design phase of a system, he said, rather than a retrospective analysis of a system that has already been designed. This would improve the efficiency of designing safe, effective systems. The final speaker in the session, Ann Bisantz (see p. 39) described how cognitive engineering methods that can represent highly complex systems, such as health care, can facilitate an understanding and model strategies based on the experiences of practitioners to improve communication and collaboration in health care settings.

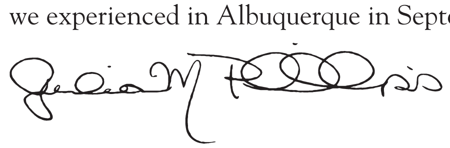
The session on understanding and countering the proliferation of weapons of mass destruction was chaired by Greg Hebner and Scott Goldstein. The first speaker, Steven Nixon, described the urgent need for significant adaptation in the U.S. national security posture to meet the challenges of globalization. Charles Beames then presented case studies of three industry leaders in innovation, Google, Apple, and IBM, which he used to determine common cultural characteristics that might be applicable to improving the nation’s ability to develop innovative countermeasures to the asymmetric technologies that are increasingly being used by our adversaries. Joseph Martz concluded the session by noting the critical importance of science and engineering to nuclear deterrence in the 21st century.

The technical talks were followed by extended, enthusiastic Q&A sessions. The program this year also featured 90-minute breakout sessions of groups of 10 to 15 individuals, each of whom described the most important advance he or she hoped to achieve in the next 10 years, as well as the most important advance someone else might make that would contribute to meeting that goal. Each group then explored the connections between ideas and identified linkages between their very different disciplines, technologies, and employment sectors. These highly interactive educational exchanges of information stimulate ideas for new avenues of exploration.

The dinner speaker this year was, for the first time, an alumnus of the FOE program. Dr. Alton D. Romig, executive vice president and deputy laboratories director for integrated technologies and systems, Sandia National Laboratories, spoke on energy policy, the role of technology in national security, and the intimate connection between policy and engineering.

This year’s symposium was supported by Sandia National Laboratories, University of New Mexico School of Engineering, The Grainger Foundation, Air Force Office of Scientific Research, Defense Advanced Research Projects Agency (DARPA), Department of Defense–DDR&E-Research, National Science Foundation, Microsoft Research, Sun Microsystems, IBM, Intel, Alcatel-Lucent/Bell Laboratories, Corning Inc., Cummins Inc., and NAE member John A. Armstrong.

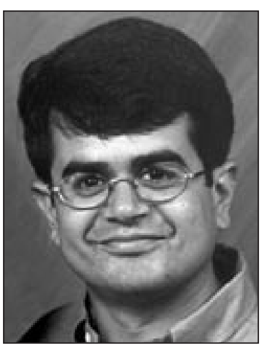
FOE symposia are interdisciplinary, diverse, and stimulating gatherings for everyone who attends. I hope the six papers in this issue convey a sense of the excitement we experienced in Albuquerque in September.



Macromolecular drugs can be delivered with painless, patient-friendly alternatives to injections.

Recent Developments in Needle-Free Drug Delivery

Samir Mitragotri



Samir Mitragotri is a professor of chemical engineering at the University of California, Santa Barbara.

Delivering medicines to patients in a safe, effective, and compliant way can be a major challenge (Langer, 2003). Pills and injections are the most common modalities for administering drugs. Although pills can only deliver small molecules, they are generally accepted as a convenient mode of drug delivery (Morishita and Peppas, 2006). Macromolecular drugs such as peptides and proteins, which cannot be taken orally, must be administered by injection. For some drugs, however, systemic administration to healthy tissues can be toxic, regardless of how they are administered. These drugs are only effective if they act directly on specific diseased tissues (Vasir and Labhasetwar, 2005).

The ability of drugs to reach target tissues from the point of administration via pills or injections is limited by the body's multiple barriers, including enzymatic degradation in the stomach, absorption across the intestinal epithelium, hepatic clearance, and accumulation in non-targeted tissues. These barriers have a range of lengths (from the tissue to the organelle level) and time scales.

Collectively, these conditions have made the conversion of potent biomolecules into medical therapies very challenging. The field of drug delivery has grown in response to these challenges and is now a significant component of the overall drug-development process.

In the past several decades, tremendous progress has been made toward the development of safe, effective, and convenient means of drug administration. Advances have been possible, at least in part, because of our improved understanding of the human body. This article focuses on some key developments in the field of drug delivery, especially those that deal with the development of painless, patient-friendly alternatives to injections for the delivery of macromolecules (Figure 1).

The Need for Better Methods of Drug Delivery

Needles and syringes are the most common method of administering macromolecular drugs; an estimated 12 billion injections are given annually worldwide (Kermode, 2004). Despite their common use, needles have several limitations, including needle phobia (Nir et al., 2003) and accidental needle sticks (Rosenstock, 2000). In addition, concerns have arisen about the unsafe use of needles, as exemplified by the overwhelming number of HIV, hepatitis C, and hepatitis B infections that are thought to originate each year from the re-use of needles and syringes (Kane et al., 1999).

Noncompliance with medical treatment regimes is also a significant issue. It has been estimated that most patients do not adhere to prescribed dosing regimens, even in developed countries. Noncompliance is linked to several factors, including pain, needle phobia, and forgetfulness, and can result in serious medical complications. In fact, noncompliance is a leading cause of hospitalizations when the carefully designed drug concentration profile is altered in a way that becomes harmful to the patient.

Typically, the blood concentration levels of both injectable and oral drugs that are administered repeatedly vary, depending on the schedule of their administration and the speed at which they are absorbed and distributed by the body. Deviations from the therapeutic range of blood concentrations cause undesirable effects. For these reasons, it is important that drug developers, in addition to considering the efficacy and safety of a drug, must also carefully consider how a drug-delivery system may affect patient compliance.

The limitations of conventional methods of drug delivery can potentially be overcome by needle-free delivery of drugs through the skin or mucosal surfaces of the mouth, nose, or lungs (Varmus et al., 2003). Although these represent viable alternatives to needle-based methods, these surfaces also present significant barriers to drug entry into the body, and breaching them in a safe, effective way is a major goal of drug-delivery research. This article, provides a brief review of past efforts, a description of the current status, and prospects for the future, with an emphasis on transdermal and oral drug delivery.

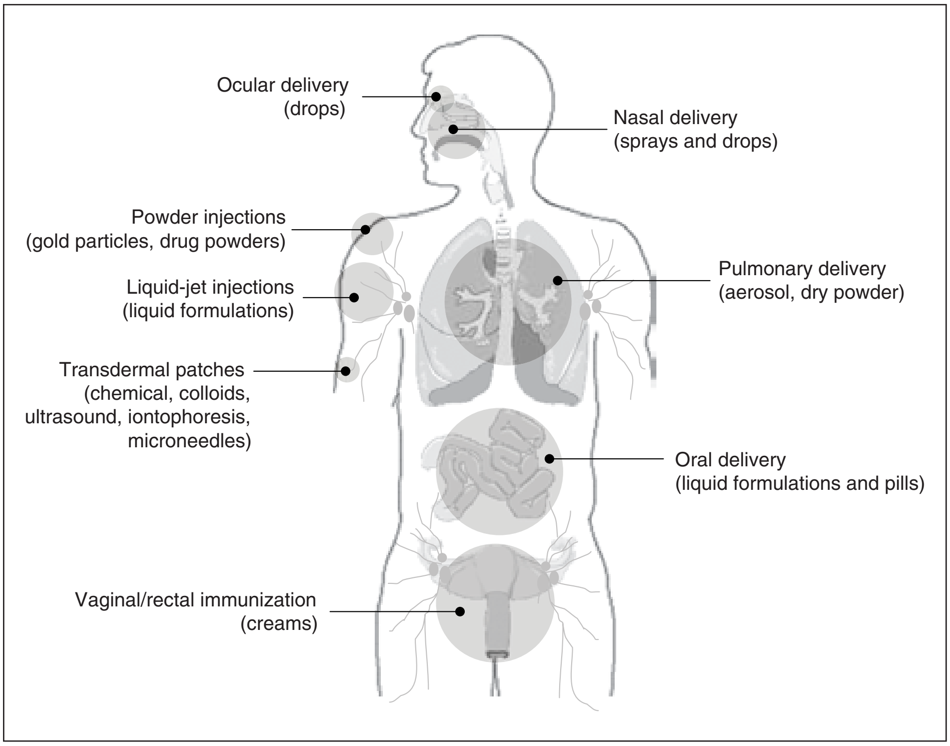


FIGURE 1 Various modes of needle-free drug delivery. Source: Adapted from Mitragotri, 2005.

Transdermal Drug Delivery

Skin, the largest human organ, provides a painless, compliant interface for systemic drug administration (Zaffaroni, 1991). However, because skin evolved to impede the flux of toxins into the body, it naturally has low permeability to the movement of foreign molecules (Wertz and Downing, 1989). A unique, hierarchical structure of lipid-rich matrix with embedded corneocytes in the stratum corneum (the upper strata

[15 µm] of skin), is responsible for this barrier (Wertz and Downing, 1989).

Corneocytes, cross-linked keratin fibers (about 0.2–0.4 microns thick and about 40 microns wide) held together by corneodesmosomes, provide structural stability to the stratum corneum. Lipids, which provide the primary barrier function in the stratum corneum, consist of several components; the primary constituents are ceramides, cholesterol, and fatty acids. The layer of lipids immediately adjacent to the corneocytes is covalently bound to them and plays an important role in maintaining the barrier function. The stratum corneum is continuously desquamated, with a renewal period of about one week, and is actively repaired by the secretion of lamellar bodies following the disruption of the barrier properties or other environmental insults (Prausnitz et al., 2004).

Transdermal drug delivery involves placing a drug on the skin in the form of a patch, cream, or lotion wherein the drug permeates across the skin and enters the bloodstream. Key advantages of transdermal delivery include the easy accessibility of skin, which encourages patient compliance, avoidance of the gastrointestinal tract, and sustained release over extended periods of time (Prausnitz et al., 2004).

A number of drugs, including scopolamine, nitroglycerin, nicotine, clonidine, fentanyl, estradiol, testosterone, lidocaine, and oxybutinin, are routinely delivered transdermally by skin patches (Prausnitz et al., 2004). The patches, which generally last from one to seven days, depending on the drug, have enabled new therapies and reduced first-pass effects and severe side effects. For example, estradiol patches, which are widely used, have eliminated liver damage, which was a side effect of the drug when it was delivered orally. Transdermal clonidine, nitroglycerin, and fentanyl patches also have fewer adverse effects than the same drugs delivered orally. Nicotine patches have prevented, or at least reduced, smoking and increased lifespans (Prausnitz et al., 2004).

Two classes of transdermal patches are currently available: (1) reservoir-type patches and (2) matrix-type patches. A reservoir-type patch holds the drug in a solution or gel, and the rate of delivery is governed by a rate-controlling membrane. Reservoir-type patches offer more flexibility in terms of drug formulation and tighter control over delivery rates than matrix-type patches. However, they are usually associated with greater design complexity. In matrix-type patches, the drug, adhesive, and mechanical backbone of the patch are combined into a single layer. Thus matrix-type patches are easier to fabricate, but they pose even more significant design constraints than reservoir-type patches (Prausnitz et al., 2004).

Drugs that are currently administered transdermally have two common characteristics—low molecular weight and high lipophilicity. Opening the transdermal route to large hydrophilic drugs, a major challenge in the field of transdermal drug delivery, will require the development of technologies that enable the controlled, reproducible transdermal delivery of macromolecular drugs.

Drugs delivered transdermally have two common characteristics—low molecular weight and high lipophilicity.

Passive Methods

Technologies that facilitate transdermal drug delivery can work either passively or actively, depending on whether an external source of energy is used to facilitate skin permeation (Figure 2). Passive methods include chemical enhancers, micelles, liposomes, and peptides (Chen et al., 2006; El Maghraby et al., 2006; Karande et al., 2004; Schreier and Bouwstra, 1994; Schuetz et al., 2005). Examples of chemical enhancers include fatty acids, fatty esters, solvents, and surfactants (Williams and Barry, 1992). These enhancers facilitate transdermal transport by making drugs more soluble, increasing partitioning into the skin, fluidizing the crystalline structure of the topmost layer of skin, or dissolving skin lipids.

Although individual chemical enhancers have had some success, combinations of chemical enhancers are more effective. However, so far, the rational design of combinations of enhancers has been limited by the lack of information on interactions between individual chemical enhancers and the stratum corneum. The number of randomly generated formulations for binary mixtures is in the millions, and the number for higher order formulations (for example, ternary or quaternary mixtures) is even higher. Screening of these formulations is beyond the scope of traditional methods (e.g., Franz diffusion cells).

High-throughput methods of screening transdermal formulations can open this bottleneck and may lead to the discovery of previously unknown mixtures. A new high-throughput method for screening transdermal formulations (Karande et al., 2004) is > 100-fold more efficient than Franz diffusion cells (Bronaugh, 1989); with this method, up to 1,000 experiments a day can be conducted, an experimental space well beyond the scope of traditional tools (Karande and Mitragotri, 2001). Recent studies have also shown that peptides may effectively increase skin permeability. Specifically, peptides discovered using phage-display methodology have been shown to deliver macromolecules, such as insulin, *in vivo* (Chen et al., 2006).

Chemical enhancers are relatively easy to incorporate into transdermal patches and can be calibrated to deliver predetermined amounts of a drug by changing the application area. However, passive methods cannot dynamically control the drug dose.

Active Methods

Active methods can be controlled in real time by varying appropriate parameters. The device and application parameters can also be adjusted to match the patient's skin properties. A growing number of researchers are now exploring transdermal devices with active mechanisms for skin permeation, such as microneedles, jet injectors, ultrasound, iontophoresis, and electrophoresis (Arora et al., 2007; Bashir et al., 2001; Doukas and Kollias, 2004; Habash et al., 2006; Kalia et al., 2004; Karande et al., 2004; Mitragotri et al., 1995; Prausnitz et al., 1993; Zhang et al., 1996).

Microneedles are arrays of micrometer-sized shallow needles that penetrate only into the superficial layers of skin, thereby eliminating the pain associated with standard hypodermic needles (Prausnitz, 2004). Microneedles have been made from a variety of materials, including metals, semiconductors, polymers, and glass, and have been shown to be effective in drug delivery. They have also been produced in solid and hollow forms. Solid microneedles are used to render

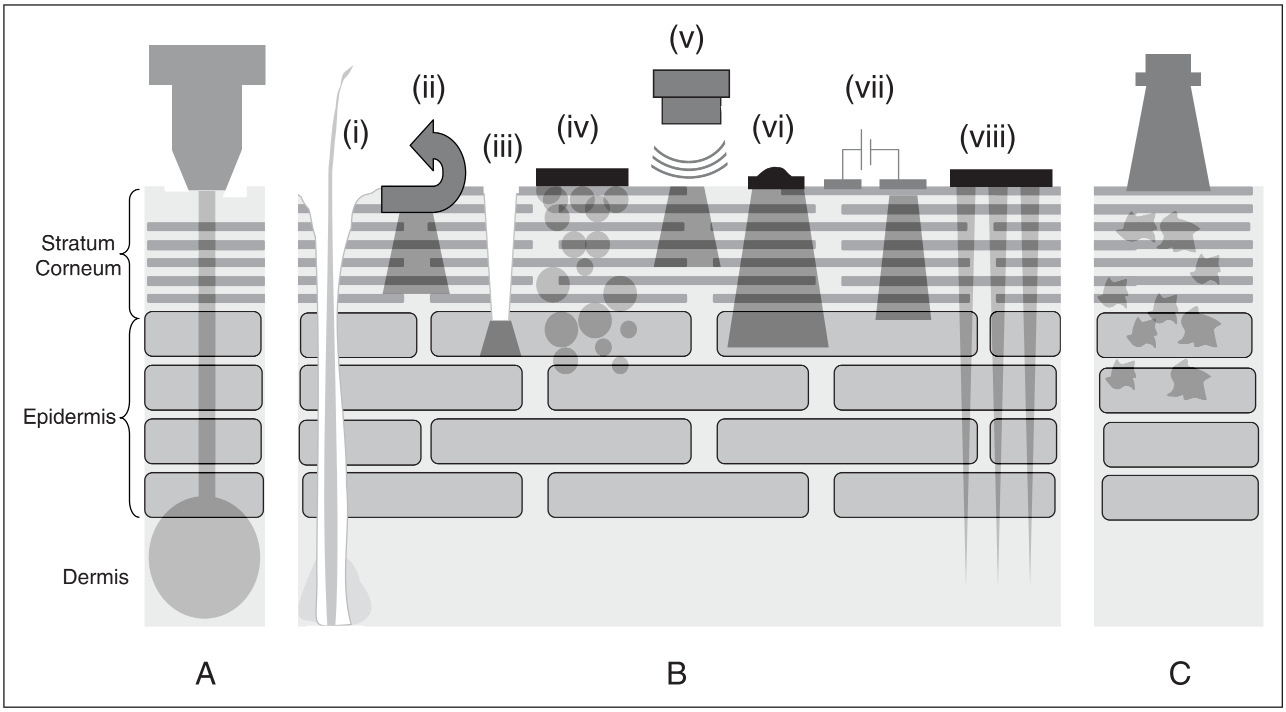


FIGURE 2 Various modes of transdermal drug delivery. (A) Liquid-jet injections deliver drugs into intramuscular, subcutaneous, or intradermal regions. (B) Permeability-based methods of transdermal drug delivery: (i) delivery through hair follicles; (ii) tape-stripping removes the stratum corneum and facilitates drug absorption; (iii) thermal or radio frequency wave-mediated ablation of the stratum corneum creates micropores that enhance drug delivery; (iv) colloidal carriers, such as microemulsions and transfersomes, enhance the dermal absorption of topically applied drugs; (v) low-frequency ultrasound increases drug delivery by making the skin more permeable; (vi) chemical enhancers or peptides for drug delivery; (vii) electroporation of the stratum corneum enhances drug delivery into the epidermis; (viii) microneedles penetrate into the epidermis to deliver drugs. (C) Powder injection delivers dry drug powders into superficial skin layers (epidermis and superficial dermis). Source: Adapted from Mitragotri, 2005.

skin permeable, whereas hollow microneedles actively deliver drugs into the skin at a controlled rate.

In contrast, jet injectors deliver a high-velocity liquid jet stream into the skin, delivering drugs into various skin layers, depending on the jet parameters (Mitragotri, 2006). Jet injectors have a long history, particularly in the delivery of vaccines, insulin, and growth hormone. Ultrasound enhances skin permeability by cavitation, which temporarily disrupts skin structure (Paliwal et al., 2006; Tezel and Mitragotri, 2003). Iontophoresis and electroporation use electric fields to alter skin structure and/or provide additional driving force for drug penetration through the skin (Banga and Prausnitz, 1998; Guy et al., 2000).

Combined Technologies

Although many individual technologies have been shown to facilitate transderml drug transport, combinations of technologies are often more effective than any of them alone (Mitragotri, 2000). A combination of two or more technologies may not only increase the enhancement, but may also potentially be safer. Understanding the synergies between technologies and selecting the right combinations is a fruitful area for research that is still largely unexplored.

Summary

In the last decade, significant new insights have been developed into the structural organization and barrier formation of the skin. In the past, skin was considered primarily a barrier, but it is now known to be a smart material that controls its own structure and function in response to the environment (Menon, 2002). This new knowledge must be incorporated into the future development and evaluation of transdermal technologies.

Oral Drug Delivery

Oral drug delivery is the most common, and the preferred type of drug administration. A large number of small molecules, including those prescribed for the treatment of pain, heart disease, and blood pressure, are already delivered orally. Drugs delivered orally are typically absorbed across the intestinal epithelium into the bloodstream via two mechanisms. The transcellular route involves the transport of drugs through the cell membrane to cross the barrier, either by partitioning of the drug into cell membranes or through the generation of small pores in the outer cell membrane, which allows entry into the cell.

Alternatively, the drug may permeate through the paracellular pathway, which entails transport through the tight junctions between epithelial cells (Cano-Cebrian et al., 2005). A tight junction is a dynamic network of tightly packed proteins in the interstitial spaces of a cell monolayer. Tight junctions have been likened to gatekeepers, as their primary function is to maintain the barrier properties of the epithelium and only permit the transport of very small molecules (< 4 nm in diameter).

A third possibility is that drugs may be actively transported across the epithelium through receptor-mediated endocytosis (Figure 3).

Proteins and Peptides

The oral delivery of proteins and peptides has elicited a great deal of interest in recent years because of the availability of novel therapeutics through the advent of recombinant DNA technology. Proteins and peptides are macromolecules with a wide variety of functions in biological catalysis, the regulation of cellular processes, and immune-system protection.

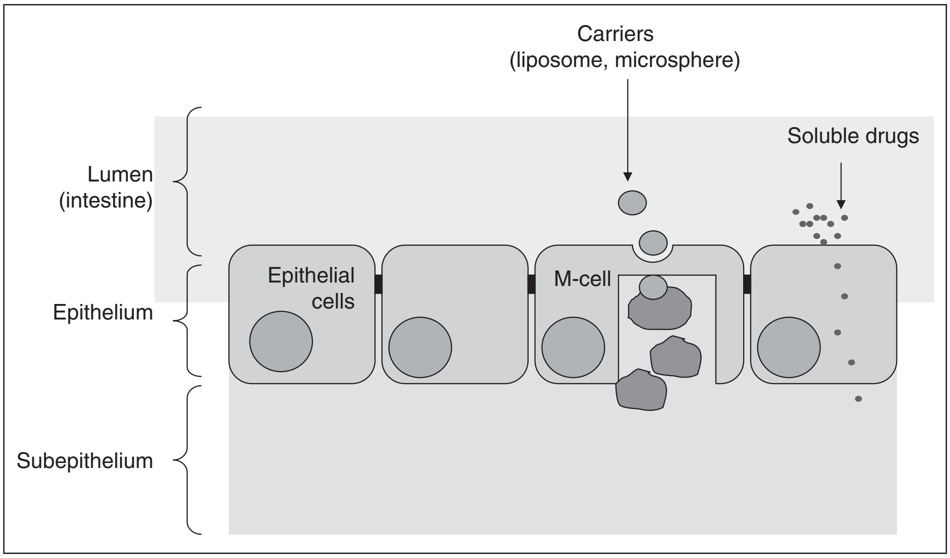


FIGURE 3 Pathways of drug absorption across the intestinal epithelium. Source: Adapted from Mitragotri, 2005.

Effective oral delivery of a protein or peptide requires that a therapeutic molecule be delivered to the site of interest and cross the intestinal epithelium barrier intact before being transported to the portal circulation system. Unfortunately, this process is difficult and results in only a small fraction of drug being absorbed in the bloodstream. The delivery of proteins and peptides is further limited by their susceptibility to enzymatic degradation in the gastrointestinal tract (Morishita and Peppas, 2006).

The scientific community has made a major effort in recent years to overcome the obstacles to oral delivery through the development of a large number of new, innovative drug-delivery techniques (Hosny et al., 2002; Luessen et al., 1995; Lyu et al., 2004; Sinha et al., 2004; Whitehead and Mitragotri, 2008; Whitehead et al., 2004, 2008a;b). These methods include enzyme inhibitors, permeation enhancers, mucoadhesive polymers, chemical modification of drugs, targeted delivery, and encapsulation.

With engineering tools at hand, the future of drug delivery looks brighter than ever.

Enzyme Inhibitors

Enzyme inhibitors are used to counteract the natural functions of the enzymes of the gastrointestinal tract that break down ingested proteins. Many studies have been performed in which inhibitors were co-administered with a drug (Bernkop-Schnurch, 1998), but these strategies have seldom been successful unless they included absorption enhancers.

Permeation enhancers have also been used, similar to the way they are used in transdermal drug delivery (Carino and Mathiowitz, 1999). Permeation enhancers, such as surfactants, fatty acids, and bile salts, either disrupt the epithelial membrane of the intestine or loosen the tight junctions between epithelial cells. While numerous studies have demonstrated that certain enhancers can be very potent delivery aids, safety concerns abound (Aungst, 2000).

Mucoadhesives

Mucoadhesive strategies have also been used to localize drugs to a small, defined region of the intestine through attractive interactions between the carrier and the intestinal epithelium. This kind of localization results in a high concentration gradient of the drug across the epithelial barrier, which improves drug bioavailability. In addition, a strong adhesion force prolongs the residence time of the dosage at the site of drug absorption, which reduces the dosing frequency and, in turn, increases patient compliance.

Certain mucoadhesive polymers, such as polycarbophil and chitosan derivatives, have been shown to simultaneously act as permeation enhancers and enzyme inhibitors (Luessen et al., 1995; Sinha et al., 2004).

Encapsulation Technologies

Encapsulation technologies are another alternative for the oral administration of drugs. Using commercially available pH-sensitive polymers, it is possible to target particular regions of the intestine (e.g., jejunum or colon) for drug delivery. Enteric coatings made from these pH-sensitive polymers enable drug-delivery devices to pass through the acidic environment of the stomach unscathed and rapidly dissolve in the intestine. Studies to evaluate these polymers for targeted oral delivery are ongoing in various laboratories (Hosny et al., 2002; Lyu et al., 2004).

Other techniques involve the targeting of M-cells in the intestine to improve mucosal vaccine delivery. M-cells, which are present in the Peyer's patches of the intestine, have the unique ability to take up antigens; targeting can be achieved by using M-cell-specific lectins in combination with a drug-delivery formulation.

Other encapsulation strategies, including microparticles (Mathiowitz et al., 1997), nanoparticles (Carino et al., 2000), and liposomes (Iwanaga et al., 1999), have been developed. These strategies can protect proteins from enzymatic degradation in the intestine and/or facilitate protein uptake across the epithelium (Carino and Mathiowitz, 1999).

Areas for Ongoing Research

Novel, painless, patient-friendly methods of drug delivery represent an unmet need in the field of health care. Discoveries in the last decade have demonstrated the feasibility of using several different methodologies for enhancing drug delivery through skin and other mucosal surfaces. These methods have shown the potential to deliver several molecules, including macromolecules such as insulin and vaccines.

The development of mathematical models to describe and predict transport across the skin and mucosal barriers is another area of active research that has provided useful insights into the development of novel strategies. With the variety of engineering tools at hand, the future of drug delivery looks brighter than ever. The challenge is to convert these discoveries into useful products.

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New drug-delivery strategies will lead to safer, more effective treatments for previously intractable diseases.

Targeted Polymeric Nanotherapeutics

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Jeff Hrkach

This paper provides an overview of steps being taken by BIND Biosciences Inc. to translate innovative research conducted at the Massachusetts Institute of Technology (MIT) and Harvard Medical School into novel, targeted, polymeric nanotherapeutics.

Advances in drug delivery have significantly affected the lives of patients afflicted with a variety of diseases. New drug-delivery strategies can improve the efficacy, safety, and/or compliance of existing approved medicines and can lead to the development and approval of new drugs with inherent properties (e.g., solubility, bioavailability, off-target side effects) that might otherwise keep them from being approved. In many cases, these improvements are the result of changes in formulation leading to, for example, longer lasting action or a change in delivery modality (e.g., transdermal or inhalation).

Particle-based drug delivery, particularly polymeric particle systems wherein delivery is achieved by encapsulation, or physical entrapment, of a drug within the particle matrix, has been a very active area of interest that has resulted in several successful products. One example is Risperdal CONSTA®, which is indicated for the treatment of schizophrenia.[1]

Risperdal delivers the drug risperidone encapsulated in poly(lactide-*co*-glycolide) (PLGA) biodegradable polymeric microspheres with a particle

[1] *http://www.risperdalconsta.com.*

diameter of about 100 microns via intramuscular injection once every two weeks. The drug is released over time from the particles by slowly diffusing out of the polymeric matrix as water diffuses in and as the polymer chains degrade via hydrolysis, causing particles to lose their structure and fall apart. PLGA-based particle drug-delivery systems can be tailored to the properties of the drug, appropriate dosage, and the mechanism of action for releasing the encapsulated drug over a period of weeks or months in a controlled way.

Nanoparticles can deliver therapeutic payloads directly to the disease site.

Risperdal®, the original risperidone product, is taken orally by patients with schizophrenia on a daily basis. In most cases, the simplicity of taking a pill is very strongly preferred as a method of administering a drug, and designing a drug-delivery system to change the administration from oral delivery to a more complicated (e.g., inhalation) or painful (e.g., injection) delivery, would normally be unsuccessful (unless the oral drug had a significant shortcoming).

For patients with schizophrenia, however, taking a pill every day can be problematic, and missing a dose one day can lead to a downward spiral of missing more doses. In this case, intramuscular injection administered by a doctor or nurse once every two weeks has not only increased patient compliance, but also improved the efficacy of the drug, resulting in a significant improvement in the treatment of patients with schizophrenia.

Microparticle delivery systems, such as Risperdal CONSTA, are too big to be administered intravenously. Their particle size would result in very fast clearance by the body's defense mechanisms or could potentially pose a significant safety risk if they were to lodge in capillary beds in the heart or lungs. Nanoparticle-based drug delivery systems, in which particle sizes generally range from about 20 to 200 nanometers, are being investigated for delivering therapeutic agents, imaging diseased tissues or organs, and sensing the effectiveness of drug delivery or the status of disease. As a point of reference, a nanometer is one-billionth of a meter or one-millionth of a millimeter. Because of their very small size, nanoparticles administered systemically (i.e., by intravenous injection or infusion) circulate through the bloodstream carrying their therapeutic payloads directly to the site of disease in the body.

Nanoparticle-Based Drug-Delivery Systems

Diseases associated with defects or irregularities in the endothelial cells of blood vessels in the diseased area, creating what is called "leaky vasculature," may be particularly susceptible to treatment by nanoparticle-based drug-delivery systems. These include inflammatory diseases (e.g., rheumatoid arthritis, atherosclerosis), infectious diseases (e.g., tuberculosis), and cancer. Once nanoparticles reach the affected area, they can passively diffuse from the bloodstream across the leaky vasculature to deliver drugs directly to the disease site.

However, because nanoparticles are foreign bodies circulating in the bloodstream, the natural defense mechanisms of the body attempt to remove them. The way the body protects itself from nanoparticles or other foreign particulate matter circulating in the bloodstream is through the mononuclear phagocytic system (MPS), sometimes also called the reticulo-endothelial system, in which phagocytic cells located primarily in the liver and spleen engulf the nanoparticles. High levels and fast rates of nanoparticle clearance by the MPS lead to an accumulation of nanoparticles in the liver and spleen, thus removing them from circulation before they are able to reach the site of disease and effectively deliver their therapeutic payloads. In addition, if the drug being delivered has potential specific toxicities in the liver or spleen, the clearance of nanoparticles by these organs may exacerbate those effects making the drug less tolerable or more dangerous.

The optimization of nanoparticle properties, therefore, is critical to the development of a safe nanoparticle drug-delivery system. Particle-surface characteristics (e.g., chemical composition, charge) have a strong influence on the detection of nanoparticles by the MPS. Therefore, one way to minimize MPS clearance is to construct nanoparticles with poly(ethylene glycol) (PEG), a biocompatible polymer, on the surface, a technique that has been successfully used to increase the circulation time of biodegradable polymeric nanoparticles (Gref et al., 1994). The hydrophilic, uncharged nature of PEG can interfere with phagocytic recognition and the uptake of nanoparticles or proteins resulting in prolonged circulation times and more opportunity for the drug to reach the intended disease target.

DOXIL®, a liposomal formulation of the drug doxorubicin that uses a PEG surface to prolong circulation time,[2] is approved for treatment of ovarian cancer, AIDS-related Kaposi's sarcoma, and multiple myeloma. Doxorubicin, like many drugs, does not have a long circulation time in the bloodstream but instead can diffuse throughout the body in a way that can cause untoward side effects and that limits the amount of drug delivered to the tumor, thus decreasing its efficacy. By encapsulating doxorubicin in PEGylated liposome nanoparticles, DOXIL allows for longer circulation times than the drug has in its free, unencapsulated state, in fact long enough for the particles to diffuse into and deliver doxorubicin to the tumor vasculature.

A potential downside of nanoparticle-based drug-delivery systems is that they can deliver more drug to certain parts of the body than the free drug would normally deliver, which can result in either new side effects or an exacerbation of existing side effects. For DOXIL, the result is an increase in the incidence of hand-foot syndrome (a skin irritation that usually occurs on the hands and feet) compared to doxorubicin alone. The apparent cause is that the long-circulating nanoparticles eventually land in the capillary beds of the hands and feet where they deliver liposome-encapsulated doxorubicin in greater amounts than would be delivered by free, unencapsulated doxorubicin.

To repeat, nanoparticles can passively diffuse from the circulating bloodstream through the leaky defects in tumors or areas of infection or inflammation to deliver their therapeutic payloads. Although effective, this passive targeting can have limitations in that nanoparticles may also diffuse out of the disease site through the defects back into circulation. Considerable research is being conducted to improve nanoparticle drug-delivery systems by trying to actively target the nanoparticles to diseased cells (Allen, 2002; Heidel et al., 2007; Peer et al., 2007). These approaches attempt to take advantage of the presence of unique or highly up-regulated cell-surface receptors on diseased cells by functionalizing the surface of nanoparticles with ligands that promote cell-specific recognition and binding.

The intent is that once the particles successfully migrate through the bloodstream to the disease site, targeted nanoparticles will then anchor themselves to the disease cells, keeping the nanoparticles in place long enough to deliver their payloads. The choice and properties of the cell-surface receptor may even allow for the uptake of intact nanoparticles into the cell. The resulting intracellular drug delivery can greatly increase the effectiveness of the drug.

For some drugs and therapeutic applications, intracellular delivery may be necessary, thus requiring intracellular nanoparticle trafficking. One example of this is the new class of short-interfering RNA (siRNA) drugs, which are being developed to inhibit the production of disease-causing proteins through RNA interference (RNAi).

The BIND Targeted Nanoparticle

BIND Biosciences Inc. (BIND), a biopharmaceutical company that was founded upon the research of two pioneers in nanoparticle drug delivery, Professor Robert Langer of MIT and Professor Omid Farokhzad of Brigham and Women's Hospital of the Harvard Medical School, has developed methods of engineering targeted nanoparticles composed of biodegradable and biocompatible polymers with precise biophysicochemical properties optimized to deliver drugs for specific therapeutic applications (Gu et al., 2008).

The foundational research by Langer and Farokhzad put BIND in a position to pursue the development of targeted polymeric nanotherapeutics for treating several diseases. BIND's lead program is focused on translating their innovative academic findings into improved treatments for patients with cancer. The BIND technology offers a unique combination of long-circulating nanoparticles with the capability of targeting diseased cells specifically and releasing drugs from nanoparticles in a programmable, controlled way.

Figure 1 is a schematic diagram of a BIND targeted nanoparticle. The targeting ligand enables the nanoparticle to recognize specific proteins or receptors on the surface of cells involved in disease, or in the surrounding extracellular matrix, and bind, with high

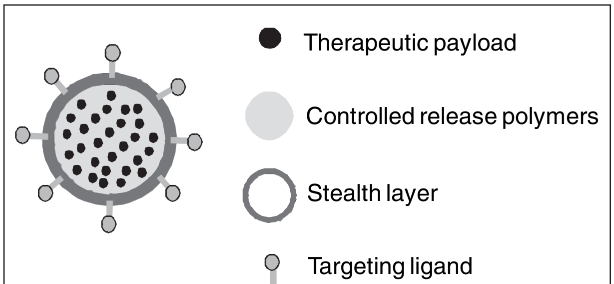

FIGURE 1 Schematic diagram of a BIND targeted polymeric nanoparticle.

[2] *http://www.doxil.com/.*

specificity and avidity, to its intended cellular target site. Many types of cancer have been shown to have cell-surface receptors that are highly expressed on the cancer cells (e.g., prostate cancer [prostate-specific membrane antigen, PSMA], breast cancer [human epidermal growth factor receptor 2, HER-2], and lung cancer [epidermal growth factor receptor, EGFR]), and many drugs are being evaluated that might improve treatment outcomes.

Surface Functionalization

Surface functionalization imparted by a PEG component shields the targeted nanoparticles from MPS immune clearance, while providing an attachment site for the targeting ligand on the particle surface at precise, controlled levels through proprietary linkage strategies. A key to the successful development of BIND targeted nanoparticles is the optimization of the nanoparticle surface, which requires a precise balance between the targeting ligand and PEG coverage so the nanoparticle surface is masked enough to provide circulation times long enough to reach the disease site and enough targeting ligand on the surface to effectively bind to the target cell surface receptors. This delicate balance requires precise control over the nanoparticle production process. It also requires the discovery and selection of ligands that are potent and specific enough to bind selectively to the targeted disease cells while remaining bound to the nanoparticle surface.

The right combination of polymer properties is critical to an optimal drug-release profile.

The polymer matrix, the bulk of the nanoparticle composition, encapsulates the drug in a matrix of clinically safe, validated biodegradable and biocompatible polymers that can be designed to provide appropriate particle size, drug-loading level, drug-release profile, and other critical properties. A variety of drugs or therapeutic payloads can be incorporated into the targeted nanoparticles, including small molecules, peptides, proteins, and nucleic acids, such as siRNA.

Drug-Release Profile

The drug-release profile is a critical factor for the effective delivery of targeted nanoparticles. If the drug leaks out of the nanoparticle too quickly, it will be released into the bloodstream and essentially delivered as free, unencapsulated drug, thus losing the advantages of nanoparticle delivery. If the drug is not released in the appropriate time frame after the nanoparticles have reached the disease site, it may not reach an efficacious level. Thus it is critical that the right combination of polymer properties be tailored to ensure the optimal drug-release profile. BIND targeted polymeric nanotherapeutics can be engineered with different physicochemical properties, mechanisms of action, and dose requirements to provide effective drug delivery for a variety of diseases with different indications.

Regulatory Requirements

When a start-up company is founded based on academic research, the initial scientific efforts are focused on transferring the technology from academic laboratories to the company, where researchers can establish the capabilities of the technology and reproduce the results. Shortly thereafter, with a baseline understanding of the technology in hand, the translational aspects of the research begin. The company focuses on defining the most suitable disease indications to pursue and the specific characteristics required.

At this point, the regulatory requirements dictated in the United States by the Food and Drug Administration (FDA) for pharmaceutical development of drug product candidates must be taken into consideration. Since its inception in early 2007, BIND has undertaken a combinatorial optimization approach resulting in a number of enabling improvements to nanoparticle formulation, as well as the nanoparticle production process to meet the needs of its lead targeted oncology candidate.

The optimization approach includes evaluating the performance of nanoparticles using in vitro cell-based assays and in vivo preclinical testing, as well as several chemistry, manufacturing, and controls (CMC) requirements mandated by current manufacturing practices and the FDA to ensure, among other things, batch-to-batch reproducibility and shelf-life stability. Meeting these requirements entails testing a variety of properties, such as particle size, content of the targeting ligand, drug-loading level, and the stability of the nanoparticles and the drug under storage and in-use conditions. As pharmaceutical development progresses, the CMC requirements become more stringent. However, even at this early stage, the company begins testing critical parameters.

To establish an acceptable level of safety and tolerability to support the initial evaluation of a candidate drug product in human clinical studies, the FDA requires formal safety testing in animal models. This is the first major step in the FDA-regulated area of pharmaceutical development. It also represents the company's first efforts at scaling-up the formulation and process capabilities of the drug. Whereas research at MIT/Harvard and initial efforts at BIND were conducted on nanoparticle batches prepared on the bench-top milligram scale, BIND nanoparticle production batch size has been scaled up three orders of magnitude for the animal safety and tolerability tests that support clinical studies.

The critical, long-term stage of pharmaceutical development is clinical testing. Through a progression of studies, the safety, tolerability, and efficacy of a drug product candidate are established; the tests are accompanied by a series of submissions to and discussions with the FDA.

For BIND targeted polymeric nanotherapeutic drug candidates based on improving the performance of existing marketed drugs, the clinical testing period is likely to be shorter than for a completely new drug candidate, because the history and data established for the existing drug provide valuable reference points for BIND and the FDA. Nevertheless, several clinical studies are required, all CMC requirements must be met, and the nanoparticle production process must be scaled-up to the kilogram level to supply the drug for clinical studies and ultimately, if successful, to supply the approved, marketed drug to doctors and patients.

Thus a long, challenging, very exciting pathway lies ahead for BIND Biosciences in translating the novel targeted polymeric nanoparticle drug-delivery research by Professors Langer and Farokhzad into medicines that can improve, and even save, the lives of patients suffering from serious diseases.

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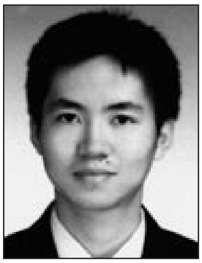
Printable microscale and nanoscale inorganic materials, such as crystalline semiconductor nanowires, provide both high performance and air stability.

Roll Printing of Crystalline Nanowires for Integrated Electronic and Sensor Arrays

Zhiyong Fan, Johnny C. Ho, Roie Yerushalmi, and Ali Javey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Fabrication of printable sensor arrays on bendable/flexible substrates may enable the development of a wide range of new technologies, including flexible displays, radio frequency identification tags, sensor tapes, artificial skin, and more (Friedman et al., 2005; Huang et al., 2001; Lee et al., 2005; McAlpine et al., 2005; Reuss et al., 2005; Service, 2000; Someya and Sakurai, 2003). Tremendous progress has been made in this field in the past decade, mainly through the exploration of organic materials as active semiconductor components. However, the short lifetimes and low carrier mobility of these materials, as compared to crystalline inorganic semiconductors, have been major obstacles to applications that require high speed, low

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power, and long lasting electronics (Reuss et al., 2005; Service, 2000; Someya and Sakurai, 2003). Therefore, a new printable electronic materials technology with improved performance and air stability is of great interest for the future of printable electronics.

Recently, new methods of "printing" microscale and nanoscale inorganic structures have been proposed and developed. Unlike their organic counterparts, inorganic materials provide air stability as well as high performance (Ahn et al., 2006; Bryllert et al., 2006; Fan et al., 2008a,b; Ford et al., 2008; Friedman et al., 2005; Huang et al., 2001; Javey et al., 2007; Lee et al., 2005; McAlpine et al., 2005; Wang et al., 2007; Yerushalmi et al., 2007). One such inorganic material is the crystalline semiconductor nanowire (NW). In this paper, we review recent advances in the assembly and integration of NW arrays on foreign substrates that can be integrated into electronic devices and sensors.

Crystalline Semiconductor Nanowires as Building Blocks for Electronics and Sensors

To date, a variety of functional NWs have been synthesized and integrated as building blocks of single-component devices, such as field-effect transistors (FETs), sensors, photodiodes, and electromechanical systems, to mention just a few (Ahn et al., 2006; Bryllert et al., 2006; Fan et al., 2008a,b; Ford et al., 2008; Friedman et al., 2005; Huang et al., 2001; Javey et al., 2007; Lee et al., 2005; McAlpine et al., 2005; Wang et al., 2007; Yerushalmi et al., 2007). These chemically derived single-crystalline nanostructures (the majority of them synthesized by chemical vapor deposition [CVD]) have unique advantages over conventional semiconductors. They enable the integration of high-performance device elements on virtually any substrate (including mechanically flexible plastics) with scaled on-currents and switching speeds comparable to or higher than those of state-of-the-art, planar silicon (Si) structures.

For example, *p*-type FETs based on heterostructured Ge/Si NWs and n-type FETs based on InAs NWs have demonstrated a carrier mobility about10 times higher than that of Si transistors (Bryllert et al., 2006; Ford et al., 2008; Xiang et al. 2006). These high-mobility NW materials are ideal platforms for high-performance, printable electronics. Uniquely, the electrical properties of NWs are extremely sensitive to their chemical/biological and electromagnetic surroundings because of their miniaturized dimensions, large surface-area-to-volume ratio, and finite carrier concentration. As a result, sensors based on NWs are also highly sensitive. For example, NWs made of Si and In_2O_3 have been extensively studied for use in biological and chemical sensors capable of detecting analytes down to the level of single molecules (Zheng et al., 2004, 2005). CdSe and ZnO NWs, which are optically active and have

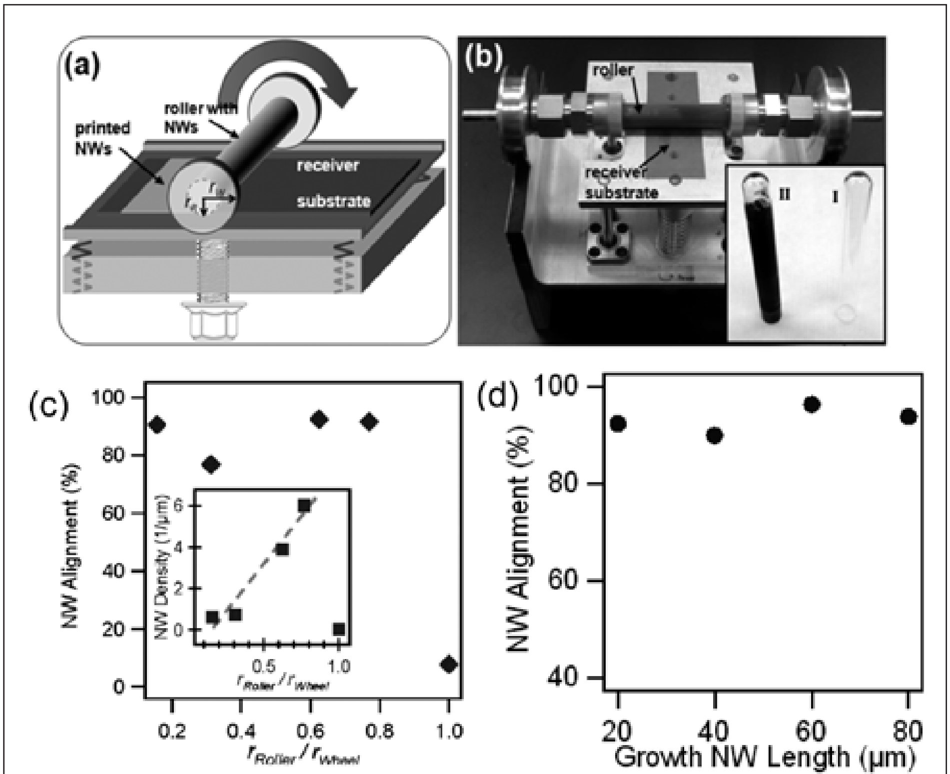

FIGURE 1 Differential roll printing of NWs. (a) Schematic drawing of the printing setup. (b) Optical photograph of the assembled apparatus (top view). The inset shows the blank and NW-coated glass tubes used as rollers (I and II, respectively). (c) The NW alignment and density (inset) as a function of roller-to-wheel size ratio. (d) The alignment of the printed film is nearly independent of NW length. Source: Yerushalmi et al., 2007. Reprinted with permission.

been investigated in the past, have demonstrated a significantly higher photo-response than their thin-film or bulk counterparts (Fan et al., 2008a; Yu et al., 2008).

Although NWs are obviously promising materials for high-performance nanoelectronics and sensors, a major challenge to their integration into large-scale devices/circuits is perfecting their controlled assembly on substrates. In recent years, many approaches have been investigated with varying degrees of success. These approaches include liquid-flow alignment, Langmuir-Blodgett technique, alternating current (AC) dielectrophoresis, blown-bubble method, contact and roller printing, and others. In this article, we review recent progress on a highly efficient, scalable approach for the ordered, uniform assembly of NW arrays on substrates for integration in multifunctional circuits.

Roll Printing of Nanowires on Substrates

We recently developed an NW roll-printing technology to address the need for large-scale assembly of aligned NW arrays on foreign substrates (Fan et al., 2008b; Yerushamli et al., 2007). The overall process involves (1) optimized catalytic growth of the desired crystalline NWs by CVD on a cylindrical substrate (i.e., roller), and (2) patterned transfer of NWs directly from the roller to a receiver substrate via differential roll printing, as illustrated in Figure 1.

The grown NWs stick out of the surface of the roller with random orientation. The length of the NWs is controlled by the growth time and is typically 20–80 µm for optimal printing results; the diameter (10–100 nm) is controlled by the size of the catalytic nanoparticles used as seeds for CVD growth. The roller is connected to a pair of rotating wheels and brought into contact with a stationary receiver substrate. As the roller is turned under a constant pressure and at a constant speed, NWs are transferred to the receiver substrate, which is coated with a photolithographically patterned photo-resist layer that enables the patterned assembly of NWs (Yerushalmi et al., 2007).

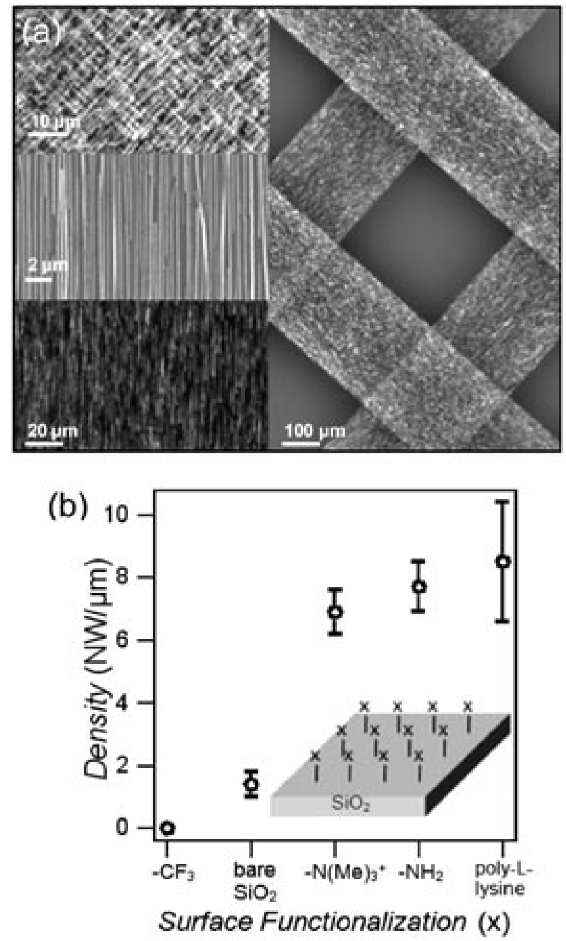

FIGURE 3 (a) Optical (left) and scanning electron microscope (middle) images of printed Ge NW arrays. The printed NWs are ~30 nm in diameter. (b) Printed nanowire density as a function of the surface functionalization of the receiver substrate. Source: Fan et al., 2008b. Copyright 2008 ACS.

FIGURE 2 Printed NW arrays on unconventional substrates: glass and paper (left) and plastic (right). Refer to Figure 3 for high-magnification images. Source: Yerushalmi et al., 2007. Reprinted with permission.

An important aspect of this printing process is the mismatch between the radius of the roller and the radius of the wheel (r_R, r_W, respectively), which causes a shear motion of the roller on the stationary substrate in addition to the rolling motion (Yerushalmi et al., 2007). In traditional roll-printing methods, such a mismatch would be highly undesirable and would distort the printed features. However, the relative sliding motion caused by the mismatch generates the required directing field and shear force to effectively "comb" the NWs, resulting in aligned transfer to the receiver substrate. Without the shear force, a negligible number of NWs are transferred, and their alignment is random, as shown in Figure 1c. This is consistent with the hypothesis that, as randomly aligned NWs on the growth substrates are dragged across the surface of the receiver substrate, they become aligned by mechanical combing.

Once the NWs are anchored by van der Waals forces, they are detached from the growth substrate and transferred to the receiver substrate. Interestingly, the density of the printed NWs shows a near linear dependence on r_R/r_W for $r_R/r_W<1$, as shown in the inset of Figure 1c. This trend is to be expected because the total number of NWs available for transfer is $(2\pi r_R)nW$, where n is the density of NWs on the roller substrate and W is the width of the contact area. Since the printed area covered per revolution is $(2\pi r_W)W$, the maximum printed density is $n(r_R/r_W)$. If we compare the slope of the density of printed NWs with r_R/r_W, we get $n\sim 9$ NW/μm (Yerushalmi et al., 2007).

We have observed that, in the range of 20–80 μm, the length of as-grown NWs does not change the printing alignment significantly, as shown in Figure 1d. The high degree of alignment (~90 percent) is independent of the length of the NW and is highly favorable for the scalability of device applications (Fan et al., 2008b). During the printing process, NWs are assembled on both the photo-resist and patterned regions of the substrates. The patterned photo-resist is later removed by a standard lift-off process using a solvent, leaving behind assembled NWs at the predefined locations (Fan et al., 2008b; Yerushalmi et al., 2007).

This process can be used for a wide range of NW materials, including Si, Ge, and compound semiconductors, and for the entire NW diameter range (10–100 nm) that has been explored. It is also compatible with a wide range of rigid and flexible receiver substrates, including glass, Si, plastics, and paper (Figure 2). Thus this approach is a highly scalable, low-cost, efficient method of assembling functional NWs on substrates and may point the way toward the realization of high-performance, flexible electronics based on printed, single-crystalline, high-mobility nano-engineered materials. Notably, the printed NW arrays are highly aligned in the direction of rolling and are limited to a monolayer (Figure 3) with no uncontrolled aggregations.

To shed light on the transfer mechanism and the process dynamics, and to gain better control of the printing process, we have explored the effect on the density of printed NWs of modifying the surface chemical of the receiver substrate (Fan el al., 2008b). As shown in Figure 3b, for the $-CF_3$ terminated SiO_2 surfaces (which are highly hydrophobic and not sticky), we observed almost no significant transfer of NWs ($<10^{-3}$ NW/μm) from the donor to the receiver substrate. Using an identical printing process on $-NH_2$ and $-N(Me)_3^+$ terminated SiO_2 (which are highly hydrophilic and sticky), we observed a high-density transfer of NWs, approaching ~8 NW/μm (Fan et al., 2008b). This major modulation of printed NW density by ~4 orders of magnitude demonstrates the importance of nanoscale chemical interactions during the printing process.

A lubricant (octane and mineral oil, 2:1, *v:v*) is applied to all surfaces during printing. The lubricant, which serves as a spacing layer between the two substrates, minimizes NW-to-NW friction, uncontrolled breakage, and detachment of NWs. The results suggest that during the printing process NWs are dragged across a receiver substrate and are eventually detached from the roller as they are anchored to the surface-functional groups of the receiver substrate by van der Waals forces.

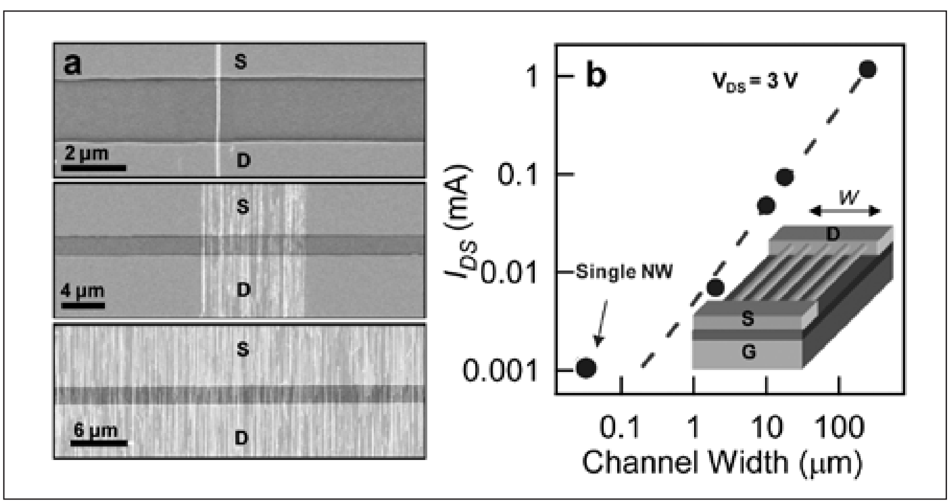

FIGURE 4 Devices based on printed NW arrays. (a) From top to bottom, scanning electron microscope images of back-gated, single GeNW FET, 10 μm and 250 μm wide, parallel arrayed NW FETs. (b) On-current as a function of channel-width scaling, showing a highly linear trend. Source: Fan et al., 2008b. Copyright 2008 ACS.

Printed Nanowire Arrays for Integration in Electronic Devices

We have successfully demonstrated highly uniform assembly of parallel arrays of NWs on the wafer scale, which is crucial for the fabrication and integration of high-throughput devices (Fan el al., 2008b). After patterned printing of NW arrays on the receiver substrates, which can be crystalline Si, low-cost glass, or bendable/flexible plastic, device structures can be fabricated using conventional lithography methods, with each device consisting of a parallel array of NWs.

In the most commonly explored device configurations, metal source/drain (S/D) and gate contacts are deposited by evaporation and liftoff. Because NWs are randomly positioned, not all of the printed NWs in a given region bridge the S/D electrodes. Since there is minimal NW-to-NW crossing or bundling in our assembled NWs, only the NWs that directly bridge S/D electrodes contribute to conduction. This technology is most relevant for printable macroelectronics with channel widths on the order of tens of microns or more and does not cause large device variations or degrade performance.

By tuning the width of the patterned regions for the assembly, the on-current can be readily modulated so more NWs will be involved in conduction (Figure 4) (Fan et al., 2008b). The observed linear dependence of the on-current on the device width illustrates the uniformity and reproducibility of NW printing technology over large areas. Specifically, a standard deviation σ~15 percent in the on-current (for a width of ~200 µm) was observed (Javey et al., 2007).

Heterogeneous Assembly for Integration in Multifunctional Circuits

In addition to device integration, there is a great deal of interest in the development of a versatile method of heterogeneous integration of crystalline materials on substrates to add functionality to a device (e.g., combining sensing capability with conventional electronics). Because NW printing technology is done at ambient temperatures, it is uniquely suited for the heterogeneous assembly of crystalline NWs on substrates for integration in multifunctional circuits (Fan et al., 2008a).

For instance, high-mobility Ge NWs can be printed at certain locations on the receiver substrates to enable high-performance transistors, while optically active CdSe NWs (direct band gap, Eg~1.8eV) can be printed at other pre-defined sites to enable efficient photo detection (Fan et al., 2008a). This is in distinct contrast to conventional Si processing for which the integration of crystalline-compound semiconductors has proven to be challenging because of lattice mismatches and interface problems.

The fabrication of heterogeneous NW circuits involves two-step printing of heterostructured Ge/Si and CdSe NWs at pre-defined locations on substrates, followed by device and circuit fabrication using conventional microfabrication processing. As a proof of concept of the feasibility of using NW printing technology

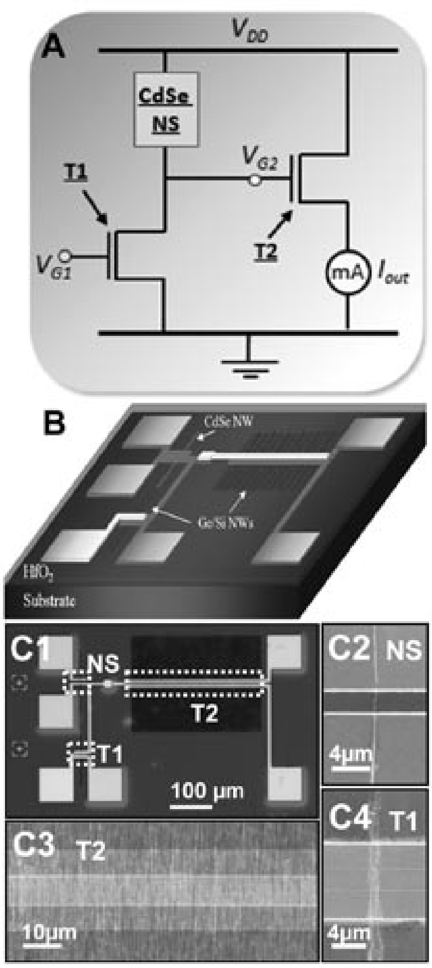

FIGURE 5 Heterogeneous NW assembly for all integrated sensor circuitry. (A) Circuit diagram for the all-NW photo detector, with high mobility Ge/Si NW FETs (T1 and T2) amplifying the photo response of a CdSe nanosensor. (B) Schematic drawing of the all-NW optical-sensor circuit based on ordered arrays of Ge/Si and CdSe NWs. (C1) An optical image of the fabricated NW circuitry, consisting of a CdSe nanosensor (NS). (C2) Two Ge/Si core/shell NW FETs (T2 and T1). (C3) and (C4) channel widths of ~300 µm and 1 µm, respectively. Each device element in the circuit can be independently studied for dynamics and circuit debugging. Source: Fan et al., 2008a. Reprinted with permission.

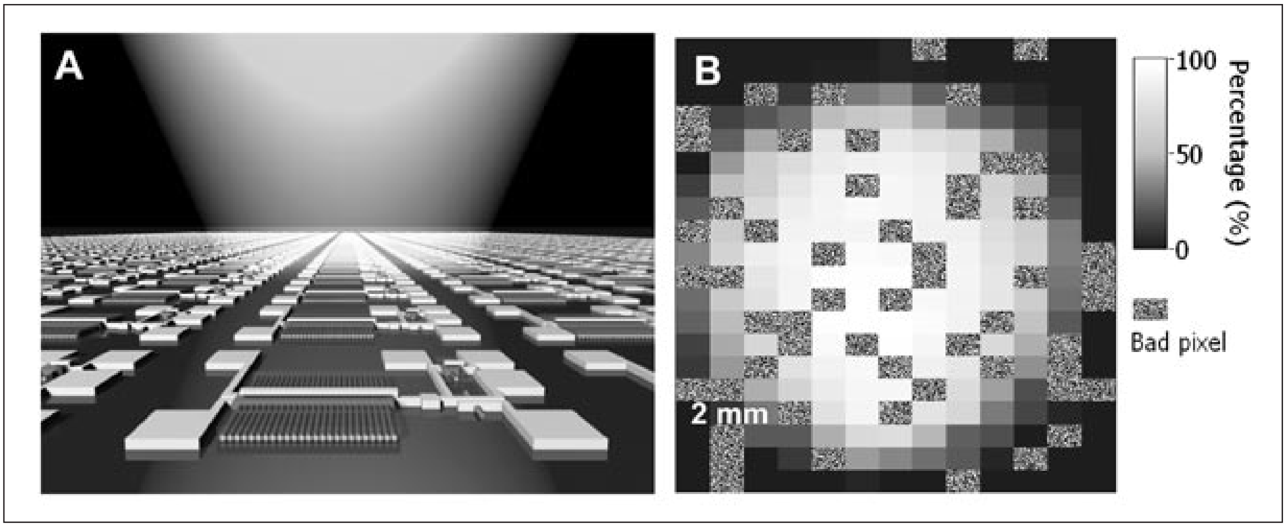

FIGURE 6 NW sensor circuitry with imaging functionality. (A) Schematic diagram. (B) An output profile of the integrated imager for a circular light spot (gray pixels represent defective sites). Source: Fan et al., 2008a. Reprinted with permission.

for heterogeneous circuitry, we fabricated Ge/Si NW amplifiers and CdSe photo detectors that are integrated on-chip on Si substrates (Figure 5). The CdSe NW photo detectors were shown to be highly responsive to white light (~100x reduction in resistance upon irradiation to ~4 mW/cm^2), and the integrated Ge/Si NW FETs amplified the signal of the sensors by ~1000x.

For this demonstration, we fabricated large arrays of the proof-of-concept circuits on substrates; each circuit was used as an individual pixel to detect light and amplify the signal. Owing to the high uniformity and reproducibility of the printing process, a relatively large matrix (13 x 20) of the all-NW sensor circuits was fabricated on a chip (with a yield of greater than 80 percent) and used as an integrated imager (Figure 6) (Fan et al., 2008a). In the future, the yield can be significantly improved by optimizing NW synthesis and fabrication processing.

To demonstrate the imaging capability, a circular halogen light source was focused and projected onto the center of the array, and the circuit output current was measured and normalized on a 0–100 scale with "0" and "100" representing the minimum and maximum measured intensity. The output profile map clearly matches the variation in spatial intensity of the light source, with the intensity decreasing from the center to the outer edge of the circuit (Fan et al., 2008a). Each pixel size can be further down-scaled in the future by reducing the feature sizes, such as channel and interconnect lengths and widths. This work not only demonstrates NW device integration at an unprecedented scale, but also presents a novel system based on printed NW arrays that may have a number of technological applications with NWs as building blocks.

Conclusion

Significant progress has been made in the roll printing of NWs for highly ordered assembly of crystalline semiconductors on foreign substrates with high uniformity, regularity, and tunable density. Parallel arrays of NWs have been shown to be high-performance building blocks for diodes, transistors, and sensors that can be readily integrated into functional circuits on unconventional substrates, such as bendable plastics. In addition, heterogeneous integration can be achieved using a multi-step printing process at ambient temperatures. This approach may lead to the development of a wide range of novel printable electronics that are unattainable with conventional Si processing.

Acknowledgment

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DNA and peptide nucleic acids are attractive assembly linkers for bottom-up nanofabrication.

The Role of DNA in Nanoarchitectonics

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In the last several decades, the scaling of complementary-metal-oxide-semiconductor (CMOS) technologies has fueled multiple industries, which have produced new industrial and defense products. However, the International Technology Roadmap for Semiconductors (ITRS) anticipates that scaling will necessarily end, perhaps by 2016, with a 22 nanometer (nm) pitch length (9 nm physical gate length). To address that eventuality, ITRS defines several potential avenues for research, such as bio-inspired assembly, that could lead to new paradigms and alternative technologies. The ultimate goal is the development of highly controlled, high-throughput fabrication of nanoelectronics as stand-alone devices/systems or components/devices that could be integrated heterogeneously onto existing device platforms.

Deoxyribonucleic acid (DNA) and peptide nucleic acids (PNAs), which have base sequences that offer specificity, are attractive assembly linkers for bottom-up nanofabrication. Recent publications on bio-assembly describe ex-vivo-assembled discrete devices, such as DNA-single-walled carbon nanotubes (SWNTs) and virus-nanocrystal (NC) nanoarchitectures for electronics components (Tseng et al., 2006; Wang et al., 2006) and the

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programming of nucleic-acid sequences for the large-scale assembly of nanostructures (Akin et al., 2007; Ruan et al., 2007).

We believe that novel routes, which would be available with self-assembly processing and highly integrated materials, could circumvent current challenges of CMOS to achieve environmental friendliness, thermal balance, dielectric quality, and manageable capital costs of next-generation fabrication facilities—if we can develop massively parallel integration of SWNTs and semiconducting, defect-tolerant nanowires.

Assembly based on biomolecular recognition is a promising approach for constructing complex architectures from molecular building blocks, such as SWNTs and NCs (Ravindran et al., 2003). In the Ozkans' laboratories at the University of California, Riverside (UCR), researchers are using a "tiered" approach to the nanomanufacturing of molecular electronics to address several issues: gaining an understanding of charge-carrier transport across bio-inorganic interfaces; ensuring error-free repeatability of the synthesis of hybrid building blocks; and directing the integration of nanoscale components (including assembled architectures, nanowires, and nanodevices) on silicon (Si) platforms. Figure 1 shows two novel devices fabricated at UCR: (a) a virus-NC memory device with write-erase cycles, and (b) a resonant tunneling diode based on DNA-SWNT architectures.

Carbon Nanotube-Based Functional Nanostructures

The synthesis of hybrid nanoarchitectures based on SWNT-DNA or SWNT-PNA conjugates may offer unique possibilities for nanoelectronics and biotechnology (Figure 2). New structures would combine the electrical properties of SWNTs with the self-assembling properties of oligonucleotides or other biomaterials, such as proteins, enzymes, and viruses. For example, we recently demonstrated that SWNT-DNA-SWNT conjugates can be used to fabricate resonant tunneling diodes (Wang et al., 2006). Based on this result, we expect that novel devices and applications, such as bio-electronic devices, DNA sensors, mechanical actuators, templates for hierarchical assembly, and others, can be derived.

Several studies have reported using SWNTs for imaging probes in scanning force microscopy (Bernholc et al., 2002; Wong et al., 1998), and electrochemical studies have shown that SWNTs can be used as enzyme-based

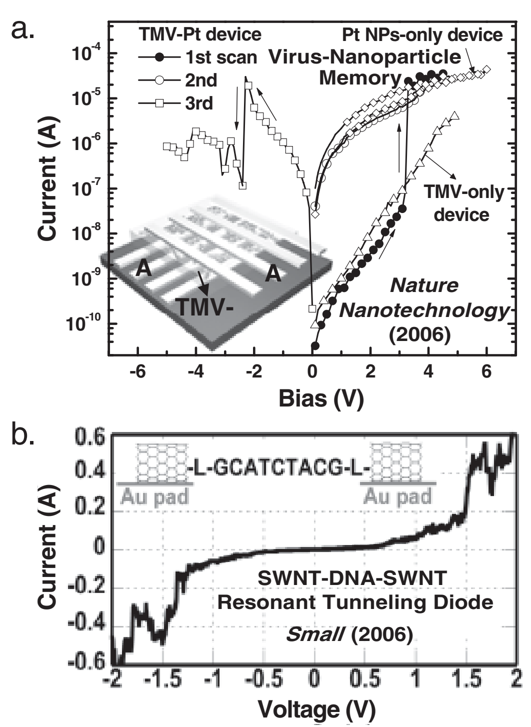

FIGURE 1 (a) Tobacco Mosaic Virus (TMV) for cross bar-memory applications. (b) DNA-CNT nano architectures for resonant tunneling diodes.

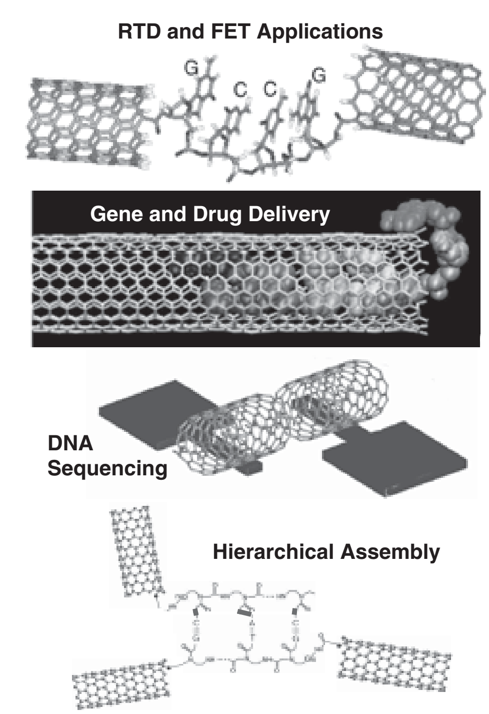

FIGURE 2 SWNT-DNA sensors for hybrid nanoelectronics, biosensors, and bottom-up nanofabrication.

sensors and DNA sensors (Britto et al., 1996; Davis et al., 1997; Melle-Franco et al., 2004; Wang et al., 2004c; Zhao et al., 2002). Because SWNT electrodes have demonstrated catalytic properties, they could also be used as electrodes in fuel cells and electrochemical detectors in medical and military settings (Que et al., 2004; Rubianes and Rivas, 2003; Sherigara et al., 2003; Wang et al., 2004a,b; Wohlstadter et al., 2003).

Functionalized nanotubes have been used in fabricating field-effect transistors for use in nanoelectronics and biosensors (Bradley et al., 2004; Javey et al., 2003; Star et al., 2003); and several studies have shown that SWNTs and multi-walled nanotubes (MWNTs) can accommodate the encapsulation of nanoparticles, fullerenes, and metallized DNA fragments (Cui et al., 2004; Davis et al., 1998; Dennis and Briggs, 2004; Gao et al., 2003). Other studies have suggested that organic and inorganic molecules might be conjugated to the side walls of carbon nanotubes (CNTs) (Hirsch, 2002; Lin et al., 2003; Sarikaya et al., 2003; Shim et al., 2002).

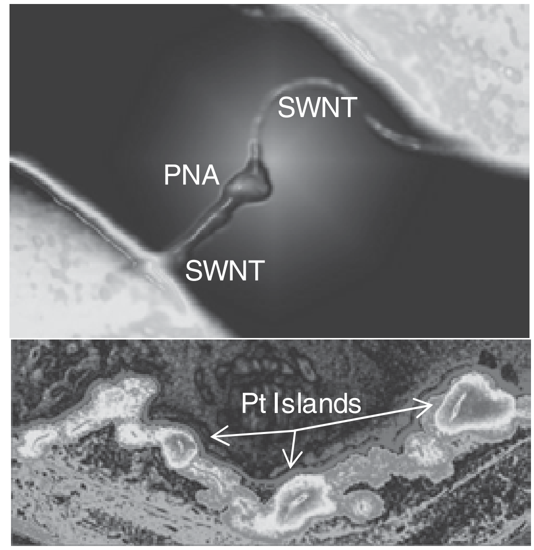

FIGURE 3 (Top) Electron microscopy image of end-to-end assembly of two SWNTs via PNA. (Bottom) Electron microscopy image of Pt metallized PNA strand. Notice formation of Pt islands during the metallization process.

Bottom-up Fabrication: Hybrid Nanoarchitectures

SWNTs are being used as active components in solid-state nanoelectronics (Tsukagoshi et al., 2002), and individual SWNTs have been used to realize molecular-scale electronic devices, such as single-electron (Postma et al., 2001) and field-effect transistors (Tans et al., 1998). Several SWNT-based devices have been successfully integrated into logic circuits (Bachtold et al., 2001) and transistor arrays (Javey et al., 2002). However, the difficulty of determining the precise location and interconnection of nanotubes has so far stymied progress toward the integration of larger scale circuits.

The search for alternative routes based on molecular recognition between complementary strands of DNA has prompted an exploration of the electronic properties of DNA for use in molecular electronics and templated nanostructures (Arkin et al., 1996; Coffer et al., 1996; Heath and Ratner, 2003; Seeman, 1998, 1999, 2003). We have synthesized SWNT-DNA and SWNT-PNA conjugates, in which DNA or PNA sequences are covalently bonded to the ends of SWNTs to form a viable bio-inorganic interface (Figure 3).

Research on the fabrication of oligonucleotide-based nanoarchitectures has been focused mostly on non-covalent interactions between DNA fragments and SWNTs (Dwyer et al., 2002; Zheng et al., 2003). Because the intrinsically low conductivity of DNA limits its usefulness in electronic circuits, some investigators have attempted to distribute metal particles on the backbone of DNA to lower its resistance (Spyro, 1980; Winfree et al., 1998).

The synthesis of end-specific SWNT-DNA and SWNT-PNA complexes (Figure 3) is a novel concept that was studied for the first time at UCR (Wang et al., 2006). In the preliminary experiments, we used ssDNA with a nine-base configuration of [5'(NH2)GCATCTACG] and ssPNA with a custom sequence of (NH2)-Glu-GTGCTCATGGTG-Glu-(NH2). In order to preserve the superior electrical characteristics of SWNTs, their side walls must be free of damage or defects. Therefore, functionalization of SWNTs only at the ends, before the assembly process, is critical. Our work demonstrates the first successful end-to-end assembly of SWNTs using nucleic acids. After placing physical metallic contacts on SWNTs, we investigated the electrical characteristics of this heterojunction. The results show negative resonance tunneling behavior that can be adopted to fabricate resonant tunneling diode circuits.

Metallized Nanoarchitectures

For an electrical circuit to have fast processing capability, the conductivity of circuit elements can be important. Information must be delivered to the other parts of the circuit with no delay (or loss). To achieve this, we adjusted the conductivity of the assembled circuit elements. In functional assembly such as SWNT-PNA-SWNT, the PNA link may have to be engineered to make it more conductive. We used a metallization procedure to improve the conductivity of nucleic acid-based linkers.

In one case, we developed a platinum (Pt) metallization process. The synthesis of Pt-decorated SWNT-ssDNA complexes requires a two-step chemical reduction and the deposition of metallic colloids (Mertig et al., 1998, 1999; Pompe et al., 1999; Richter et al., 2000). In the first step, SWNT-ssDNA conjugates were mixed with a salt solution (e.g., K2PtCl4 solution). After this activation step, the Pt (II) was reduced to metallic platinum. In the reduction process, Pt dimers formed heterogeneously on DNA molecules, and the initial heterogeneous Pt nuclei quickly developed into bigger particles, consuming the metal complex feedstock in the solution (Ciacchi, 2002) to create metallized linkers (Figure 2). Because oxidized SWNTs have higher adsorption capacities for heavy metal ions (Braun et al., 1998), the Pt ions would be absorbed on SWNTs if the metallization process was done after assembly.

Modeling of Band Structures and Carrier Transport for Bio-inorganic Interfaces

An analysis of high-lying occupied molecular orbitals (HOMO) and low-lying unoccupied molecular orbitals (LUMO) reveals the structural and electrical properties of bio-inorganic interfaces, such as CNT/protein, quantum dot (QD)/DNA, QD/protein, metal/DNA, and metal/protein systems. In a recent study, the electrical properties of the interfaces between SWNT-ssDNA and SWNT-ssPNA were deduced via density functional theory (DFT) calculations (Singh et al., 2006; Wang et al., 2006), in which two unit cells of zigzag (10,0) oxidized CNT were linked to a DNA sequence with amine to form an amide linkage.

When the highest HOMO and lowest LUMO surface plots (shown in Figure 4) were generated, the HOMO-LUMO gap was found to be about 3.1 electron-volts (eV). For comparison, the HOMO-LUMO gap of SWNT alone is ~3.1 eV. The large gap is the result of the shortness (just two unit cells) of the modeled SWNT. For an extended (10,0) CNT, the bandgap is ~0.98 eV. The HOMO orbital is confined on the SWNT, while the LUMO orbital extends across the amide link, suggesting a good possibility of electron transfer across the amide bridge for n-type SWNTs.

Similar calculations for SWNT-ssPNA revealed that, although the HOMO orbital is confined to the glutamate link, the LUMO orbital extends over the SWNT, suggesting that SWNT-ssPNA conjugates might be used to build hole-conducting devices. Thus these preliminary studies suggest that bio-inorganic interfaces achieved by conjugating SWNTs with ssDNA and ssPNA might lead to the fabrication of n-type and p-type devices, which might someday provide an alternative or an enhancement to conventional CMOS technology.

Nanopatterning via Dielectrophoresis Using Micro- and Nano-Arrays

Micro- and nano-array platforms can be used to control the electrophoretic manipulation of (bio)molecules, particles, and micro-light emitting diodes (LEDs) as electronic elements. The platform shown in Figure 5 is used for electric-field-assisted manipulation and the assembly of nano-elements, such as metallic and semiconducting SWNTs, QDs, dendrimers, and/or conjugation molecules, such as DNA fragments. The nanochip platform (shown in Figure 5) enables rapid, parallel transport within seconds to a specific location on the chip array by providing independent current or voltage control on each electrode.

Current commercialized applications of this platform include DNA hybridization and DNA analysis for molecular diagnostics via fluorescence detection using fluorophore-labeled reporters (Akin et al., 2007; Dubois and Nuzzo, 1992; Ruan et al., 2007; Salem et al., 2004). Commercial uses of DNA detection include highly multiplexed, fully validated assays and panels for

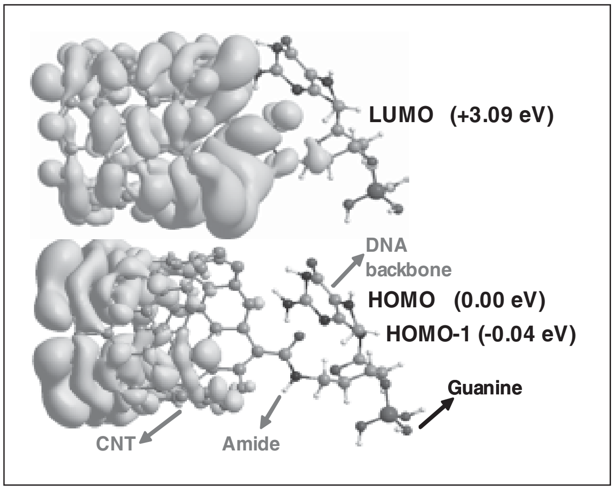

FIGURE 4 HOMO-LUMO calculation of SWNT. The gap is found to be 3.1eV. Similar modeling studies can reveal electrical characteristics of organic-inorganic interfaces.

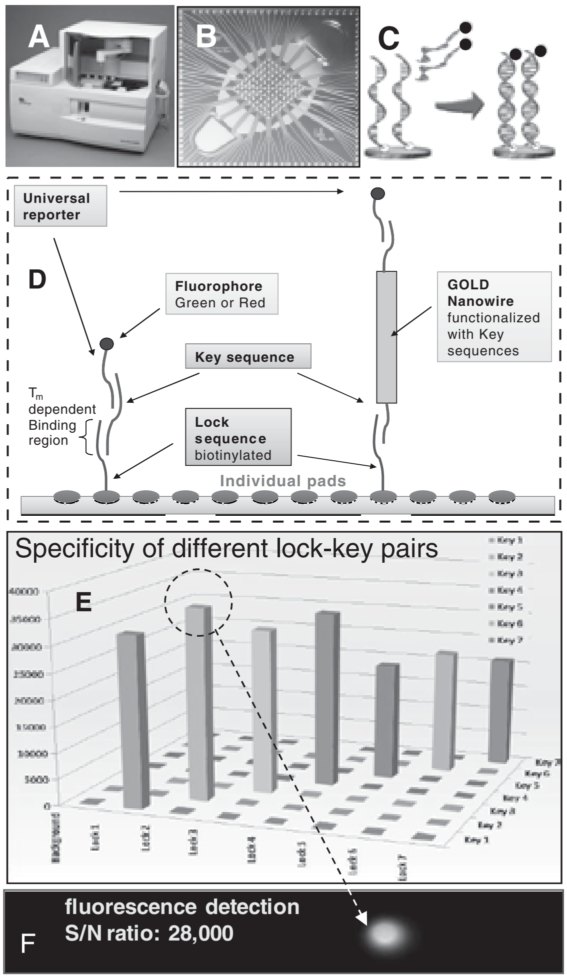

FIGURE 5 (A)–(C) Nanogen platform and microarray device for dielectrophoresis applications. (D) Assembly of ssDNA sequences and functionalized nanowires onto Si arrays. (E) Specificity of assembly of different lock and key ssDNA sequences. (F) High S/N ratio is obtained.

identifying cystic fibrosis, respiratory viruses, hereditary hemochromatosis, and other medical conditions.

So far, different types of arrays (with 10,000, 400, and 100 sites) have been developed using silicon micromachining with fully automated and robotized fluidics. Figures 5c and 5d show the in-situ assembly for the manipulation, direction, and assembly of nanoelements using electric-field assembly. The electrode array, with geometry configurable to the desired application, is energized to attract and combine different types of nanoelements (Figure 5b). When electric-field assembly is used, the process is significantly different from self-assembly in a static solution, because it enables site-specific assembly.

In the future, the controlled parallel assembly of nanowires and nanotubes could be investigated by attaching one end of a nanowire to the target DNA immobilized on the nanoarray and the other end to a reporter-DNA sequence equipped with a fluorescent tag (Figure 5d). Upon hybridization, the presence of fluorescence could be used to assess and record in-situ assembly.

Conclusions

Clearly, chemical and biological assemblies are promising technologies. However, many new technologies must be developed and much science must be learned for that promise to be fully understood and realized. We anticipate that new engineering concepts will be discovered in the near future that will enable the massively parallel assembly of nanodevices. The future of assembly engineering (and hierarchical fabrication) may depend on being able to manipulate and control more than one type of molecular force. We anticipate that the first applications in this area will be enabled by top-down approaches for integrating assembled components onto existing device platforms.

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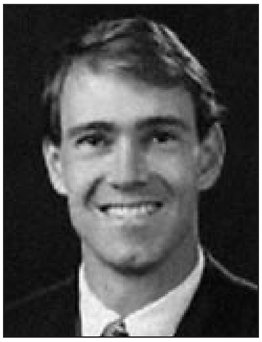
A driver's attention is a limited, critical resource that can be compromised by distractions.

Driving Attention: Cognitive Engineering in Designing Attractions and Distractions



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Driving confronts people with many of the same demands as other high-tempo, high-consequence, complex activities. People who provide health care, manage power plants, and control aircraft face similar multitasking demands, many of which are mediated by technology (Hollnagel et al., 2006; Moray, 1993; Vicente, 1999). Drivers must divide their attention among navigation, hazard detection, speed control, and lane maintenance. In addition, drivers often engage in non-driving activities, such as conversing with passengers and adjusting entertainment systems. In this multitask situation, a driver's attention is a limited, critical resource, and safety can be compromised when a driver fails to direct attention to the right place at the right time.

A recent study based on detailed data on 100 vehicles for a year showed that distractions and inattention (e.g., fatigue) contributed to approximately 80 percent of crashes and that distraction contributed to approximately 65 percent of rear-end crashes (Klauer et al., 2006). Unfortunately, this problem is likely to get worse, because driver distractions are likely to increase with rapid advances in wireless, computer, and sensor technologies (Regan et al., 2008). Not only will drivers have to manage cell phones, radios, and CD players, but they may also be tempted to use text messaging, select from MP3 music catalogs, and retrieve information from the Internet. Rapid changes in vehicle design are being made to accommodate these new devices. Nearly 70 percent of new 2007 vehicles are compatible with MP3 players, and all

2009 Chrysler vehicles will have wireless connections to the Internet (Bensinger, 2008). These infotainment devices have the potential to make driving time more enjoyable and productive, but they also have the potential to distract drivers.

Sensor, data fusion, and control technologies promise to improve driving safety by mitigating the distraction potential of infotainment devices. Increasingly, vehicles are being equipped with sensors that monitor surrounding vehicles to identify potential collisions, warn drivers, and even respond with emergency braking. Similar technologies that can automate driving during routine situations include adaptive cruise control that accelerates and decelerates the vehicle to maintain a constant speed or constant distance from the vehicle ahead (Walker et al., 2001).

Other devices can assist drivers with emergency braking, help them keep the car centered in the lane, and attend to potential threats of collisions (Norman, 2007). Although these developments are promising, driver-support technologies may not deliver the promised safety benefits because (1) they often respond imperfectly and (2) they may encourage people to pay less attention to driving if they think the system will protect them from distraction-related lapses (Evans, 2004; Stanton et al., 1997).

As new technology has done in other domains, the introduction of infotainment and driver-support technology will fundamentally change driving. The complex array of factors that affect driving safety means that focusing simply on improving technology (e.g., designing a more capable automatic braking system) will not ensure that driving is safer, not only because technology will remain imperfect, but also because safety ultimately depends on leveraging a driver's capabilities. Technologies must be designed in a way that attracts a driver's attention to what matters most and does not annoy or distract a driver from safety-critical events.

Figure 1 illustrates the challenges of combining people and technology. The top diagram shows the complementary capacities of humans and technology—both are limited and may overlap to some degree. The middle diagram shows an effective combination of human and technological capacity—in combination, both perform better than either does alone. The bottom diagram shows a dysfunctional situation in which combined human/technology performs worse than either does alone; this can occur if the person does not capitalize on the capacity of the technology (on the left) or relies on the technology inappropriately (on the right). The disuse and/or misuse of technology often occurs when a new technology is introduced (Parasuraman and Riley, 1997). In addition, some technologies, such as warning devices, can annoy people and undermine product acceptance (on the left). Poorly coordinated technology can also interfere with a driver's ongoing response to a situation (on the right).

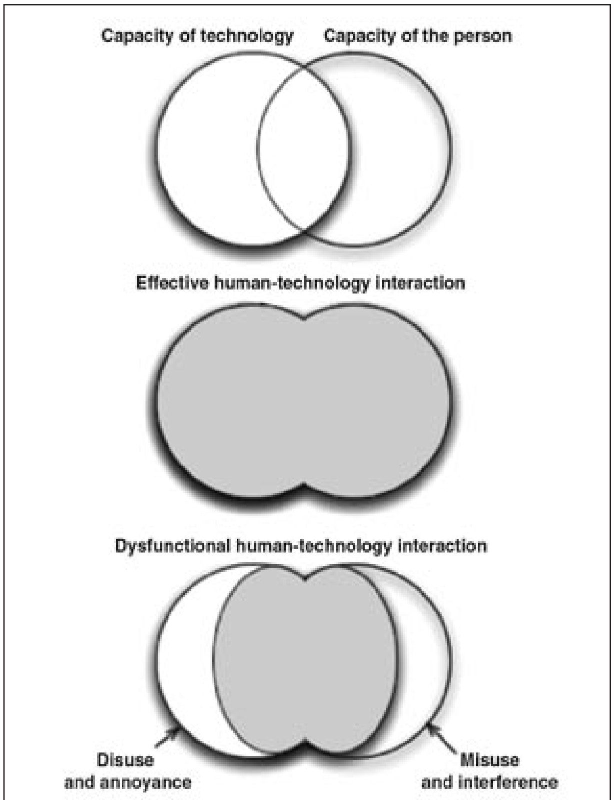

FIGURE 1 The complementary capacities of technology and humans. When properly integrated, the combination is more effective than either of them alone. When poorly integrated, the combination is less effective than either of them alone.

Achieving an effective human/technology combination requires a deep understanding of how technology mediates human attention and decision making (Lee, 2006). The dynamics of attention can be considered as a multilevel process (Michon, 1989; Sheridan, 1970). At the operational level, attention is modulated over a span of milliseconds to seconds; at the tactical level, modulation may take many seconds or minutes; and at the strategic level, it may take hours or even months. Technology can have a powerful influence at any of these levels.

Figure 2 shows the dynamics of how technology influences attention to driving and competing tasks

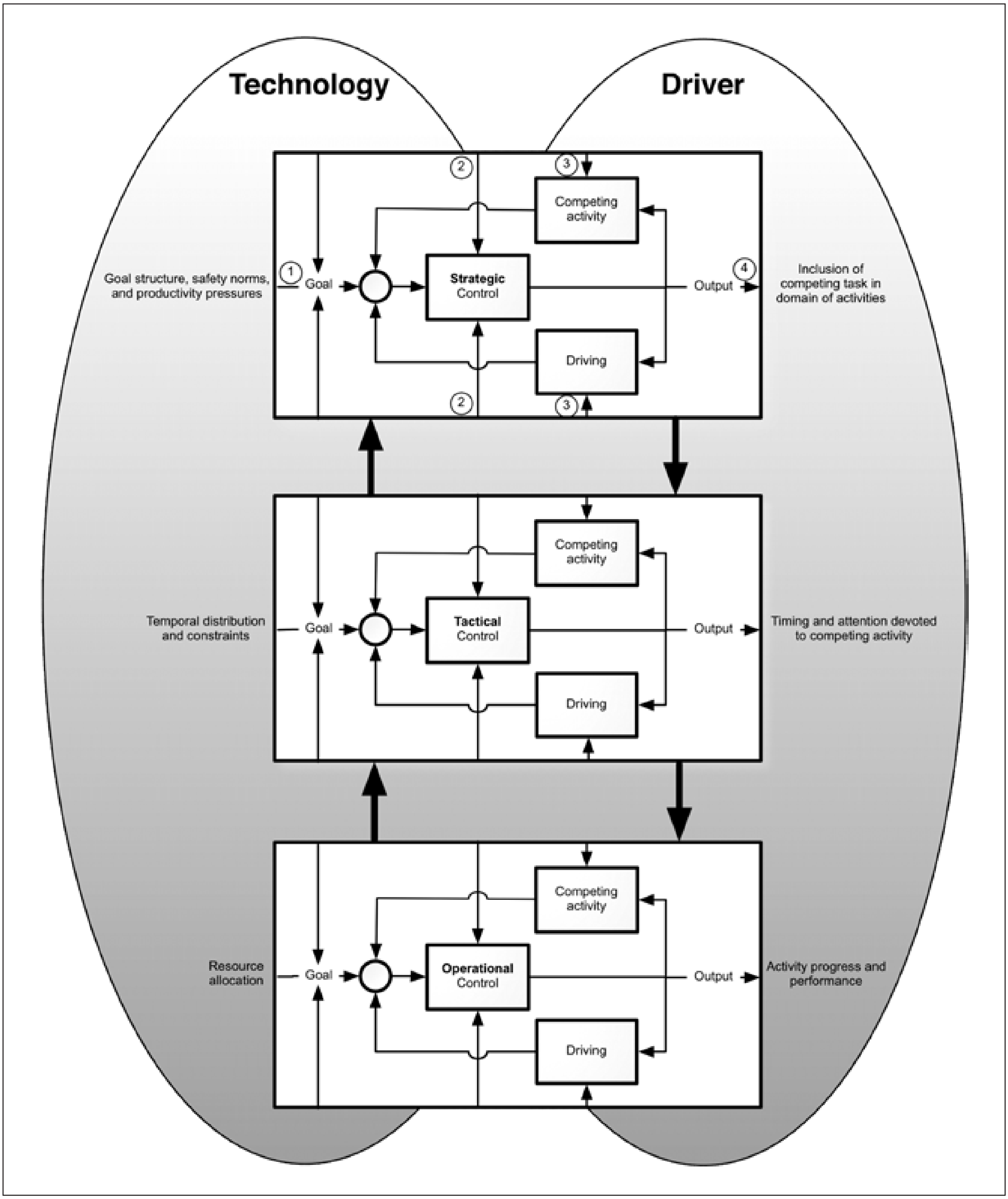

FIGURE 2 Technology-mediated attention. Numerals indicate interactions between levels: (1) adaptive control in which the output of one level affects the goal of another level; (2) feed-forward control in which the output of one level affects expectations and appropriate response schema at another level; (3) cascade effects in which the output of one level influences the control dynamics of another level; and (4) the output supports feedback control for a given level and adaptive control for other levels. The numerals at the strategic level apply also to the tactical and operational levels. The heavy lines between levels encapsulate these interactions. The ellipses in the background represent the joint control of the driver and the technology. Source: Adapted from Lee et al., 2008.

through feed-forward, feedback, and adaptive control. With feed-forward control, drivers and technology anticipate upcoming demands and direct attention accordingly. Feedback control directs attention according to the evolving demands of the situation. Adaptive control directs attention based on changing goals and priorities. As technologies become more sophisticated and ubiquitous, they also increasingly influence drivers at all levels of attention and for each type of control.

Figure 2 shows some of the complexities associated with determining how technology mediates attention. Because both technology and humans are imperfect in directing attention to the right thing at the right time, a reliable human/technology system must perform better than either performs alone. Achieving such a design goal requires attention to the driver/technology combination rather than attention to the technology alone.

Augmentation Rather Than Automation

Cognitive engineering is engineering with a sensitivity to human cognitive characteristics to improve safety, performance, and satisfaction. For example, rather than using technology to automate an action in an effort to eliminate human error, a more beneficial approach, and one that may yield greater safety benefits, would be to augment, rather than automate, human capabilities.

Technology makes it possible for a vehicle to monitor both the roadway and the driver. Thus it could augment the driver's awareness of the roadway conditions and improve the driver's awareness of his or her capacity to respond to those demands. Technology might improve safety by measuring the degree to which the driver is distracted and then directing a distracted driver's attention by alerting the driver to roadway demands. In the following descriptions of how emerging vehicle technologies might mediate a driver's attention, the reader should keep in mind that similar approaches might also apply to other high-tempo, multitask activities.

Using Model-Based Distraction Estimates to Improve Self-Awareness

In a survey of 1,000 drivers, 80 percent said they thought they drove more safely than the average driver (Waylen et al., 2004). This sense of confidence and, perhaps, complacency is one factor that encourages drivers to divide their attention between the roadway and infotainment systems. Augmenting a driver's awareness of his or her attention to the roadway might be an effective way of mitigating distraction and helping drivers make better decisions about if and when they can safely engage in a distracting activity.

Estimating the degree of distraction experienced by a driver may be critical in helping that driver manage distraction. Figure 3 shows the output of a model of a driver switching attention between the roadway and an in-vehicle device (Hoffman, 2008). This model is based on dynamic field theory (Erlhagen and Schoner, 2002) and captures the time-varying factors that cause drivers to persist in looking away from the roadway (e.g., task inertia) and factors that draw a driver's attention back to the roadway (e.g., increasing uncertainty about the roadway situation).

The top-down, or model-driven, estimate (described above) of how drivers distribute their attention can complement a bottom-up, or data-driven, approach to estimating a driver's state based on real-time driving performance data. Bayesian networks and support vector machines are effective data-driven techniques for estimating distraction based on eye movements and steering behavior (Liang et al., 2007, in press). Increasingly instrumented vehicles provide an enormous volume of data that can be used as feedback to drivers and designers, provided those data are interpreted correctly.

Estimates of impairment related to distractions, such as text messaging, can augment a driver's awareness of impairment in three ways (Donmez et al., 2006, 2007). First, a model-based prediction of distraction could alert a driver to upcoming conflicts so that he or she can direct attention to the roadway proactively. Second, the history of distraction and the associated decrements in driving performance could be shared with drivers after a drive to help them calibrate their own estimate of how well they can manage distractions. A third approach takes into consideration the current state of the driver when redirecting his or her attention to demanding roadway situations. This approach is described in the following section.

Alerting and Informing a Driver to Enhance Roadway Awareness

Sensor and algorithm technologies have made it possible for a vehicle to detect hazards and alert or inform the driver, thus reducing his or her reaction time to an imminent collision (Lee et al., 2002). Unfortunately, these systems also generate many false alarms—signaling a hazard where none exists—which can annoy and distract drivers. However, making such systems more useful and trusted will require more than a technological fix.

For example, based on our knowledge of human reactions, we know that drivers perceive seat vibrations as less annoying than auditory alerts (Lee et al., 2004). In addition, not all false alarms are created equal. False alarms that drivers associate with events in the environment lead them to trust the system and thus become more likely to comply with subsequent alerts. False alarms that appear as if they occur randomly tend to have the opposite effect (Lees and Lee, 2007). Drivers respond differently to alerts, even though they might all be labeled “false alarms” from a technological perspective.

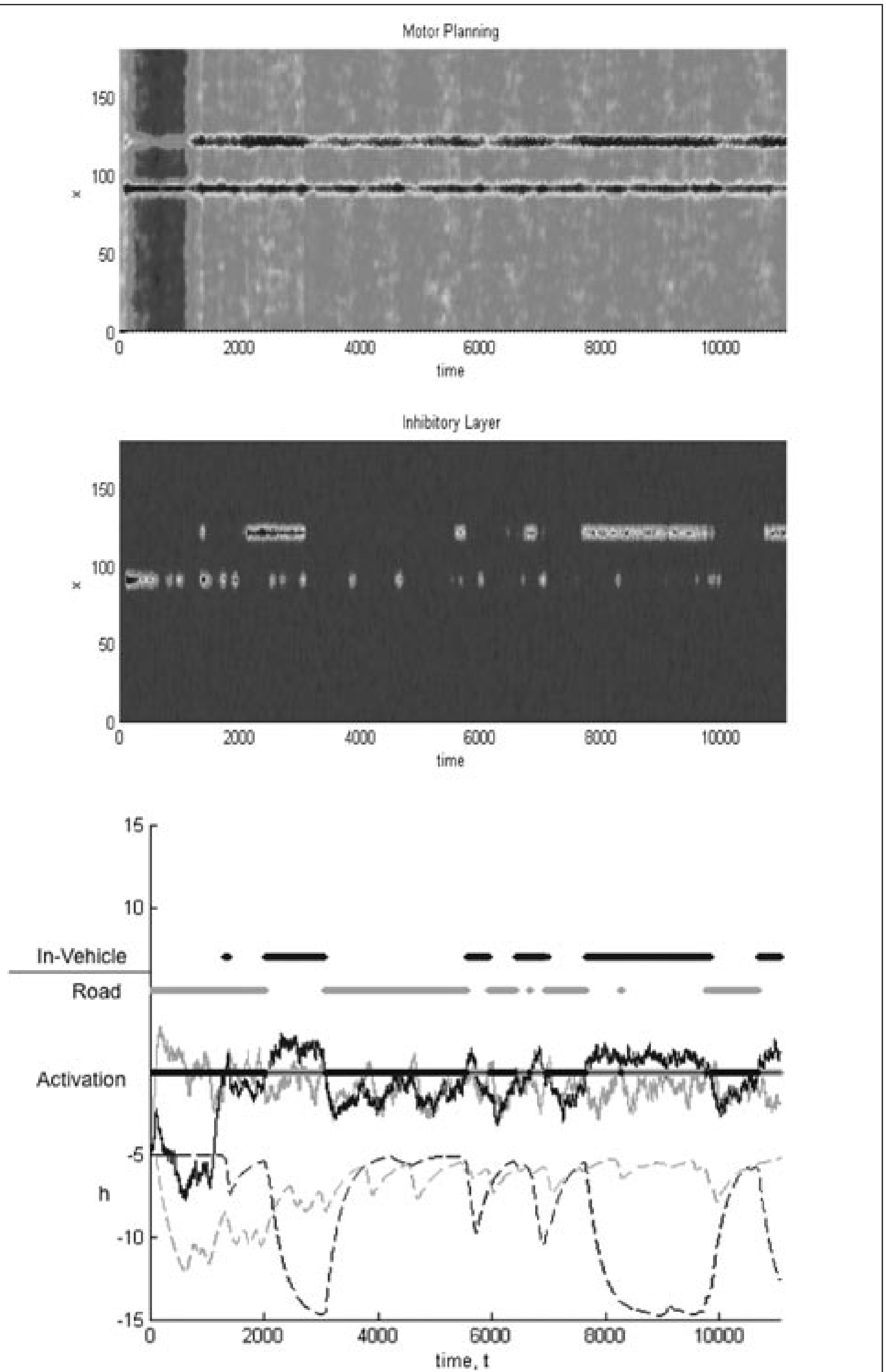

FIGURE 3 A theoretical approach to describing the dynamic distribution of attention between the roadway and an in-vehicle device.

Adapting a threshold for alerts based on the degree of driver distraction could reduce false alarms by raising the threshold for attentive drivers. This approach could lead to an interesting paradox in that the drivers who most need alerts are also the most likely to consider them false alerts. For example, a distracted driver might not notice a hazard (even with the alert) and so might not appreciate the value of the alert. Providing a driver with information on roadway demands and hazards after a drive, similar to the post-drive feedback for distraction, could help him or her understand the reason for the alerts. More generally, drivers are more likely to benefit from vehicle technology that augments driver attention by informing through continuous information rather than alerting through discrete warnings.

Recent studies suggest the potential benefits of post-drive feedback (McGehee et al., 2007; Tomer and Lotan, 2006). In one study, teenage drivers drove with a camera that captured abrupt braking and steering responses. The resulting video and a summary of events was shared with their parents weekly, leading to an 89 percent reduction in the number of events triggered by risky drivers compared to the baseline period. Even after the feedback was removed, the rate of events remained low until the end of the study six weeks later. Whether feedback would be accepted or effective in helping experienced drivers manage distracting technology remains to be seen.

Conclusion

Technology changes the nature of driving by introducing new vulnerabilities and capacities (Woods and Dekker, 2000). Infotainment systems introduce new distractions that can undermine safety. Driver-assistance technologies promise to mitigate these distractions and improve safety. But we will not reap the potential benefits of these devices with a technology-only approach. Drivers tend to reject or misuse imperfect technologies that automate driving rather than augmenting driver capabilities. Cognitive engineering methods can show the way to using technology to leverage human capabilities to improve the safety and performance of complex systems by enhancing self-awareness and the awareness of potentially distracting technology.

Increasingly pervasive and powerful driving technologies, as in other domains, can blur the boundaries between the human and the technological, posing practical, theoretical, and philosophical issues about safety and performance, which increasingly depend on a complex interaction of driver, in-vehicle technology, and the driving situation (Lees and Lee, 2008).

Cognitive engineers face the following challenges:

- Philosophical issues relate to technologies that generally help but can also interfere with human performance. Driver-assist emergency braking, for example, generally improves crash outcomes, but, in rare instances, can impede a driver's responses.
- Practical concerns include how to draw meaning from large, complicated streams of sensor data in real time and from petabytes of accumulated data to provide feedback to operators and designers.
- Theoretical concerns relate to the dynamics of attention and how technologies can affect those dynamics and, generally, how the nature of cognition changes as technology shapes and is shaped by human activity.

Acknowledgments

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Cognitive engineering methods can improve human performance in the complex health care environment.

Cognitive Engineering Applications in Health Care

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The goal of cognitive engineering is to support the cognitive activities associated with behavior, particularly in complex working environments, through the design of system components, such as user interfaces, automation, decision aids, and training. Health care is an environment with classic complexities—time pressure, risk, uncertainties, and many interacting components. The health care environment is further complicated by multiple levels or domains of concern. For instance, even an individual patient consists of numerous, interacting systems that may not all be well understood and for which only limited or indirect information may be available.

The complexity of the patient domain is compounded by the complex socio-technical working environment that addresses the patient's needs—the health care system—which is comprised of many people working both individually and in teams, who must coordinate their actions and who have different, sometimes competing goals (e.g., health care providers vs. government regulators vs. insurance companies vs. hospital administrators). In the health care environment, individuals interact with a variety of information sources and technologies, ranging from handwritten charts to pagers and phones to electronic medical records and digital imaging systems. Resources in the health care environment, such as caregiver time and hospital beds, are limited, and demands on the system (i.e., incoming patients and their conditions) are unpredictable.

Methods in cognitive engineering have been developed to uncover and represent both complexities in high-consequence fields such as health care and the knowledge and strategies experienced practitioners use to perform successfully (Bisantz and Burns, 2008; Bisantz and Roth, 2008; Crandall et al., 2006; Vicente, 1999). The results of cognitive engineering analyses can have a critical impact on the design of information, tasks, and training that will enhance, rather than disrupt, successful work practices and allow practitioners to respond appropriately to diverse, unpredictable events.

Cognitive engineering research in health care environments, which has a general goal of supporting safe and effective performance, has followed different research paths, including (1) characterizing complexities in the environment and demands on practitioners, sometimes with a focus on preventing medical errors; and (2) focusing on the design and/or impacts of new technologies. Understanding demands on practitioners, the strategies they use to meet those demands, and the role of information from different sources and technologies in work practice is essential to designing new information systems that can improve patient care.

Poor communication is a frequent cause of medical errors.

Characterizing Complexity: System Structure, Strategies, and Communication

A common method of representing the complexities of the work domain (i.e., the abstraction hierarchy, see Rasmussen et al., 1994; Vicente, 1999) is to represent high-level goals, balances and priorities, processes, and physical structures. In the individual patient system, for instance, researchers have modeled physiological functions and anatomical structures, as well as methods of controlling them, to support diagnostic decision making, understand information needs among clinicians, and design monitoring displays (Hajdukiewicz et al., 1998; Miller, 2004; Sharp and Helmicki, 1998; Watson and Sanderson, 2007).

Enomoto et al. (2006) and Burns et al. (2008) conducted a study of the tasks of cardiac-care telehealth nurses, as well as the underlying patient structure and processes, to identify the challenges they faced and the strategies they used in diagnosing cardiac patients based on phone interviews. Various innovative visualizations were designed and tested, alternately emphasizing mapping symptoms to diagnoses, clusters of co-occurring symptoms, and symptom severity. Hall et al. (2006) used similar techniques to simultaneously represent aspects of a surgical team, the patient, and the equipment used to compare problem-solving strategies used by anesthesiologists.

A particular complexity of interest in medicine is the need for multiple individuals (e.g., physicians, nurses, technicians, support staff) to communicate with each other to coordinate patient care, particularly in hospital settings. Poor communication has been cited, for example, as a frequent cause of errors in the administration of medications (c.f. Rogers et al., 2004). Numerous cognitive engineering-oriented studies in medical environments have been conducted on communication functions, patterns, and sometimes breakdowns.

For example, Fairbanks et al. (2007) described aspects of communication, such as the type of partner, communication mode (e.g., face-to-face, phone), duration, and location of communication in a hospital emergency department (ED). They shadowed 20 caregivers (including attending physicians, residents, ED nurses, and charge nurses) to construct networks showing the communication pathways radiating from, and connecting, caregivers. Results provided insights into typical patterns of communication and the individuals or positions that were key communication nodes in the ED. For instance, nurses played a central role in communication; most communication was face-to face; and overall, there were frequent communications of short duration.

Potential gaps in information flow were also identified. For instance, triage nurses and ambulance personnel (emergency medical services [EMS]), who have initial contact with patients, were observed to communicate primarily with charge nurses (responsible for workflow and patient assignment) but not with the physicians who would care for the patients. This gap may indicate an opportunity for intervention, such as a change in training or procedures or the development of new technologies, such as real-time patient information systems that can be accessed by both EMS and ED staff.

Similarly, Moss et al. (2002) characterized the mode, recipient, and topic of communications by an operating room charge nurse responsible for coordinating patient, surgical team, equipment, and room preparation; the goal of the study was to suggest how electronic scheduling systems could be shared and used effectively. Guerlain et al. (2007) found that training surgeons in specific types of communication and teamwork skills, such as methods of conducting pre-operative briefings, improved communication.

Several studies have investigated communication strategies during shift changes and other transitions, when one group of caregivers must transfer information about patient status to another (Nemeth et al., 2006; Patterson et al., 2005; Sharit et al., 2005; Wears et al., 2003). Patterson et al. (2005) observed nurses during shift changes in acute-care units to identify the strategies and technologies they used to obtain necessary information. Audiotaped and face-to-face communications led to different strategies. For instance, if the information was audiotaped, incoming staff could not directly question outgoing staff; however, incoming nurses tended to listen to audiotaped information as a group and talk about the status of patients, which could result in a shared awareness of patient states and team coordination to meet patients' needs.

Wears et al. (2003) contrasted two transitions between ED physicians. In one, the transition was the source of error recovery because incoming physicians suggested an alternative, ultimately correct, diagnosis. In the second, poor communication was the source of a breakdown because critical information about the state of a medication order was misunderstood, and an essential treatment was delayed.

New Technologies and Unintended Consequences

Advanced technology has often been advocated as a way to reduce errors and adverse events in health care (Aspden et al., 2004; IOM, 1999, 2001). In many cases, however, new technologies are designed without an in-depth understanding of the work they need to support, or they are designed to address functions other than patient care (e.g., record keeping, billing). Unless the designers understand how new technologies will be used in practice and are aware of potential barriers to their use, these technologies can lead to unanticipated, undesirable consequences (Ash et al., 2004, 2007; Bisantz and Wears, 2008; Webster and Cao, 2006), such as increased workload (because of the need for new processes or workarounds to integrate them into the workflow), or serious safety compromises (if new systems are bypassed or abandoned or if critical tasks are interrupted).

For instance, in a study of new operating room technology that integrated multiple monitoring systems into a single electronic display, Cook and Woods (1996) found that the change forced practitioners to adapt their activities, as well as some aspects of the new system, to ensure that the critical information was displayed at appropriate times.

New technologies can sometimes have unintended, undesirable consequences.

In another case, Patterson et al. (2002, 2006) studied unanticipated effects and workarounds developed after the implementation of a system intended to reduce errors by using bar codes on medications and patient wristbands to confirm the type, dosage, and timing of medication administration. Unanticipated effects included fewer physician reviews of current medications, because it was more difficult for them to access information in the computerized system than in the old paper record; and nurses feeling pressured to administer medication "on time," even when other higher priority tasks were necessary (both of which increased the chances of adverse events).

A key workaround was that nurses would type a patient's bar code number into the system or scan a secondary wristband kept separate from the patient to save time and avoid several problems. First, the cart with the scanner was difficult to maneuver, and in some cases a computer had to be plugged in to maintain battery life. Second, they no longer had to disturb sleeping patients. Finally, scanning the second wristband was often more reliable than scanning the wristband on the patient, especially for long-term patients whose wristbands had become worn or smudged. In addition, nurses could "pre-pour" medications (place medications in cups for many patients at once, rather than scanning a wristband, scanning and administering medication(s), and moving to the next patient), to increase efficiency. Scanning medications in batches also made it more likely that medications were recorded as administered "on time" (which eliminated the work associated with documenting late medications).

In the end, although the bar code system could reduce the chances that the wrong type or dosage of medication would be chosen, the workarounds could increase the chances of a medication being given to the wrong patient. The researchers suggested both changes in the system design (e.g., simplifying the system interface; using wireless or easily maneuverable scanners; and using longer lasting computer batteries) and changes in procedures (e.g., using more realistic times for medication administration) that could reduce the likelihood of unanticipated effects or workarounds that would increase the chances of errors.

Learning from Existing Tools and Technologies

Understanding how extant tools and artifacts work in a system is a critical step in designing new systems to support the functional purposes of an artifact, rather than merely duplicating its surface features (Nemeth, 2004; Pennathur et al., 2007; Xiao, 2005). Bauer et al. (2006) conducted a detailed analysis of an artifact used in intensive care to inform the design of an electronic system. The artifact, a patient flow sheet, is a paper form that accommodates both structured and unstructured data capture (e.g., grids for sequential vital signs and free-form notes). By observing the flow sheet in use, they were able to identify the characteristics that had to be included in an electronic system.

Some features may not have been included if the new system had simply duplicated the surface features of the form. For instance, the paper form allowed information to be entered flexibly, rather than sequentially, allowed unstructured annotations (e.g., information did not have to be entered in a particular place or with keyboard characters), and allowed users to leave information out (for a discussion of the functionality of paper artifacts, see Sellen and Harper, 2003). The paper form also supported work because it was portable, grouped information in ways that allowed comparisons to be made easily, allowed flexible annotations to accommodate unique circumstances, and allowed data to be represented in familiar notation.

An electronic system could provide additional functionality, such as automated data analysis and calculations, and could give multiple caregivers access to the information at the same time. However, the new technology still had to support flexibility in annotation and commonly used notations and comparisons.

Some of our own work has focused on the implementation of new technologies in hospital emergency

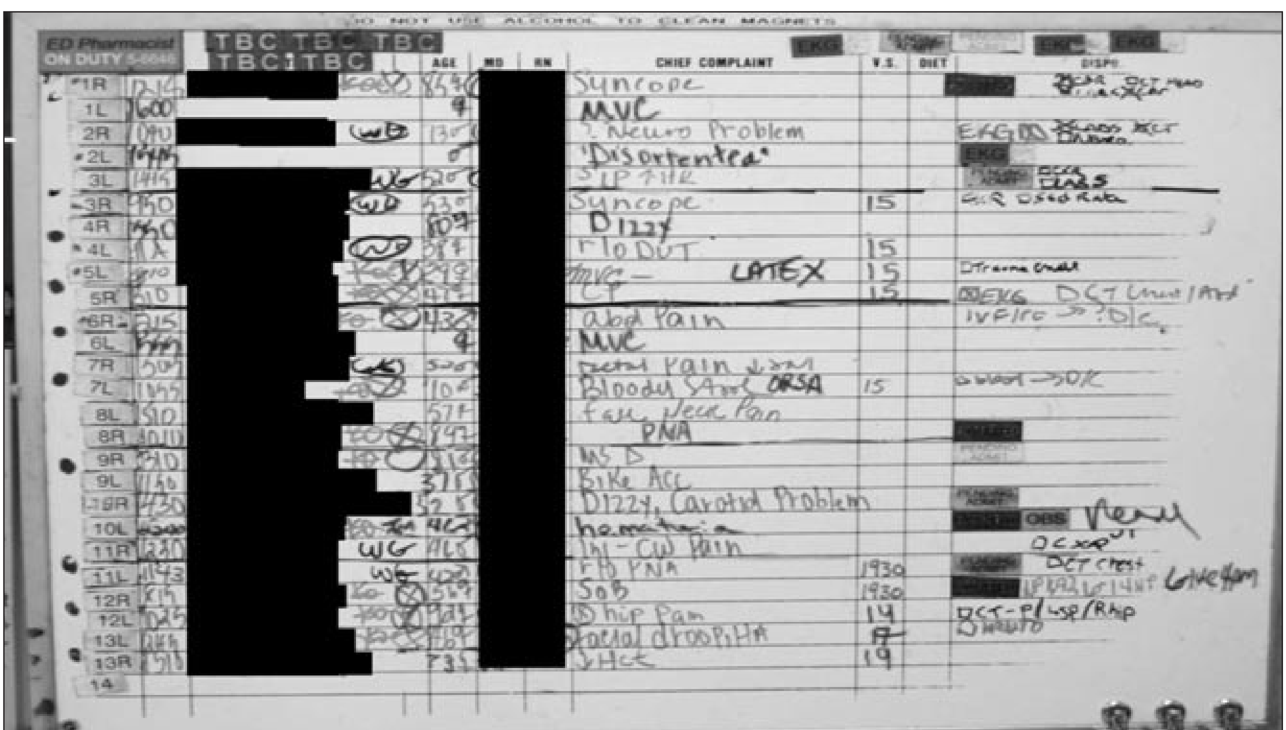

Figure 1 Manual whiteboard with the names of patients and providers obscured. Reprinted from *Proceedings of the Human Factors and Ergonomics Society Annual Meeting, 2008.* Reprinted with permission.

rooms (Pennathur et al., 2007, 2008a,b; Wears et al., 2005), where electronic patient-tracking systems are replacing manual status boards ("whiteboards"). Manual status boards (see Figure 1) provide medical and logistical information about patients and information about patient status (e.g., designated providers, treatment status, test and laboratory results, location), as well as higher level information about hospital states (e.g., number of patients in the ED, admitted patients still in the ED, available ED beds, rooms that need cleaning) and team coordination information (e.g., assignments of providers to patients or bed zones; status of on-call providers). Information on whiteboards is encoded in locally developed (e.g., by providers in the hospital or department) and locally meaningful ways. Whiteboards are used to track the process of patient care through annotations that indicate potential diagnoses, progress through treatment plans, the need for consultations or tests, and admission or discharge processes. Typically, they are located in central areas of the ED so that information is available to all care providers and can be used to coordinate activities across individuals and time (Figure 2).

Figure 2 A whiteboard being viewed by multiple providers in an ED.

Electronic status boards may mimic the look and layout of manual boards (see Figure 3), support automated recording keeping and reporting, and allow information to be accessed at different locations in the hospital, but they also impose new constraints. The ability to add or change information is limited by available computer terminals, which typically require sign-on sequences; the form of information is limited to the characters or icons available on a keyboard or through the interface, and local methods of encoding are often lost; and the length and placement of entries is prescribed (e.g., free-form annotations cannot be added).

We studied the transition from manual to electronic status boards in two university-affiliated, urban hospital EDs (Pennathur et al., 2007, 2008b; Wears and Perry, 2007; Wears et al., 2005). One hospital had made the transition 10 months prior to our study but had continued to use manual boards along with the new system. We studied the second hospital before and after the transition. In this hospital, the manual boards were removed and replaced with the electronic system. We conducted a combination of semi-structured interviews, focus groups, and observations with care providers, secretaries, information technology specialists, and administrators. We also took photographs or screen shots of the status boards at one hospital, so we could make detailed comparisons of the content and form of information in both systems.

The results of our studies indicated a number of problems related to the transition to a new technology. Shortly after the electronic system was implemented at the second hospital, providers felt that the change had a negative impact on communication and their ability to "make sense" of the overall state of the ED, in part because the system could only be viewed on desktop screens, which had limited room for displaying information and limited flexibility for documenting information about treatment plans and diagnoses. For instance, a limited number of entries were visible in the column showing treatment plans, and providers could no longer use hand-drawn checkboxes to

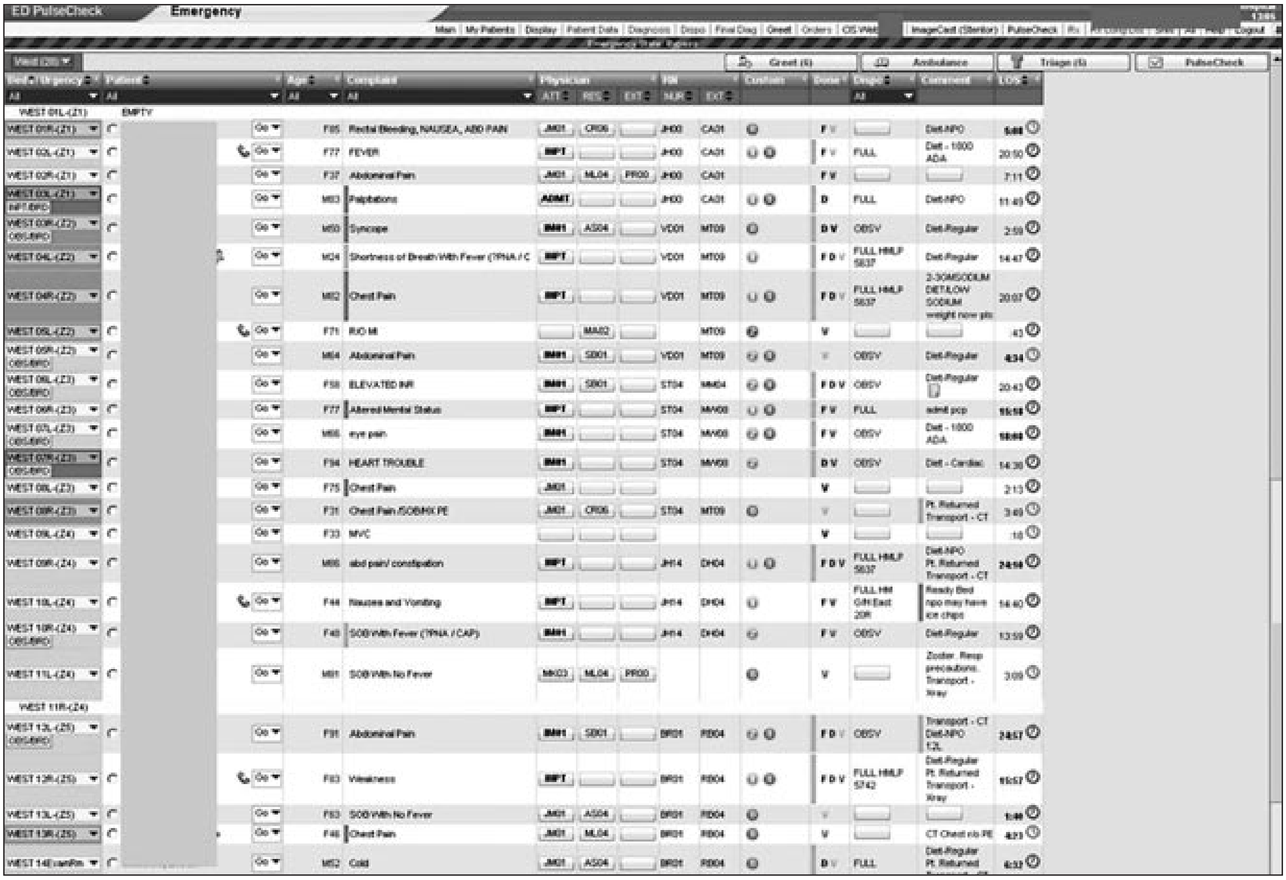

Figure 3 Electronic patient-tracking system screen. Source: *Proceedings of the Human Factors and Ergonomics Society Annual Meeting, 2008*. Reprinted with permission.

indicate progress. Because it was more difficult for providers to document and track patient progress, some providers resorted to carrying notes; this supported the work of individual providers, but the information was no longer publicly available, thus decreasing support for coordination among caregivers.

The staff also found an unanticipated use for the system—tracking patients' dietary needs and providing a printed list of diets to the meal-delivery staff. Although this function provided a benefit to some caregivers/staff, the constraints on space in the area where dietary information was entered meant that others could not use that space to display critical clinical information (e.g., lab values). In fact, at the first hospital, where both electronic and manual boards were used, clinicians tended to rely on the manual boards, while non-clinical staff used the electronic system for administrative functions, such as finding patients or assessing room status.

Some of these difficulties could be traced to the particular implementation and interface for the system, but others were more fundamental (e.g., the removal of a public, easily modified information source that supported relatively simple coordination for each individual and among individuals).

We subsequently decided to investigate the impact of electronic patient-tracking systems on caregivers' understanding of the overall ED state, as well as specific patient information. We developed a simulation-based tracking system that allows system parameters to be varied and tested by ED staff in a laboratory setting (Pennathur et al., 2008a). Immersive, simulated environments like this are used by cognitive engineers in many domains, such as aviation and driving, to test the impact of technology designs, situations, and tasks on human operators' activities and performance (Lee et al., 2002; Sarter and Woods, 2000).

The tracking simulation we developed is based on a discrete-event simulation model of a real hospital ED and incorporates both clinical information and operational information that can be used by study participants. Historic data on patient volume and the severity of their medical conditions were used to develop the model.

This model was used to generate sets of patients with medical conditions of different levels of severity, process events (e.g., waiting, registration, triage, caregiver visits, and laboratory tests), and the duration of those events. The simulated information was augmented with demographic information, medical complaints, and time-indexed medical information (e.g., tests, results, admission decisions, and the resulting information that would be shown on a whiteboard) to create "scripts" for each simulated patient.

Different scenarios were created based on different levels of demand for ED services. The scenarios were used as input to a patient-tracking display that was created for use by participants during experiments. The scenarios were augmented with secondary tasks (e.g., phone calls or pages that had to be answered) and simulation-freeze techniques for measuring participants' awareness of information represented in the system (Endsley, 1995).

This integrated experimental system can be used to test the impact of different display-related variables (e.g., display size, mode, and format of information); operational parameters (e.g., type of caregiver, number of patients); operational tasks (use of overall monitoring and monitoring during care transitions, such as a shift change); or how ED personnel interact with and interpret information on the electronic system.

Conclusion

The health care system has critical needs for improvements in efficiency, effectiveness, and safety. To meet those needs, we must first understand the complexities faced by health care workers and the knowledge, strategies, and tools they use. Cognitive engineering provides methods and tools for developing and implementing new technologies for this environment.

Acknowledgments

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NAE News and Notes

Seven NAE Members Receive National Medals of Science and Technology

Leonard Kleinrock, 2007 National Medal of Science Laureate.

Andrew J. Viterbi, 2007 National Medal of Science Laureate.

Paul Baran, 2007 National Medal of Technology and Innovation Laureate.

David Cutler, 2007 National Medal of Technology and Innovation Laureate.

President George W. Bush presented the 2007 National Medals of Science and National Medals of Technology and Innovation in the East Room of the White House on September 29, 2008. Seven NAE members were among the recipients of these prestigious awards.

A **2007 National Medal of Science** was awarded to **Leonard Kleinrock**, professor, Computer Science Department, University of California, Los Angeles, "for his fundamental contributions to the mathematical theory of modern data networks, and for the functional specification of packet switching, which is the foundation of Internet technology. His mentoring of generations of students has led to the commercialization of technologies that have transformed the world."

A **2007 National Medal of Science** was awarded to **Andrew J. Viterbi**, president, Viterbi Group LLC, "for his development of the maximum-likelihood algorithm for convolutional coding, known as the 'Viterbi algorithm,' and for his contributions to Code Division Multiple Access (CDMA) wireless technology that transformed the theory and practice of digital communications."

A **2007 National Medal of Technology and Innovation** was awarded to **Paul Baran**, chairman, NovoVentures Inc., "for the invention and development of the fundamental architecture for packet switched communication networks which provided a paradigm shift

Armand Feigenbaum, 2007 National Medal of Technology and Innovation Laureate.

Adam Heller, 2007 National Medal of Technology and Innovation Laureate.

from the circuit switched communication networks of the past and later was used to build the ARPANET and the Internet."

A **2007 National Medal of Technology and Innovation** was awarded to **David N. Cutler**, senior distinguished engineer, Microsoft Corporation, "for having envisioned, designed and implemented world standards for real-time, personal and server-based operating systems for over 30 years, carrying these projects from conception through design, engineering and production for Digital Equipment Corporation's RSX-11 and VAX/VMS and for Microsoft's Windows NT-based computer operating systems, and for his fundamental contributions to computer architecture, compilers, operating systems and software engineering."

A **2007 National Medal of Technology and Innovation** was awarded to **Armand V. Feigenbaum**, president, General Systems Company Inc., "for leadership in the development of the economic relationship of quality costs, productivity improvement, and profitability and for his pioneering application of economics, general systems theory and technology, statistical methods and management principles that define the Total Quality Management approach for achieving performance excellence and global competitiveness."

A **2007 National Medal of Technology and Innovation** was awarded to **Adam Heller**, research professor, Chemical Engineering Department, University of Texas at Austin, "for fundamental contributions to electrochemistry and bioelectrochemistry and the subsequent application of those fundamentals in the development of technological products that improved the quality of life of millions across the globe, most notably in the area of human health and well-being."

A **2007 National Medal of Technology and Innovation** was awarded to **C. Grant Willson**, Rashid Engineering Regents Chair, Department of Chemical Engineering, University of Texas at Austin, "for creation of novel lithographic imaging materials and techniques that have enabled the manufacturing of smaller, faster and more efficient microelectronic components that better the quality of the lives of people worldwide and improve the competitiveness of the U.S. microelectronics industry."

C. Grant Willson, 2007 National Medal of Technology and Innovation Laureate. *All Photos by Ryan K Morris, National Science and Technology Medal Foundation.*

NAE Newsmakers

Nathaniel Arbiter, Professor Emeritus of Mineral Engineering, Columbia University, was awarded the prestigious **IMPC Council Award** by the International Mineral Processing Congress at its September meeting in Beijing, China, for his outstanding and noteworthy contributions to the activities of the Council and its various activities.

David A. Edwards, Gordon McKay Professor of the Practice of Biomedical Engineering, Division of Engineering and Applied Sciences, Harvard University, has been elected to the Order of Arts and Literature of France. Dr. Edwards will receive the knighthood designation, **Chevalier de l'Ordre des Arts et des Lettres**. Dr. Edwards gained recognition in France for creating le Laboratoir, which provides a venue for creative thinking by scientists, beyond the constraints of specialization and grant applications. Professor Edwards describes it as "the first experiment-driven art and science incubator."

The Remote Sensing and Photogrammetry Society of the United Kingdom presented the **Taylor & Francis Best Letter Award** to Professors **Farouk El-Baz** and Eman Ghoneim for their paper, "Largest Crater Shape in the Great Sahara revealed by Multi-spectral Images and Radar Data," which was published in the *International Journal of Remote Sensing*. The award was presented at the society's Annual Conference at the University of Exeter Cornwall Campus near Falmouth, U.K.

Liang-Shih Fan, Distinguished University Professor and C. John Easton Professor in Engineering, Department of Chemical and Biomolecular Engineering, Ohio State University, was honored at the 25th International Pittsburgh Coal Conference, September 29–October 2, 2008, with the **2008 International Pitt Award for Innovation in Coal Conversion**. Dr. Fan was cited for his outstanding "contributions to Direct and In-Direct Clean Coal Technology and his inventions of OSCAR, CARBONOX, and CaRS-CO_2 processes for pollutant control of coal combustion flue gas, and Coal-Direct, Syngas, and Calcium Chemical Looping Gasification Processes for coal conversion to hydrogen, liquid fuels, chemicals, and electricity."

The Inamori Foundation presented the 24th Annual **Kyoto Prize for "Advanced Technology"** to **Richard M. Karp**, Senior Research Scientist, International Computer Science Institute, in recognition of his lifelong contributions to society. Dr. Karp was honored for fundamental contributions to the theory of "computational complexity" (a method of categorizing problems by their degree of difficulty) and for his early work on the theory of NP-completeness. His work on the analysis and design of computing algorithms has led to the solution of problems in the field of information science and a host of other fields—from the optimization of distribution networks for delivering water, gas, and electricity to data showing the correlation between gene structures and disease. The prize includes a diploma, a 20-karat gold medal, and a cash prize of approximately $500,000.

The **Millennium Technology Prize** has been awarded to **Robert Langer**, Institute Professor, Massachusetts Institute of Technology, for his invention and development of innovative biomaterials for controlled drug release and tissue regeneration that have saved many lives and improved the lives of millions of patients. Dr. Langer's innovations have had a significant impact on the treatment of cancer, heart disease, and numerous other diseases. The Millennium Technology Prize, is awarded every other year by The Millennium Technology Fund (a partnership between Finnish industry and government) in recognition of technological innovations that provide answers to the challenges of our time and improve quality of life. The winner receives €1 million.

Henry Petroski, Aleksander S. Vesic Professor of Civil Engineering, and professor of history, Duke University, was recently named a **Distinguished Member of the American Society of Civil Engineers** (ASCE). Formerly known as honorary membership, distinguished membership, the society's highest honor, is bestowed on individuals who have achieved eminence in a branch of engineering. The active roster of distinguished members includes only 193 of the more than 140,000 ASCE members worldwide. Dr. Petroski was honored for his advancement of the practice of civil engineering and civil engineering education, his achievements as a renowned educator, author, researcher, and lecturer, and his efforts to improve the public understanding of the importance of engineering through his published works.

2008 NAE Annual Meeting

Class of 2008.

NAE members, foreign associates, and guests gathered in Washington, D.C., this October for the 2008 NAE Annual Meeting. The meeting began on Saturday afternoon, October 4, with an orientation session for new members. That evening, the NAE Council held a dinner in the Great Hall of the Academy to honor 65 new members and nine new foreign associates.

NAE chair **Irwin M. Jacobs** opened the public session on Sunday, October 5, with brief remarks on "Continuing Innovations in K–12 Education and Wireless Technology" (see p. 53). President **Charles M. Vest** then delivered his annual address to the members and guests. His talk included observations about the current political scene and a discussion of advice the engineering community should offer the next president of the United States, whose ability to govern effectively and provide world leadership, he said, will depend profoundly on advancing and using the knowledge and tools of science, engineering, and medicine (see *www.nae.edu* for text of the address, and p 55). President Vest's address was followed by the induction of the NAE Class of 2008, with introductions by NAE Executive Officer **Lance Davis**.

The program continued with the presentation of the 2008 Founders Award to **Robert M. Nerem**, Parker H. Petit Professor and director, Institute for Bioengineering and Bioscience, Georgia Institute of Technology for "seminal research on fluid mechanics and atherogenesis, being a pioneer in the field of tissue engineering, founder of the American Institute of Medical and Biological Engineering (AIMBE), and leadership in engineering nationally and internationally."

Former NAE President Wm. A Wulf, Anita Jones, former NAE President Robert M. White, and Mavis White.

Robert M. White receiving his 40 year anniversary pin from President Vest.

The 2008 Arthur M. Bueche Award was presented to **G. Wayne Clough**, secretary, Smithsonian Institution, for "outstanding accomplishments advancing civil engineering and higher education, and for leadership promoting U.S. international competitiveness." Acceptance remarks by Drs. Clough (see p. 59) and Nerem (see p. 61) followed.

After a break, Dr. Vest introduced the Armstrong Endowment for Young Engineers-Gilbreth Lecturers, which are presented by outstanding young engineers who have given presentations at the NAE Frontiers of Engineering symposia. Mohan Manoharan, manager, Coatings and Surface Technologies Lab, Ceramics and Metallurgy Technologies, GE Global Research, spoke on "Nanotechnology and Industrial Research." Cynthia Breazeal, associate professor of media arts and sciences, LG Career Development Professor of Media Arts and Sciences, Massachusetts Institute of Technology, spoke on "Designing Socially Intelligent Robots."

The distinguished guest speaker was Professor Francis S. Collins, former director, National Human Genome Research Institute. The title of his talk was "Genomics and the Revolution in Personalized Medicine." The day ended with a reception for members and guests.

At the Annual Business Session for members on Monday morning, Dr. Vest spoke about administrative and programmatic matters of current interest at the Academy. He described actions taken by the NAE Council to modify membership processes and gave a broad outline of program priorities, both specific to NAE and in cooperation with the National Research Council.

Herwig Kogelnik, celebrating 30 years as a foreign associate of NAE.

The business session was followed by a symposium, "Grand Challenges for Engineering—Moving to Action." Aaron Brown, former ABC News and CNN anchor, was the moderator of a discussion about efforts to encourage the public, media, policy makers, and presidential candidates to become more active in implementing the findings of an NAE blue-ribbon committee on the Grand Challenges for Engineering (*www.engineeringchallenges.org* also see p. 64).

Committee members who participated in the symposium included the project chair and former U.S. Secretary of Defense **William J. Perry**, futurist and inventor **Ray Kurzweil** (by video from China), former head of the National Institutes of Health and Red Cross and current *US News & World Report* columnist Bernadine Healy, and chairman of the U.K. House of Lords Science Committee **Lord Alec Broers**.

Other participants in the discussion were author and *New York Times* columnist Thomas Friedman, CBS News science and technology correspondent Daniel Sieberg, former CEO of Hewlett-Packard Carly Fiorina (representing the McCain campaign), and former U.S. Under Secretary of Defense **Paul Kaminski** (representing the Obama campaign).

On Monday afternoon, members and foreign associates participated in NAE section meetings at the Keck Center. The final event of the meeting was the annual reception and dinner dance, held at the JW Marriott. Entertainment was provided by The Capitol Steps with music by the Odyssey Band.

The next annual meeting is scheduled for October 4–5, 2009, in Irvine, California.

Continuing Innovations in K–12 Education and Wireless Technology, Remarks by NAE Chair Irwin M. Jacobs

Irwin M. Jacobs

It is my pleasure to welcome all of you here today and extend a special welcome and congratulations to the new class of 2008, your families, and friends. This is a very special day for me as well—my first annual meeting as chairman of the National Academy of Engineering. So far I'm enjoying it very much, and I look forward to many opportunities for us to work together.

One of the roles of the academy is to increase awareness of the importance of engineering and its key role in our economy, particularly these days. The academy has proposed 14 Grand Challenges for Engineering, which President Vest will discuss further. One key challenge is to advance learning, to expand on the efforts of many NAE members to improve education, especially K–12 education, to increase our competitiveness, and, in so doing, to make more effective use of technology.

Although U.S. competitiveness remains strong, it has been weakening as measured by various metrics, such as the declining percentage of U.S. patent applications that originate in the United States. This issue is examined in the report, *Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future*, which was published in 2007 by the National Academies Press. For the United States to regain momentum and strengthen an increasingly international economy, we must increase the number and broaden the background of engineering students at the university level.

A variety of efforts are under way throughout the country, in which many of you are involved, to bring business, universities, and government together to support improvements in education at the local and national level. These activities often focus on broadening the pool of students who are motivated to undertake college studies in math, science, technology, and engineering, and of course to make sure that K–12 students have the necessary background to pursue those studies. I will briefly describe two of those efforts, although there are clearly many others that might be featured.

The first, a project called K-Nect, involves the use of technology, in this case smart phones, to assist in teaching 9th grade algebra. Four high schools in low-income areas of North Carolina participated last year. Each student was provided with a personal phone that had region-wide broadband connectivity. Most of these students did not have cell phones or access at home to high data-rate Internet connections. Plans are under way to extend the project to 8th and 9th grade algebra and 10th grade geometry classes.

Why smart phones? I admit, of course, to a long-term interest in the application of cell phones to education. Phones have a number of advantages, despite their small displays and keypads, because they are highly reliable and inexpensive enough that a phone can be provided to each student for use at school and at home. Smart phones are now powerful computers that have camera and camcorder capabilities and high-speed, region-wide (and increasingly worldwide) connections to the Internet.

With these capabilities, students in the K-Nect project were able to participate in school-oriented social networking—the exchange of ideas, and even videos taken with their phones, to discuss and solve problems at home, school, or even on the bus. Thus the phones provided an important way for students to motivate one another. They reported that they used their phones at least one hour every day to complete their algebra work. They also reported an increase in parental support and communication with their teachers.

Although it is not surprising for first-time educational experiments, the four Project K-Nect classes outperformed other classes taught by the same teachers on the North Carolina End-of-Course algebra exam. With further improvements in course materials, this form of personal learning can indeed be improved.

Innovation with smart phones is scalable. The International Telecommunication Union estimates that there will be 4 billion mobile subscribers by the end of 2008, approximately 61 percent of the worldwide population, up from

12 percent in 2000. Note that approximately one-third of them will be in the BRIC nations, that is Brazil, Russia, India, and China.

The second project involves the establishment of a charter school system called HIGH TECH HIGH that involves five high schools, two middle schools, a primary school, and a graduate school of education in San Diego County, with affiliations in other regions, including two in my home town of New Bedford, Massachusetts. The intent of HIGH TECH HIGH is to reach students early enough in their schooling to motivate them to take the more difficult math and science classes that will prepare them to pursue college majors in science, math, and engineering. The program has since expanded to include international and media arts studies. Students are not selected based on IQ or prior performance. They are chosen by lottery, and admissions are spread among all of the zip codes in the participating city.

In the words of Larry Rosenstock, founding principal and CEO, "the path to success was to prepare young people for college and beyond, but in a different way: through project-based learning, smaller classes, close student-teacher relationships, and a diverse student body with no tracking and with high expectations for all." HIGH TECH HIGH also exposes students to outside business and nonprofit organizations, and 167 student interns have been placed in 90 different organizations. The program has proven to be very successful. This year, there were 4,750 student applications for the 400 slots available in the first five schools. In addition, the program has been popular with teachers. There were 1,000 teacher applications this year for 36 openings. The four-year graduation rate for participating students is 98 percent, and of those 99 percent go on to college, 74 percent to four-year schools and the remainder to two-year colleges. Of HIGH TECH HIGH college students, 84 percent have graduated or are on track to graduate, compared to a 50 percent national rate. Most important from our point of view, 33 percent are majoring in math or science.

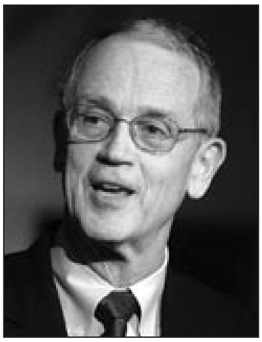
Since HIGH TECH HIGH is a charter school system, its expenditures per student are slightly lower than in the public school system, because a small number of dollars is set aside to pay interest on some of the startup costs. But why is the program so successful? Clearly there are many reasons, but one is that social networking among students, driven by a wide range of student projects, fosters comradeship and peer support. One notable project involved several classes and resulted in two books now available on Amazon.com: *San Diego Bay: A Story of Exploitation and Restoration* and *Perspectives of San Diego Bay: A Field Guide*, both five-star rated. A second reason is, of course, great teachers. HIGH TECH HIGH is able to hire people with excellent academic and/or business backgrounds and then allow them to be credentialed while teaching.

The program has now established the HIGH TECH HIGH Graduate School of Education, which offers master's degree programs in teacher leadership and school leadership to both HIGH TECH HIGH employees and other local educators, all of whom will spread the successful ideas to a wider audience. With the master's degree program, HIGH TECH HIGH can greatly increase its impact by offering training to teachers from other schools. Finally, HIGH TECH HIGH organizes a summer program for teachers and administrators from schools around the country to share experiences and best practices.

Clearly much remains to be done to prepare all of our children for personal success in this world, a world that is rapidly changing but which is filled with opportunities. It is especially important now, with the financial crisis threatening our country, that we not lose sight of our long-term needs and that we increase the resources devoted to the support of innovation, education, and research and development—especially to our research universities and institutes. With your help, NAE will continue to provide this leadership.

Again, welcome and congratulations to our new members. Thank you very much.

The Challenges Ahead, Remarks by President Charles M. Vest



Charles M. Vest

It is a great pleasure to participate in this 44th induction ceremony of the National Academy of Engineering, and it is a special privilege to welcome the families, friends, and guests of those who are being inducted today as members and foreign associates of NAE. Your election signals that our members, through a very rigorous process, have concluded that you are among the most brilliantly accomplished and distinguished members of your profession. We are proud to welcome you as colleagues, and we hope that this is a deeply meaningful event in your professional lives.

Election to NAE is a rare and singular honor, but membership carries additional significance. It is an opportunity for national service. Indeed, it is a call to national service. We are chartered by the U.S. Congress, together with the National Academy of Sciences, the Institute of Medicine, and our joint operating arm, the National Research Council, to provide independent, objective advice to the federal government on matters of science, technology, and medicine. However, we are not a government organization, and we are not part of the federal government. We are an independent, nonprofit organization.

In return for providing objective analyses and experience-based advice of the nation's most accomplished engineers through objective, non-political studies, we are granted a special, respected role as advisors to the nation. We perform this function largely by conducting rigorous studies of specific issues, either when requested by the government, or, from time to time, when we ourselves choose to examine an issue we believe to be particularly important.

Of course, we call on our members to provide leadership for these studies. This is the primary service we will expect of you. As NAE members, we are participants in the world's most formidable think tank, and, as an independent organization of nearly 2,000 of the nation's most accomplished engineers, we can play an important role in securing our nation's future.

When I was elected to NAE in 1993, I received a note from **John Armstrong**, the former vice president for research at IBM. John's note said *"Congratulations on your election to the NAE. I just can't wait to put you on a committee!"* You can see that John is less subtle in these matters than I am, but the message is identical.

Part of the core mission of NAE is to *promote the technological welfare of the nation*. Engineering is critical to meeting the fundamental challenges facing the U.S. economy, environment, health, security, and way of life in the 21st century. Although industries are well aware of the centrality of engineering to the production of competitive products and the delivery of services in the world marketplace, governments at both the federal and state levels are struggling to understand and incorporate scientific and technological knowledge into policies that are, literally, matters of life and death.

In his *New York Times* column last Sunday, Tom Friedman, who will be with us tomorrow, made this point clearly in a commentary on the Wall Street bailout and the need for a green future. He wrote, "*… we don't just need a bailout. We need a buildup. We need to get back to making stuff based on real engineering not just financial engineering.*"

Letter to the New President

In case you haven't noticed, we in the United States are in the midst of a presidential election, which, blissfully, will soon be over. Our nation will have a new president who will set about the tasks of assembling an administration, refining his vision, establishing goals and strategies, and preparing a budget.

But these are not ordinary times. We are facing tectonic shifts in the world order: global economies are increasingly intertwined; levels of education and knowledge development are rising everywhere; U.S. popularity around the world is at an all-time low; our addiction to oil has created an unstable situation in which we send about $400 billion each year to other countries to purchase it; we are awakening to the need to mitigate global climate disruption and the need to adapt to it; huge swaths of public primary and secondary education are disaster zones, especially in science and math; North America, Europe, and Asia now each fund about one-third of the world's R&D (i.e., the United

States is no longer the biggest investor); the complexity of our financial systems has grown beyond our ability to fully understand it, and, coupled with some of our baser human tendencies, we are close to the brink of economic collapse; we face insidious security threats that are entirely unlike those posed by nation states for most of our lifetimes; and an inadequate supply of water is an imminent threat not only in the developing world, but also here at home. Much more could be added to this list, but the point is that the 21st century is very different from the 20th century, and it brings with it enormous challenges—challenges on a huge, frequently global, scale.

During my first year as NAE president, I have had the opportunity to travel a lot, think about these issues, consult with leaders of various sectors and countries, be inspired by the amazing young participants in our Frontiers of Engineering programs, sit on interesting committees, and learn from my colleagues here at the National Academies. From these experiences, I have arrived at a few conclusions. First, globalization and our other major challenges bring with them extraordinary opportunities—opportunities for human advancement and opportunities for business and commerce. Second, science and engineering are at the core of the solutions to most of our challenges and problems. Third, our political process and popular worldview are largely oblivious to the centrality of science and engineering in these matters.

In this context, many in our engineering, science, and medical communities are advising, or attempting to advise, whatever new administration will be installed in January. Various organizations and publications are presenting reports or letters to the next president, and the National Academies is no exception. My colleagues, Ralph Cicerone of the National Academy of Sciences and Harvey Fineberg of the Institute of Medicine, and I sent correspondence to the two presidential candidates, and a National Research Council committee was convened to produce a document identifying the most critical posts to which the next administration must appoint leaders with science and engineering backgrounds.

In this same spirit, a magazine asked me to draft a brief letter ostensibly to our new president. Here it is:

Dear Mr. President:

Your ability to govern effectively and provide world leadership will depend profoundly on advancing and utilizing the knowledge and tools of science, engineering, and medicine.

In the 20th century, U.S. science, engineering, and medicine nearly doubled our life span, protected our nation's security, fueled most of our economic growth, sent us to the moon, fed the planet, brought world events into our living rooms, gave us freedom of travel by air, sea, and land, established instant worldwide communications, enabled ubiquitous new forms of art and entertainment, and uncovered the workings of our natural world. It was a century of speed, power, and new horizons. We have come to take all this for granted.

The 21st century will be very different. And nothing can be taken for granted. To grasp the great opportunities of our times and to meet our challenges—from economic competition to energy, from health care to education, from security to infrastructure—federal policy and action must be informed and enabled by a vibrant science and engineering enterprise. Indeed our national comparative advantage is a strong S&T base coupled to a free market economy and a diverse, democratic society. We will soon feel the full force of global competition. Jobs will follow innovation wherever in the world it is found, and innovation will follow basic research wherever it is conducted. All our children must be inspired and educated for productive, well-paying jobs in this knowledge economy.

The bipartisan America COMPETES Act was passed and signed into law in August 2007, but has not been funded. It would jump-start improvement in K–12 science and math education, strengthen and sustain long-term basic research, make the U.S. the best place in the world to study and do research, and help ensure that we remain the most innovative nation on the planet. Its cost is about 0.14 percent of the Wall Street bailout, 0.8 percent of this year's economic stimulus, or 1.8 percent of annual farm subsidies.

American science and higher education are admired throughout the world and are wellsprings of badly needed good will toward our nation. By fully exploiting our capacity in science, technology, and medicine, you can project U.S. leadership abroad, enhance the quality of life at home, and better prepare us for the uncertain challenges of a rapidly changing world.

Mr. President, the federal government must invest in our future through education, research, and innovation. I therefore believe you should take six immediate actions:

- *Use your bully pulpit constantly to establish a public vision of an America that will lead and prosper in the 21st century through knowledge and innovation.*
- *Appoint an outstanding science and technology advisor prior to your inauguration and include him or her*

at the highest tables of counsel and decision-making in a manner parallel to the national security advisor.

- *Make full funding of the bipartisan America COMPETES Act a non-negotiable first-term priority.*
- *Establish a bold national initiative engaging the private sector, academia, and government to meet our energy challenge and mitigate the advance of global climate disruption.*
- *Restore strong DOD basic research budgets and grow the NIH budget in excess of inflation.*
- *Work with Congress to eliminate academic earmarking.*

My colleagues in industry, academia, and government stand ready to support your new administration with fact-based advice and to provide the knowledge and innovation required for U.S. prosperity and improved life around the world.

Respectfully,
Charles M. Vest

I hope this message is consistent with the views of most NAE members. It certainly is reflective of the National Academies report, *Rising Above the Gathering Storm: Energizing and Employing America for a Brighter Economic Future*, which was drafted by a committee ably led by **Norm Augustine** and is the primary basis of the America COMPETES legislation. The letter also draws in large measure on the message our three academy presidents sent to the candidates. It succinctly lays out an agenda that I hope you can support.

Grand Challenges for Engineering

Niccolo Machiavelli said many things, most of which I won't repeat today, because you might fear that just one year in Washington has already corrupted my psyche and distorted my values. But there is one very important thing Machiavelli famously said, "*Make no small plans because they have no power to stir the soul*." This is very good advice for us as we think about the relationship between engineering and society, promote a broad public understanding of what we do and why it is important, and especially as we seek to inspire young men and women to become engineers.

Whether or not Machiavelli inspired him, during **Bill Wulf's** presidency, NAE formed a committee of extraordinarily innovative, successful, and diverse engineers, scientists, entrepreneurs, and one medical doctor. Former U.S. defense secretary and NAE member **Bill Perry** chaired the committee, and it was ably organized by Randy Atkins. The committee's charge was to develop a list of a modest number of grand challenges for engineering. These were not to be outrageously distant challenges, but challenges of great importance that the committee believed could actually be met in the next few decades if we set our minds and resources to doing so. The committee also established an interactive website that enabled a wide audience to suggest challenges and join in the project.

Ultimately the committee established 14 grand challenges:

1. Make solar energy economical.
2. Provide energy from fusion.
3. Develop carbon-sequestration methods.
4. Manage the nitrogen cycle.
5. Provide access to clean water.
6. Restore and improve urban infrastructure.
7. Advance health informatics.
8. Engineer better medicines.
9. Reverse-engineer the brain.
10. Prevent nuclear terror.
11. Secure cyberspace.
12. Enhance virtual reality.
13. Advance personalized learning.
14. Engineer the tools of scientific discovery.

These challenges basically fit into three categories: (1) energy, sustainability, and global climate change; (2) medicine, health informatics, and health care delivery systems; and (3) reducing our vulnerability to natural and human threats and advancing the human spirit and capabilities. Think about these challenges. Meeting some of them is imperative for human survival. Meeting others will make us more secure against natural and human threats. Meeting any of them will improve quality of life.

The Grand Challenges for Engineering were announced last February, and in the following day or two only a few small paragraphs appeared in mainstream U.S. print media. But in Europe and Asia, they received very substantial coverage. This is an all-too-familiar syndrome—complacency at home and enthusiasm elsewhere in the world. NAE then posted the Grand Challenges on the interactive website where visitors can help prioritize them. So far, the website has had about 170,000 visit from people in 40 countries. More recently, the challenges were published by NAE in a booklet with an essay on each.

I'm pleased to report that this project has created a good bit of stir in the blogosphere, and a brief video about the project can be found on YouTube as well as on our own website. This is good news, because it means we are reaching and engaging young people. The challenges will also play a central role in a documentary movie, *Imagine It*. This robust, fast-paced film deals with a new generation, global challenges, and the power of imagination.

Several engineering schools and departments have informed us that they have mounted project courses based on the Grand Challenges for Engineering. Next March, Duke University, in partnership with the University of Southern California and Olin College, will hold a summit of leading engineering, science, humanities, and social science scholars from across the nation to articulate the challenges and opportunities of the science, technology, and policy related to each NAE Grand Challenge and to propose solutions. They also intend to stimulate conversations on the importance of engineering and science in maintaining and enhancing our quality of life.

At our symposium tomorrow afternoon, we will bring together the themes of political realities of 2008 with the far-reaching Grand Challenges through a conversation among some of the committee members and a distinguished group of journalists and representatives of the McCain and Obama campaigns. Committee members **Lord Alec Broers**, Bernadine Healey, and **Ray Kurzweil** will be joined by author and *New York Times* columnist Tom Friedman and Daniel Sieberg of CBS News. Former Hewlett-Packard CEO Carly Fiorina will represent the McCain campaign, and former U.S. Undersecretary of Defense **Paul Kaminski** will represent the Obama campaign. Aaron Brown, former ABC and CNN news anchor, will moderate the conversation and audience participation. It should be a fascinating symposium, and we hope that all of you will join us (see summary on pp. 65–66).

Conclusion

In conclusion, I congratulate you on your election to NAE, and I hope that this is a deeply meaningful event for each of you. NAE asks that you also recognize your membership as an opportunity to serve your nation and the world through providing well-informed, objective, and independent advice on important issues involving technology. Developing and transmitting such advice is an important form of engineering leadership.

You come to this task at a moment in history when there is an urgent need to ensure the sustainment and enhancement of the technological welfare of the nation, so that we can both compete in the global, knowledge-based economy *and* maintain our prosperity. You also come to this task at a time when the frontiers of engineering, at both the small and large scale, are enormously exciting and of critical importance to meeting the great challenges of energy, environment, productivity, health care, food, water, and security.

G. Wayne Clough, Recipient of the 2008 Bueche Award, Acceptance Remarks

Irwin M. Jacobs, G. Wayne Clough, Charles M. Vest, and Linda Abriola, chair, NAE Awards Committee.

The 2008 Arthur M. Bueche Award was presented to G. Wayne Clough, *secretary, Smithsonian Institution, for "outstanding accomplishments advancing civil engineering and higher education, and for leadership promoting U.S. international competitiveness."*

Given the focus of the Arthur M. Bueche Award on active involvement in U.S. science and technology policy and enhancement of the relationship between industries, government, and universities, and the many outstanding people who make contributions in these areas, receiving this award is indeed a high honor. I accept it with deep humility and profound gratitude.

Heartfelt thanks go to the many people who helped me get where I am today, including many great teachers, my 34 Ph.D. students, my parents, and of course my wife and family. In my life, I've been fortunate to have had an array of wise mentors, including many who are former winners of the Bueche Award, such as **Chuck Vest**, **Norm Augustine**, **John Slaughter**, **Erich Bloch**, and **Ralph Gomory**. Others who have helped me along the way include the leaders of organizations, such as the Council on Competitiveness, the President's Council of Advisors on Science and Technology, the National Science Board, and the National Academy of Engineering itself. To all of them, my sincere thanks.

Today, science and technology policy and collaborations between industry, government, and universities are the subject of formal study by scholars around the world. My own involvement in these areas did not follow a formal route, but resulted from my career development. I was fortunate in my life to enjoy a degree of success in teaching and research at some of America's great research universities. And, as I mentioned, I've had many mentors. All of this motivated me to want to give back to the engineering profession, and over time I became involved in higher education administration, which ultimately opened possibilities to serve in the policy arena on the national scene. Some might say I was practicing policy without a license—but it was for a good cause! Mind you, I do not advocate a licensing procedure, but I do advocate more preparation for engineers, who will increasingly be called upon to participate in the policy arena—as they should.

Science and technology and related policy factors are becoming more important with each passing day, their reach extending into all areas of our lives—at work, at home, and at play. The importance of collaboration between our nation's universities and our industries and government is growing as we face global economic competition, and as the traditional U.S. advantages no longer sustain us. All of this is made more complex as lines between disciplines and fields become blurred, problems of society become increasingly interconnected, and solutions are only to be found in cross-disciplinary cooperation. Thus, while the need for engineers to participate in the national dialogue increases, at the same time, their participation requires an appreciation of issues and skills that are currently beyond the ken of most of them. We must become students again.

Not long ago I participated in a forum of top executives from technology companies, and we all agreed that engineers should be more engaged in policy. The sentiment, however, was that engineers would be more effective if they offered opinions only about issues in their fields of expertise.

As I listened, I realized that our local, state, and national politicians do not think this way. Every day they vote on matters of importance without being experts in that field. If they are lucky, elected officials get advice on issues from staff, constituents, experts, and outside entities. At the local and state levels such expert advice may not be available. Regardless, they are expected to vote. It is time for engineers to realize that on all levels of government we should play a larger role in this process.

Through advisory boards and nonpartisan groups, informal advice, and expert testimony, engineers can inform the issues of the day. The enduring advantage of our discipline is that we bring a problem solver's mentality to issues, and we can sort through complexities to find the core problems. But this is not enough. To serve the public better and work more effectively in the policy arena, we will have to move beyond our comfort zones.

We should appreciate that our way of thinking is useful, even when we are confronted by matters that are unfamiliar to us. A few years ago I was asked by then-Governor Roy Barns of Georgia to head a statewide task force on revising Georgia's natural gas deregulation legislation. The legislation had created a marketing nightmare that had angered Georgia's citizens. Now, I knew very little about the natural gas industry or deregulation, but I found that, with a little study, my engineering approach to the issues put me ahead of just about everyone else. I also knew enough to seek out two expert consultants and asked them to inform my task force. In the end, we produced a framework for legislation that corrected the problems.

Being willing to step outside of one's comfort zone is one part of the equation. But I believe engineers who wish to contribute to policy deliberations should also prepare themselves by developing an appreciation of the world of policy and politics. This can best be done with some degree of formal preparation.

Some of this is already being done. With support from the MacArthur Foundation, 10 universities now offer a year-long program for mid-career scientists and engineers to prepare them for policy roles. We were fortunate at my former institution, Georgia Tech, to receive a MacArthur grant for this purpose. Beyond this excellent program, I would suggest that other entities, perhaps NAE or the disciplinary professional societies, could offer shorter term programs to help individuals who arrive in executive positions and need help in getting started. Of course, NAE and the National Research Council, as part of their charter, must offer advice to the federal government as needed. Yet the need for advice goes well beyond this traditional role, and often the Academies are not asked for advice until problems arise. Besides, local and state governments need help as well.

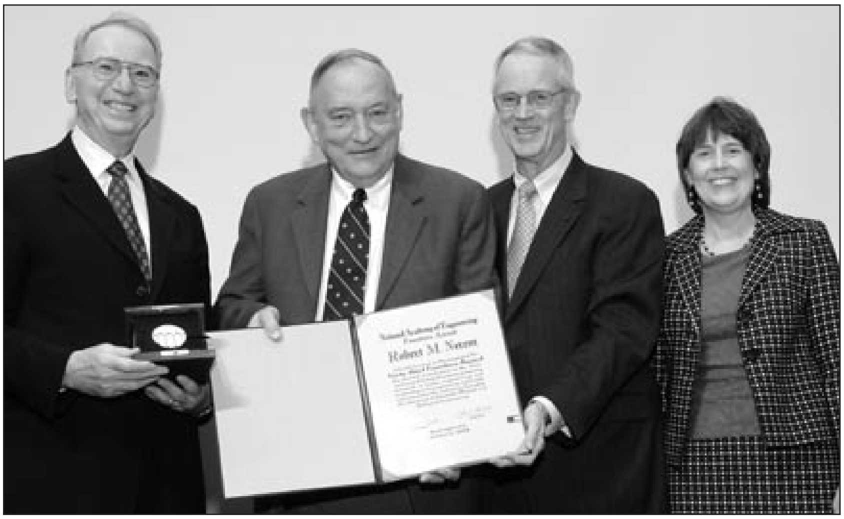
This has become increasingly clear to me in my new position as the twelfth secretary of the Smithsonian Institution. At this great institution, I am privileged to witness how technology merges with science, art, history, and culture—and always has. I learned that the first secretary of the Smithsonian, Joseph Henry, served as a science advisor to President Lincoln and as president of the National Academy of Sciences for 12 years, even as he remained secretary of the Smithsonian. The Smithsonian today is involved in education, outreach, research, the creation of new knowledge, and the preservation and documentation of 137 million scientific, historical, artistic, and cultural artifacts.

Despite the seemingly disparate nature of Smithsonian activities, technology is an essential component linking them. For example, we are in the process of digitizing our collections and creating innovative systems to allow access to them by students and teachers in the K–12 system and by research scholars around the world. This is a revolutionary prospect, moving from a world where nearly 98 percent of the 137 million objects are kept in archives and seen by only a few, to a world where they can be seen and used by millions of people everywhere. The possibilities are staggering. Needless to say, it is an exciting time to be secretary of the Smithsonian, and I look forward to working with the National Academies to re-establish the link between these great American institutions.

In hundreds of ways science and technology are changing our lives dramatically, and the policy framework to make this work has to be established, hopefully with input from those who are most knowledgeable—scientists and engineers.

Many thanks again to the academy for this great honor and many thanks to my family and friends. I thank all of you for the opportunity to share my thoughts with you.

Robert M. Nerem, Recipient of the 2008 Founders Award, Acceptance Remarks



Irwin M. Jacobs, Robert M. Nerem, Charles M. Vest, and Linda Abriola, chair, NAE Awards Committee.

The 2008 Founders Award was presented to Robert M. Nerem, Parker H. Petit Professor and director, Institute for Bioengineering and Bioscience, Georgia Institute of Technology, for "seminal research on fluid mechanics and atherogenesis, being a pioneer in the field of tissue engineering, founder of the American Institute of Medical and Biological Engineering (AIMBE), and his leadership in engineering nationally and internationally."

I thank the National Academy of Engineering for this very special honor, one that is for me very humbling. I also thank the friends who nominated and supported me, my wife, Marilyn, who has been not only supportive but also a partner for 30 years in so many ways, my family, my students past and present, my colleagues, and the communities of which I have been a part and that have nurtured my career. All of these have been "The Wind Beneath My Wings."

To start with, I am the first generation in my family to be born in this country. Both of my parents were born and raised in Norway, my father in Ålesund on the west coast and my mother in Harstad in the far north, above the Arctic Circle. My father graduated as a civil engineer from Trondheim in the mid-1920s. My parents then immigrated to the United States, and I was born in Chicago in 1937, the last of four children, although two died at a very early age. I grew up in Evanston, Illinois, outside of Chicago, with the exception of two years after World War II when we lived in Norway and I went to Norwegian schools.

In my opening words of thanks I noted the communities of which I have been a part. I used the plural because of my journey through the world of engineering. Even as an undergraduate, I was a migrant, i.e., I migrated from one engineering field to another, changing majors every semester, starting in petroleum engineering and ending up in aeronautical engineering. In fact, all of my degrees, including my Ph.D., are in aerospace engineering. My dissertation was on heat transfer during reentry, and early on my community was the fluid-mechanics and heat-transfer community, and my societies were the American Institute of Aeronautics and Astronautics and the American Physical Society Division of Fluid Dynamics.

When I received my Ph.D. and began to interview for a job, my first offer was from **Sol Penner**, last year's Founders Award recipient, who at that time was at the Institute for Defense Analyses (IDA). Even though he offered me a job, he recognized my interest in an academic career and encouraged me to pursue that dream. Thus I did not go to IDA, and my first position after my Ph.D. was at Ohio State University as an assistant professor, where I continued to pursue my research interests in fluid mechanics and heat transfer.

A few years later, due to my association with the National Aeronautics and Space Administration (NASA), I became a consultant on a research project at Ohio State on the effect of vibrations during launch on astronaut physiology. Like most consultants, I made little if any contribution to the project. However, it opened the window on a whole new world, that of biology and medicine. This led me to spend the better part of 1970 at Imperial College London working with Dr. Colin Caro and the Physiological Flow Studies Unit on problems related to blood flow and the cardiovascular system.

When I returned to Ohio State,

two things happened that shaped my career. First, the chair of my department encouraged this young academic to pursue his new passion and to enter into the world of biomedical engineering. Second, I was offered the opportunity to move my laboratory over to the Department of Veterinary Physiology, even though my appointment was still in aerospace engineering where I continued to teach. This arrangement provided me an entry into the interdisciplinary world, launched me into a new phase of my career, and brought me into both the bioengineering community and the biology community.

Initially I wanted to use my engineering knowledge to study blood flow, especially its role in disease processes. One could not, however, investigate the interaction between blood flow and the vessel wall without getting into biology, first at the level of cell biology and then at the molecular level. Ultimately this led me to tissue engineering and stem-cell technology, including both embryonic stem cells and adult stem cells. As my career has evolved, I have continually moved into new areas that in general I did not have the background to pursue. As a result, I have been a student all my life.

In 1987, I moved to Georgia Tech. Because of what might be called an antiquated system, one imposed by the State of Georgia Board of Regents, no new faculty member could be appointed with tenure. This system was subsequently changed, but when I came to Georgia Tech in 1987, I came as an untenured full professor with an endowed chair. Thus when I was elected to NAE in 1988 I was untenured.

When my election to NAE was announced in February 1988, I was at a meeting at the World Health Organization in Geneva, Switzerland. I still remember waking up in the middle of the night to a phone call from **Ward Winer** notifying me of my election to NAE. Ward also had been elected, and Ward and I were in the class of 1988 with **Dan Mote**, the 2006 Founders Award recipient. At the end of my telephone conversation with Ward I commented that "maybe this will help me get tenure." Ward responded by saying, "Oh, I wouldn't put too much significance on this!" Well, don't worry, I did get tenure; however, there was some truth in what Ward said to me. After all, election to NAE is for past achievements, but with that election comes the responsibility to continue to serve and lead.

The last 20 years have been "one hell of a ride." I have been blessed with wonderful colleagues and excellent students. In fact, it is because of the students that I have pursued an academic career, and my greatest satisfaction professionally has come from the young people with whom I have worked and whom I have had the privilege of mentoring. My students refer to themselves as SOBs, i.e., <u>S</u>tudents <u>o</u>f <u>B</u>ob. In their view, there already were identified FOBs, i.e., <u>F</u>riends <u>o</u>f <u>B</u>ob, so why not SOBs?

A few years ago my then students banded together and said to me, "You know those various rules you keep on 'spouting off'? Well, write them down." So this I have done, and I thought that in closing I would share them with you. These rules are not original, simply pulled together over the years; however, they do represent my philosophy about life. I share them with you in the hope that at least a few might be of interest.

There currently are 15 of what I call "The Rules of Life: The Planet Earth School." In this school the teachers are the persons you encounter and/or the events in which you are involved, and the "rules" are as follows.

1. There are no such things as mistakes, only lessons (i.e., a series of learning experiences). Growth is through a series of such experiences, a process that involves both successful and unsuccessful experiments.
2. An unsuccessful experiment does not represent failure, just a learning experience, and one often learns more from these than from successes. Apply the lessons of today so as to make yourself a better person tomorrow.
3. Always be open in the widest possible way to encountering a new person or a new opportunity, as these represent new teachers, new learning experiences. "Leave the screen door (to the outside world) unlatched," because you never know who or what will walk in.
4. If you encounter a closed door, simply look for another door that might be open. Life is filled with a lot of paths and doors to walk through, so don't waste time on a door that is closed. Let the "rock" in your path be a "stepping stone."
5. Your life is up to you. At birth you were provided a "canvas" onto which you have the opportunity to "paint your life." Take charge of your life and the "painting of this picture." If you don't, someone or something else will.

6. People will remember not what you said, but only how you made them feel, so strive to make a difference in the lives of others.
7. Remember that the cup is always half full, never half empty, but also remember that the only cards you can play are the ones you are dealt.
8. Look for the good in people, and try to imagine the world as it seems to the other person.
9. Never, never worry about something over which you have no control.
10. Whatever happens, place the least dramatic interpretation on the event, the incident, and/or whatever is said.
11. Never have expectations, only hopes, and welcome each and every new day, for "each dawn is a new beginning." Each day presents new opportunities and, as has been said, "a day spent without real enthusiasm, is an opportunity lost."
12. Love yourself, make peace with who you are and where you are at this moment in time; be willing to let go of the life you had planned so as to have the life that awaits you.
13. Listen to your heart. If you can't hear what it is saying in this noisy world, make time for yourself, enjoy your own company, let your mind wander among the stars.
14. Don't let your preoccupation with reality stifle your imagination. If someday, why not now, even though the impossible may take a while.
15. Finally, life's journey isn't to arrive at the grave safely in a well preserved body, but rather to skid in sideways, worn out, shouting—holy cow, what a ride!

When I look at my life, I do say "holy cow, what a ride," both personally and professionally. Personally I have my bride Marilyn and four wonderful children, two from my first marriage and two inherited through my marriage to Marilyn. I have seven grandchildren. In two days Marilyn and I will celebrate our 30th wedding anniversary, not bad for a second time around. Professionally, as I tell my students, "I am still trying to figure out what I want to do when I grow up," even though I don't think anyone believes that I actually will someday grow up.

Although the "ride" is not by any means over, it is important from time to time to stop and "smell the roses." My selection for the 2008 Founders Award has provided me the opportunity to do so. So again I thank NAE, my friends who nominated me, my colleagues, my family, the FOBs and SOBs, the communities of which I have been a part, and all those whose lives have "touched" me. They all have been my teachers on this planet Earth, and I consider myself to be truly blessed. Thank you.

Grand Challenges for Engineering Panel Discussions

William Perry, chair of the Grand Challenges committee, frames the issues.

Last February, NAE announced the results of the Grand Challenges for Engineering project, a major international effort to identify goals of worldwide significance for humanity. After months of in-person and online discussions, with input from thousands of people from around the world, 14 focus areas were chosen by a blue-ribbon committee of leading thinkers.

Instead of a symposium at the NAE Annual Meeting this year, two panel discussions were held, moderated by Aaron Brown, former anchor of ABC News and CNN, on the Grand Challenges for Engineering (*www.engineeringchallenges.org*). The discussions focused on (1) communicating the challenges to the public and (2) engaging policy makers in developing ways to address them. A very large audience included NAE members and interested members of the public; the event was also webcast.

The event was opened by NAE president **Charles Vest**, followed by an overview of the goals and findings of the Grand Challenges project by **William Perry**, chair of the Grand Challenges for Engineering Committee and former U.S. secretary of defense.

Members of the first panel included: Thomas Friedman, columnist for the *New York Times* and author of *Hot, Flat and Crowded*; Bernadine Healy, health editor and columnist for *US News and World Report* and former head of the National Institutes of Health; **Ray Kurzweil**, president and CEO of Kurzweil Technologies and a member of the Grand Challenges for Engineering Committee; and Daniel Sieberg, science and technology reporter for CBS News.

Thomas Friedman, Bernadine Healy, and Daniel Sieberg engage in a lively discussion.

The panel generally agreed that science and technology reporting in the mainstream media, a major outlet for educating the public, must be greatly improved. Sieberg pointed out the difficulties facing reporters, who must "boil complicated, important stories down to two minutes," the amount of time generally allotted by news producers. Tom Friedman argued that engaging the public will require that the challenges be framed in an inspirational way. "You can emphasize the 'challenge' and how difficult [it] is, or [you can] emphasize the 'grand.' These [challenges] are opportunities masquerading as impossible problems. But if you want to be big as a country, be big in the big things. These challenges are the biggest thing."

Committee member Ray Kurzweil joins the proceedings via teleconference from China.

Healy encouraged academics to focus on the importance of innovation. "Leadership from universities is critical," she said. "I'd love to see the presidents [of universities] get together and talk about promoting [the challenges] and ask, 'What are we doing? Do we have courses in it? Are we creating inspiration?'"

Kurzweil stressed that many technologies still on the drawing board will grow exponentially, and not simply linearly, in the next several years. In the case of solar power, he said, "the tipping point is less than five years away . . .We do get people's attention when we make this point."

The second panel was asked to consider how a substantive discussion about the challenges could be initiated in political circles and how the challenges could be addressed in policy discussions. The panel members included **Lord Alec Broers**, a member of the U.K. House of Lords and a committee member; Carly Fiorina, former CEO of Hewlett-Packard and a representative of the McCain campaign; and **Paul Kaminski**, former U.S. under secretary of defense, NAE member, and representative of the Obama campaign.

Brown opened the discussion by suggesting that political terms of

Aaron Brown moderates a panel discussion with Paul Kaminski, Alec Broers, and Carly Fiorina.

office, two, four, and six years, are not well-suited to addressing big issues. Kaminski agreed. The challenges are "long-term [and] multidisciplinary," he said. Dealing with them will require first "dealing with a number of the . . . complexities of our political systems that work on short-term scales."

The representatives of both campaigns lamented that "trivial" subjects tend to take center stage and attract excessive media coverage at the expense of more important matters, such as engineering and technological issues. However, they also agreed that this is an unfortunate, but unavoidable aspect of modern campaigning and that, once a candidate is sworn in, the focus on technical issues will intensify.

When asked if America was still seen as the world leader in engineering and science, Broers suggested that the determined U.S. focus on terrorism has, perhaps, changed the way Europeans view Americans. "But," he said "don't for one minute think that the world isn't going to turn to America as the leader to help us with these challenges."

Fiorina expressed her conviction that the market and innovators, and not the government, would drive us forward in meeting the challenges. "The innovation we need now is not command-and-control, top-down, and organized, but decentralized," she said. "America's political power in the world rests on our economic power in the world, and our economic power rests on our ability to innovate."

The purpose of the Grand Challenges for Engineering project is to raise public awareness and stimulate interest in important engineering-related issues. The symposium was one element in the dissemination of the results of the project. A podcast of the event posted on the NAE website (*www.nae.edu*), which provides worldwide access to the discussion, can be accessed via a link under "Events."

NAE president Chuck Vest talks with Aaron Brown after the event.

2008 U.S. Frontiers of Engineering Symposium

On September 18–20, 109 engineers attended the 2008 U.S. Frontiers of Engineering (US FOE) symposium at the University of New Mexico in Albuquerque; the symposium was hosted by Sandia National Laboratories. NAE member **Julia M. Phillips**, director of the Physical, Chemical, and Nano Sciences Center at Sandia National Laboratories and chair of the symposium, was instrumental in bringing the symposium to Albuquerque. The presentation topics this year were drug-delivery systems, emerging nanoelectronic devices, cognitive engineering, and understanding and countering the proliferation of weapons of mass destruction.

In the first session, on drug-delivery systems, cutting-edge researchers described how advances in materials, particularly polymer systems, have enabled more careful engineering of delivery systems. For example, engineered particles and devices can now provide sustained release of drugs, eliminating daily dosing; and micro- and nano-engineered systems can target the delivery of a therapeutic to a particular physiological system or disease site, thus minimizing systemic side effects. The presentations included an overview of drug delivery methodologies and highlights of several key technologies for targeting and controlling the release of bioactive materials.

The session on emerging nanoelectronic devices was focused on novel nanoscale materials and devices, circuit concepts, and sensor functionalities that can be harnessed to develop new technologies for information processing. Presenters described a variety of innovative ideas for post-CMOS technologies, such as molecular electronics, carbon nanotube devices, and spin devices that can be integrated with appropriate nanoarchitectures to create alternative electronic devices.

According to the Human Factors and Ergonomics Society, the goal of cognitive engineering is to improve systems design and training to support human cognitive and decision-making skills, particularly in applied, naturalistic settings. The four speakers in this session provided an overview of the field and described improvements in systems engineering designed to maximize human performance and reduce errors in driving, power-plant operations, and health-care delivery.

The last session included presentations on understanding and countering the proliferation of weapons of mass destruction. Two of the talks were focused on national and international policy issues that frame the discussion. A third described the strategy of capability-based nuclear deterrence—reliance on a small number of deployed weapons coupled with a robust, agile infrastructure enabled by science and engineering.

On the first afternoon of the meeting, participants gathered in small groups to share ideas on important advances they hope to make in the next 10 years and to "brainstorm" on discoveries that could help them reach their goals. On the second afternoon, participants were taken on tours of the Center for High-Technology Materials at the University of New Mexico and two facilities at Sandia National Laboratories, the National Solar Thermal Test Facility (aka the Solar Tower) and the Z Machine, the world's largest X-ray generator.

This year the dinner speech was on the first evening by NAE member Alton (Al) D. Romig, executive vice president, deputy laboratories director for integrated technologies and systems, and interim chief operating officer of Sandia National Laboratories. Dr. Romig, a participant in the first US FOE symposium in 1995, was the first dinner speaker who was also an FOE alumnus. His talk on energy policy and the role of technology in national security covered a variety of topics, including engineering advances that have improved our energy security and the integration and interdependency of world economics and energy markets.

Julia Phillips completed her third year as chair of the US FOE organizing committee and symposia. The chair for next year is NAE member **Andrew M. Weiner**, Scifres Family Distinguished Professor of Electrical and Computer Engineering at Purdue University. Planning is already under way for the 2009 meeting, which will be held September 8–10 at the Beckman Center in Irvine, California.

Funding for the 2008 US FOE Symposium was provided by Sandia National Laboratories, The Grainger Foundation, Air Force Office of Scientific Research, DARPA, Department of Defense (DDR&E-Research), National Science Foundation, Microsoft Research, Sun Microsystems, IBM, Intel, Alcatel-Lucent/Bell Labs, Corning Inc., Cummins Inc., and Dr. John A. Armstrong.

Since 2005, US FOE symposia, and some bilateral symposia, have been held at research centers at GE, Ford, Microsoft, Alcatel-Lucent/Bell Labs, Hitachi Global Storage Technologies, and HP Labs. Participants at these symposia have been given a first-hand look at corporate and government research facilities, and these "guest hosts" have defrayed a substantial portion of the meeting costs.

For more information about the symposium series or to nominate an outstanding engineer to participate in future Frontiers meetings, contact Janet Hunziker at the NAE Program Office at (202) 334-1571 or by e-mail at *jhunziker@nae.edu*.

Workshop on Engineering, Social Justice, and Sustainable Community Development

On October 2 and 3, 2008, approximately 80 people attended a workshop sponsored by the NAE Center for Engineering, Ethics, and Society on engineering, social justice, and sustainable community development. The goal of the workshop was to explore (1) issues related to human welfare and social and environmental justice; (2) the interface between engineering ethics and practice; and (3) implications for engineering education and professional societies.

Five sessions of presentations were held during the two-day workshop:

- **Session I: Engineering and Special Vulnerabilities.** This session addressed the technical and social constraints, as well as opportunities, facing engineers, who often work in crisis areas, ranging from the aftermath of disasters to areas of social conflict. Speakers focused on how engineers can direct or influence projects to advance humanitarian goals, as well as social justice and sustainable community development.

- **Session II: Engineering, Ethics, and Society.** The focus of this session was on the technical, political, historical, environmental, economic, and cultural factors that influence the outcome of engineering projects. One of the questions raised was how humanities and social science disciplines can be brought to bear on engineering projects in difficult circumstances.
- **Session III: Implications for Engineering Education.** Presentations addressed how educators can increase students' awareness of the social and environmental challenges facing practicing engineers. They also explored the interface between these issues and structural, programmatic, and curricular changes in engineering education.
- **Early Career Engineers Panel:** A panel of early-career engineers shared their perspectives on the factors that influenced their career choices and how their careers have been (and are still) shaped by ethical challenges.
- **Roundtable Discussion:** During a roundtable discussion on the main theme of the workshop, many subjects were raised. The focus was on areas for research and sources of support for efforts to support engineers working in complex technical and cultural circumstances.

Much of the conversation during the workshop was focused on the intersections between engineering, humanitarianism, and social science. As **Henry Hatch**, an NAE member and moderator of the first session, commented, "Take the words we've used in this session—environmental, technical, social. If we as engineers do not do everything in full recognition of those items, we will fail. We're not doing engineering for engineering's sake; we're doing it for the benefit of humankind." He added that engineers must enlist the help of social and behavioral scientists to ensure that they and their colleagues are aware of the ramifications of their work.

Anu Ramaswami of the University of Colorado, Denver, suggested that engineers who work in foreign countries face many additional issues. "We can't ignore that we're working with people in these nongovernmental organizations on the ground who have a social and political agenda," she said.

Carl Mitcham, Colorado School of Mines, pointed out that, although all engineering societies emphasize public safety, health, and welfare in their codes of conduct, engineers don't study those issues. "Engineering as it is taught and practiced is highly dependent on externally rather than *internally* derived contexts for its formally articulated professional values." This remark stimulated a great deal of discussion and debate throughout the meeting.

Linda Abriola, NAE member and dean, School of Engineering at Tufts University, addressed the group during the third session on implications for engineering education. She noted that since her school had made the paradigm shift to teaching engineering as a professional practice that can serve humanitarian and social goals, the attrition rate had dropped to zero. She attributed the change largely to service-type learning opportunities and project-based, interdisciplinary units that have great appeal to a new generation of would-be engineers, particularly women.

The two-day event was hosted by **John Ahearne**, NAE member and chair of the Center for Engineering, Ethics, and Society (CEES) Advisory Group, and Rachelle Hollander, director, CEES. The workshop was co-sponsored by the Association for Practical and Professional Ethics and partially supported by the National Science Foundation and a grant to CEES from NAE member **Harry E. Bovay Jr.** The program agenda can be found via a link on the NAE home page (*www.nae.edu*).

Christine Mirzayan Science and Technology Policy Graduate Fellow Joins NAE Program Office

Amber Carrier

Amber Carrier, a Christine Mirzayan Science and Technology Policy Graduate Fellow, joined the NAE Program Office in September. During her 10 weeks in residence at NAE, she worked with Catherine Didion on Diversity in the Engineering Workforce and the *Engineer Your Life* and *EngineerGirl!* websites and with Greg Pearson and Proctor Reid helping to lay the foundation for a cross-disciplinary project on engineering and the life sciences, a joint project of NAE and the NRC Board on Life Sciences.

Amber, who is completing her Ph.D. in biology at the University of Louisville, is pursuing research on the influence of reproductive hormones and evolution on the dynamics of microflora in the lungs of women with cystic fibrosis. She received her B.S. in biophysics from the University of Southern Indiana in 2005.

Amber was recently elected president of the Graduate Student Council and serves on the Commission on the Status of Women at the University of Louisville. She hopes her participation in these activities will help ease the transition of her fellow students into graduate and professional schools and encourage women to pursue advanced degrees.

As a Mirzayan Fellow, she learned about NAE's efforts to encourage diversity in academia and increase the public understanding of science and engineering. Her experience at NAE may also be useful in her future career in academia or as a member of an administrative or policy advisory board. In her spare time, she enjoys running, cooking, traveling, working on her house, and spending time with her family.

NSF Introduces New Business R&D and Innovation Survey

A new National Science Foundation (NSF) Survey of Business R&D and Innovation will be mailed to some 40,000 firms in the United States in January 2009.

The new, expanded survey was developed over the past three years in response to a 2005 report, *Measuring R&D Expenditures in the U.S. Economy*, by the National Research Council Panel on R&D Statistics. The report noted that R&D decision making was critical to the future of the U.S. economy and to our national well-being and concluded that it was time to implement another major redesign of the Survey of Industrial R&D, which had been used for more than 50 years. Recommendations included:

- learning more about R&D record keeping in industry
- considering web-based data collection
- collecting reliable data on industry R&D by line of business
- building the capacity to collect innovation-related data for integration with the R&D survey
- creating a panel of R&D experts to provide advice on trends and issues

Industry representatives advised the panel that they would use the survey for benchmarking if the data were more timely and were disaggregated by line of business. NSF has undertaken a major effort to ensure that industry is aware of the importance of providing full and accurate responses.

For further information, contact Raymond M. Wolfe, Research and Development Statistics Program, Division of Science Resources Statistics, National Science Foundation, 4201 Wilson Boulevard, Suite 965, Arlington, VA 22230; *rwolfe@nsf.gov* or visit the NSF website (*www.nsf.gov*).

Washington State Creates New Science Academy

The Washington state legislature has authorized the establishment of the Washington State Academy of Sciences (WSAS). Modeled after the National Research Council (NRC) to provide independent scientific, technical, and engineering advice to state policy makers, WSAS will convene study committees to analyze scientific information relevant to important public-policy questions affecting the state. The published findings of these studies will be used to inform public discussions and decision-making.

"The Washington State Academy of Sciences will not make policy recommendations," says Gordon Orians, WSAS president. "Like the NRC, it will be scrupulous to maintain non-partisan credibility. Study committee members will serve without compensation, and we will issue expert reports. But policy decisions will remain the responsibility of elected officials."

The more than 80 members of the initial WSAS class, all elected members of the National Academy of Sciences, National Academy of Engineering, or Institute of Medicine, have been drawn from in-state businesses, industry, and academic institutions. The first class was inducted in November at the first WSAS annual meeting.

For more information, visit the WSAS website at *www.washacad.org*. Media contact: Rich Murphy, 206-769-0831, *rich@rjmurphy.net*.

Calendar of Meetings and Events

December 15–19	Committee on U.S.–China Cooperation on Electricity from Renewables Meeting Beijing, China
2009	
January 2	NAE Awards Call for Nominations
January 2–30	Election of 2009 Class of NAE Members and Foreign Associates
January 15	Deadline for submission of petition candidates for NAE officers and councillors NRC Governing Board Executive Committee Meeting
January 28	Peer Committee Chair/Search Executive Workshop
February 3	Finance and Budget Committee Conference Call
February 5–6	Membership Policy Committee Meeting Irvine, California
February 6	Announcement of NAE Class of 2009
February 9–10	NRC Governing Board Committee Meeting Irvine, California
February 11–12	NAE Council Meeting Irvine, California
February 12	NAE National Meeting University of California, Los Angeles
February 15–21	National Engineers Week
February 17	NAE Awards Forum and Awards Dinner
February 17–March 3	Call for Nominations for Section Elections
February 18	NRC Governing Board Executive Committee Meeting
March 1–31	Election of NAE Officers and Councillors
March 5	NAE Regional Meeting Massachusetts Institute of Technology, Cambridge
March 11	NRC Governing Board Executive Committee Meeting
March 17	NAE Regional Meeting University of Washington, Seattle
March 30–April 10	Election of Section Leaders

All meetings are held in the Academies Building, Washington, D.C., unless otherwise noted. For information about regional meetings, please contact Sonja Atkinson at *satkinso@nae.edu* or (202) 334-3677.

In Memoriam

NATHANIEL ARBITER, 97, Professor Emeritus of Mineral Engineering, Columbia University, died on October 5, 2008. Mr. Arbiter was elected to NAE in 1977 "for contributions to research and education in processing low-grade ores and the development of new hydrometallurgical processes."

WILSON V. BINGER, 91, retired partner and chairman, Tippetts-Abbett-McCarthy-Stratton, died on April 21, 2008. Mr. Binger was elected to NAE in 1975 "for leadership in the development of large dams, water resources, soil mechanics, and foundation engineering."

LEROY L. CHANG, 72, University Professor Emeritus, Hong Kong University of Science and Technology, died August 10, 2008. Dr. Chang was elected to NAE in 1988 "for pioneering achievements in superlattices and heterostructures."

PATRICK F. FLYNN, 70, retired vice president research, Cummins Engine Company Inc., died August 19, 2008. Dr. Flynn was elected to NAE in 1995 "for advances in diesel engine design utilizing science-based methodology."

JOHN E. JACOBS, 88, Walter P. Murphy Distinguished Professor, Emeritus, Northwestern University, died on July 26, 2008. Dr. Jacobs was elected to NAE in 1969 "for advances in the development and application of ultrasound image systems and specialized computers relating to biomedical use."

Publications of Interest

The following reports have been published recently by the National Academy of Engineering or the National Research Council. Unless otherwise noted, all publications are for sale (prepaid) from the National Academies Press (NAP), 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055. For more information or to place an order, contact NAP online at <*http://www.nap.edu*> or by phone at (888) 624-8373. *(Note: Prices quoted are subject to change without notice. Online orders receive a 20 percent discount. Please add $4.50 for shipping and handling for the first book and $0.95 for each additional book. Add applicable sales tax or GST if you live in CA, DC, FL, MD, MO, TX, or Canada.)*

NASA Aeronautics Research: An Assessment. In 2006, the National Research Council (NRC) published *A Decadal Survey of Civil Aeronautics: Foundation for the Future*, which set out six strategic objectives for the next decade of civil aeronautics research and technology. In the National Aeronautics and Space Administration (NASA) Act of 2005, Congress mandated that the NRC conduct a review of NASA's efforts to pursue those objectives. Among other things, this report presents an assessment of how well NASA's research portfolio is addressing the recommendations and high-priority R&T challenges identified in the *Decadal Survey*; how well NASA's aeronautics research portfolio is addressing the aeronautics research requirements; and whether the nation will have the skilled workforce and research facilities to meet the first two recommendations.

NAE members **Meyer J. Benzakein**, chair, Aerospace Engineering Department, Ohio State University; **David E. Crow**, retired senior vice president of engineering, Pratt and Whitney, and professor of mechanical engineering, University of Connecticut; and **Eli Reshotko**, Kent H. Smith Professor Emeritus of Engineering, Case Western Reserve University, were members of the study committee. Paper, $31.75.

Test and Evaluation of Biological Standoff Detection Systems: Abbreviated Version. A biological warfare agent (BWA) is a microorganism or toxin derived from a living organism that causes disease in humans, plants, or animals or the deterioration of materials. The effectiveness of a BWA is greatly reduced if its presence is detected in time for the target population to take defensive measures. The ideal detection system will have a quick response time and be able to detect a threat plume at a distance. However, testing these systems is difficult because open-air field tests with BWAs are not permitted under international conventions and because the wide variety of environments in which detectors might be used may affect their performance. This report explores issues related to determining the effectiveness of biological standoff detection systems without open-field testing.

NAE member **Frances S. Ligler**, U.S. Navy Senior Scientist, Center for Bio/Molecular Science and Engineering, Naval Research Laboratory, was a member of the study committee. Paper, $15.00.

Evaluation of the Multifunction Phased Array Radar Planning Process. The multifunction phased-array radar (MPAR) is a potentially cost-effective way to meet the surveillance needs and mission requirements of agencies that currently rely on decades-old radar networks. These agencies include the National Oceanic and Atmospheric Administration's National Weather Service, the Federal Aviation Administration, the U.S. Department of Defense, and the U.S. Department of Homeland Security. This report analyzes the current systems, the capabilities of MPAR, technical challenges, cost issues, and possible alternatives.

NAE member **Robert J. Serafin**, Director Emeritus, National Center for Atmospheric Research was a member of the study committee. Paper, $21.00.

Desalination: A National Perspective. Recent advances in technology have made the desalination of seawater and groundwater a realistic option for increasing water supplies in some parts of the United States, and desalination is likely to be one component in the nation's future water-management portfolio. However, the permitting of desalination plants has been delayed for a host of financial, social, and environmental reasons, especially uncertainties about environmental impacts. The National Research Council, with the support of the

Bureau of Reclamation and the Environmental Protection Agency, formed a committee to assess state-of-the-art desalination technologies, identify challenges to their implementation, and recommend next steps and areas for further research.

NAE member **Menachem Elimelech**, Roberto C. Goizueta Professor, Environmental Engineering Program, Yale University, was a member of the study committee. Hardcover, $45.00.

Review of the 21st Century Truck Partnership. The 21st Century Truck Partnership (21CTP), a cooperative research and development partnership formed by four federal agencies with 15 industrial partners, was launched in 2000 with high hopes that it would dramatically advance the technologies used in trucks and buses and lead to cleaner, safer, more efficient vehicles. This review of the program evaluates progress and recommends improvements. Key recommendations include revisions and rebalancing of the research portfolio, a clear restatement of goals, and regular reviews based on available funds.

NAE members on the study committee were **Paul N. Blumberg**, consultant, Southfield, Michigan; **Andrew Brown Jr.**, executive director and chief technologist, Innovation and Technology Office, Delphi Corporation; **Joseph M. Colucci**, president, Automotive Fuels Consulting Inc., and retired executive director, Materials Research, General Motors Research and Development; **Patrick F. Flynn** (vice chair), retired vice president of research, Cummins Engine Company Inc.; and **Dale F. Stein**, President Emeritus, Michigan Technological University. Paper, $32.75.

National Academies Summit on America's Energy Future: Summary of a Meeting. In response to a growing sense of national urgency about the importance of energy to long-term U.S. economic vitality, national security, and climate change, the National Academies sponsored a meeting to discuss how the need for energy can be met without causing irreparable damage to the environment or compromising U.S. economic or national security. The summary of this two-day summit, which was part of a larger project, America's Energy Future: Technology Opportunities, Risks, and Trade-offs, is the first in a series of authoritative estimates and analyses of energy supplies and demands; new and existing technologies and their associated impacts; and projected costs. This workshop summary will be useful to federal and state policy makers, industry leaders, investors, and others who are willing to take action to solve the energy problem.

NAE members on the organizing committee were **Richard A. Meserve**, president, Carnegie Institution of Washington; **Lawrence T. Papay**, CEO and principal, PQR LLC, and retired sector vice president for integrated solutions, Science Applications International Corporation; and **Maxine L. Savitz**, retired general manager, Technology/Partnerships, Honeywell Inc. Paper, $40.00.

Transitions to Alternative Transportation Technologies: A Focus on Hydrogen. Hydrogen fuel cell vehicles (HFCVs) could alleviate the nation's dependence on oil and reduce emissions of carbon dioxide, the major greenhouse gas. Industry- and government-sponsored research programs have made substantial technical progress in the past several years, and several companies are introducing pre-commercial vehicles and hydrogen fueling stations in limited markets. However, further technological advances and commercial viability will require coordinated efforts by vehicle manufacturers and hydrogen suppliers to bring down costs, commercialize new automotive manufacturing technologies, and ensure adequate supplies of hydrogen. Reaching these goals will also require considerable funding from the federal and private sector. The study committee of this report provides estimates of the funding requirements and of the impacts on oil consumption and carbon dioxide emissions as the percentage of HFCVs in the light-duty vehicle fleet increases.

NAE members on the study committee were **Michael P. Ramage**, retired executive vice president, ExxonMobil Research and Engineering Company; **Rakesh Agrawal**, Winthrop E. Stone Distinguished Professor, School of Chemical Engineering, Purdue University; **James R. Katzer**, manager, strategic planning and performance analysis, ExxonMobil Research and Engineering Company (retired), Visiting Scholar, MIT, and independent consultant; **Lawrence T. Papay**, retired sector vice president for integrated solutions, Science Applications International Corporation, and CEO and principal, PQR LLC; **William F. Powers**, retired vice president, research, Ford Motor Company; and **Arnold F. Stancell**, retired vice president, Mobil Oil and Turner Professor of Chemical Engineering, Emeritus, Georgia Institute of Technology. Paper, $39.00.

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