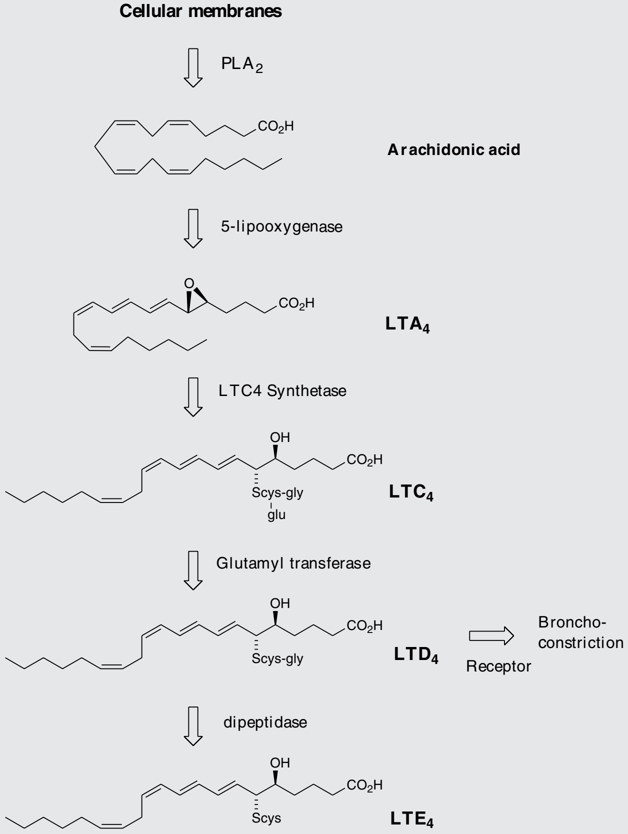
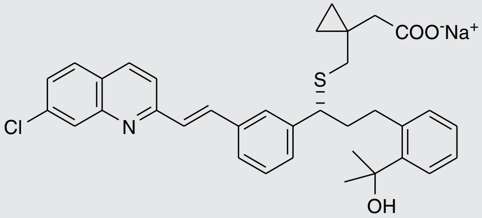
rial, the belief was that SRS-A played a key role in human asthma. In 1979, Bengt Samuelsson proposed a structure for SRS-A that was derived from arachidonic acid and the amino acid cysteine. He called it leukotriene C.



Formation of leukotrienes via the arachidonic acid cascade.

Soon after, the complete structure of SRS-A was finally determined by total synthesis. SRS-A turned out to be a mixture of 3 substances now known as leukotriene C_4 (LTC_4), leukotriene D_4 (LTD_4) and leukotriene E_4 (LTE_4) in which LTD_4 was predominant. The jump from a biological observation in 1938 to a molecular structure of LTD_4 opened the door to a novel and selective treatment for asthma. The theory was that if one could find a molecule that specifically blocked the action of LTD_4 on the lung, it would be possible to prevent the tightening of the airways found in asthma. Eighteen years after Samuelsson's proposal, after the synthesis and testing of thousands of man-made compounds, Singulair (montelukast) reached the world's pharmacies. Leukotriene modifiers are recognized to be the first important advance in asthma therapy in 25 years.



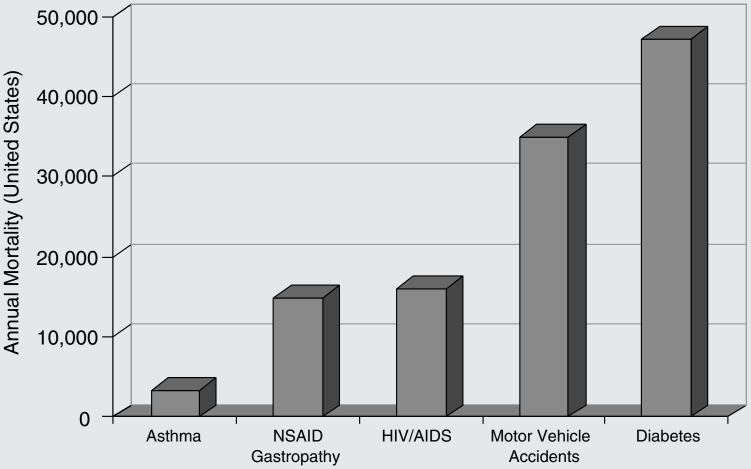
Singulair (montelukast)

This is just one example of how the chemical understanding of one of life's processes at the molecular level resulted in the solution to a 60-year-old problem. The selective LTD_4 receptor antagonist was specifically designed to take the place of LTD_4 on smooth muscle. Such approaches—where the drug molecule does only what it's intended to do, without indiscriminately binding to other receptors in the body—are aimed at selective therapies that are free of side effects. It is that selectivity, designing molecules with precision based on structural information, that characterizes the state of the art of chemistry as we enter the next millennium.

Underlying the discovery of a selective asthma therapy are numerous advances in analytical and instrumental techniques as well as synthetic methods that allow the construction of complex molecules. Practical catalytic, stereospecific, and organometallic methods that permit a high level of stereochemical control have enabled production at the multiton level of molecules previously inaccessible even at the gram scale.

Selectivity and Anti-Inflammatory Drugs

The theme of selectivity—based on detailed understanding of molecular structure and function—underlies most recent therapeutic advances. Sometimes a biochemical "revisiting" of an old discovery enables dramatic improvements in the quality of life. Among the most widely used classes of medicines are the nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen. Used for years, these pain killers and arthritis treatments work by blocking the effects of arachidonic acid on an enzyme called cyclooxygenase (COX). A major drawback to inhibiting COX is that by doing so you inadvertently block its role in protecting the gastrointestinal tract. The resulting ulcerative gastropathy is responsible for a large number of hospitalizations and deaths. Recently it was discovered that cyclooxygenase is not a single enzyme but rather a family containing at least two nearly identical members: COX-1 and COX-2. While COX-1 is responsible for the good gastroprotective effects (and shouldn't be blocked) COX-2 is the enzyme involved with pain and inflammation (the real target). The COX-2 hypothesis stated that if one could invent a specific COX-2 inhibitor, it would be an effective anti-inflammatory and analgesic medication with substantially reduced gastrointestinal (GI) toxicity compared with the classical NSAID's aspirin and ibuprofen.



Significant mortality is associated with NSAID gastropathy. G. Singh and G. Triadafilopoulos, Epidemiology of NSAID induced gastrointestinal complications, *Journal of Rheumatology,* 1999, 26, 56, 18-24, by permission of Oxford University Press.

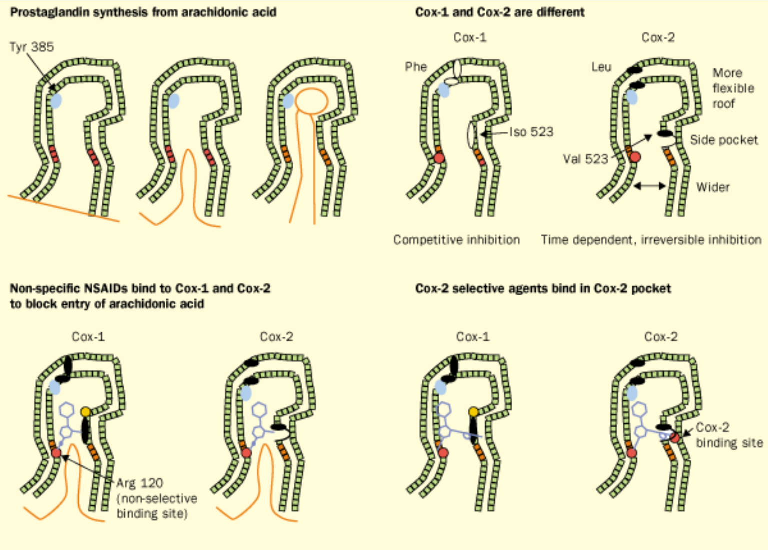
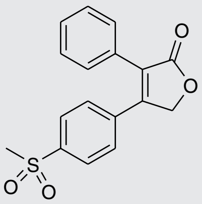
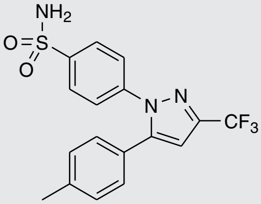


Figure reprinted with permission from Elsevier Science (*The Lancet,* 1999, 353, 307-314).

Again, detailed structural information at a molecular level was the key. Once these "pictures" were available slight chemical differences between the COX-1 and COX-2 isoenzymes could be seen: COX-2 had a side pocket while COX-1 didn't. This meant that a molecule that could dock into the COX-2 side pocket (binding site) but not into COX-1 would specifically block COX-2 without touching COX-1. In 1999 this hope was realized with the availability of COX-2 selective anti-inflammatories such as Rofecoxib and Celecoxib that can be as much as 50-fold selective for the target.



Rofecoxib



Celecoxib

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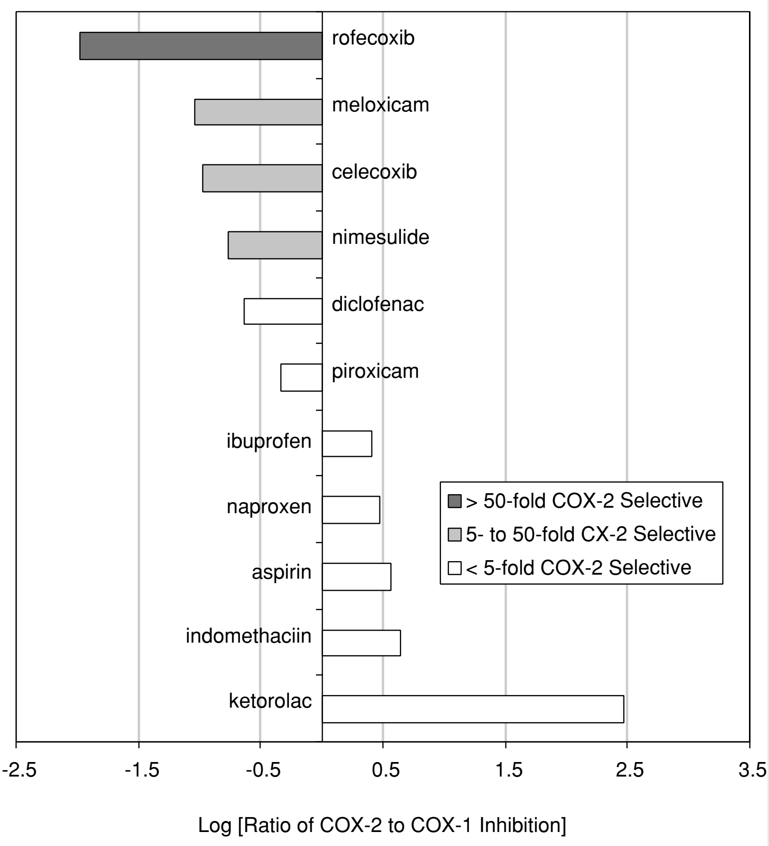
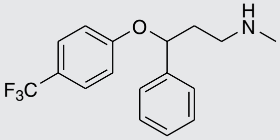


COX-2 selectivity of marketed compounds. Adapted with permission from T.D. Warner et al. *Proceedings of the National Academy of Sciences,* 96, 13, 7563 (1999). Copyright 1999 National Academy of Sciences, U.S.A.

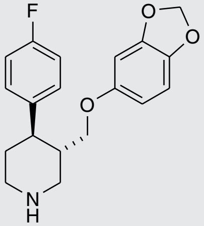
Specificity and Therapy for the Human Brain

Nowhere is the need for specificity so great as in trying to design therapies for the human brain. Here there are numerous receptors that affect our moods, sleep, alertness, memory, and coordination. Even though the importance of serotonin (5-hydroxytryptamine, 5-HT) had been known to neuroscientists for over 100 years, it wasn't until the discovery of drugs like Prozac (fluoxetine hydrochloride) and Paxil (paroxetine hydrochloride) that selective antidepressive drugs became available. The antidepressive effect results from inhibition of serotonin uptake by neurons in the brain, thus ensuring that circulating levels are adequate. The selectivity results from selective binding compared with older drugs (tricyclics) that were less discriminating in their binding to other brain receptors. The net result is fewer side effects. As the molecular basis of memory and behavior become clearer, we will see a leap in the effectiveness and specificity of drugs for the central nervous system.

The arrival of the year 2000 coincided with a milestone in modern science; many believe that deciphering the human genome will provide a road map for therapeutic intervention. We are already seeing medicines that act not directly on a target tissue but on receptors that regulate the transcription of genes. The ability to "tune" the molecular signaling that continually occurs in our bodies will eventually allow for more exquisite control of the cellular processes of life. If today's chemistry lets us turn things on or off by blocking or unblocking receptors and enzymes, tomorrow's molecules will be able to balance complex metabolic processes like growth and aging by fine tuning the regulation of genes and their products.



Prozac



Paxil

CHALLENGES AND OPPORTUNITIES FOR THE FUTURE

The opportunities for discovery and invention at the interface of chemistry, engineering, and biology are enormous, and many examples have been described in the preceding sections. This interface represents a true research frontier—one that is critical to our ability to develop new chemistry for the prevention, diagnosis, and treatment of human disease. The continuing challenge is to discover the chemical identity of all the molecules that make up living organisms and the way they bind to each other and organize into biological structure—membranes and cell structures such as nuclei, ribosomes, etc.

Ribosomes

The nucleotide sequences of the genes encoded in DNA are transcribed into the same sequences of messenger RNA, again carrying the genetic code, and these RNAs direct the synthesis of proteins with defined sequences of amino acids. Protein synthesis occurs in a cellular machine called a ribosome, which takes in messenger RNA and some amino acids linked to transfer RNA and uses base pairing to direct their assembly into a protein. The base pairing occurs because each kind of amino acid is attached to a different transfer RNA, one that carries a code for that particular amino acid. Thus messenger RNA plays the role of template for protein synthesis, and transfer RNA guides the amino acids to the correct spot. Assembling the protein still requires a catalyst to link the amino acids together.

Essentially all biological catalysts in the modern world are themselves proteins, enzymes. However, in 1989 Sidney Altman and Thomas Cech received the Nobel prize in chemistry for showing that RNA itself could act as a catalyst for some biological reactions. This led to the idea that in an earlier time, as life was evolving, RNA may have been both the information molecule (a role usually played by the more stable DNA now) and the catalyst (the role that protein enzymes now play.) Since this idea indicates that in early times the synthesis of proteins was catalyzed by RNA, not by protein enzymes, the intriguing question is whether this is still true today.

Ribosomes are complex structures consisting of one small RNA molecule and two large ones together with some 50 to 60 different proteins. Their general shape had been determined by electron microscopy some years ago, but a major breakthrough occurred in 2000. X-ray diffraction was used to determine the detailed molecular structure of a ribosomal particle that consists of almost all the molecules in a ribosome and exhibits the full catalytic and regulatory functions of a ribosome.[3] The trick was to get this large particle, about 100 times as large as a simple protein enzyme, to crystallize so the x-ray technique could be applied. The results are striking, but for the real details it is important to consult the original articles). Such a detailed structure can help medicinal chemists to develop useful drugs that bind to the ribosome, but the more important result has to do with the catalytic center.

The catalytic center of the ribosome, where the protein is actually made, is now seen to consist of RNA, not of a protein enzyme! The many

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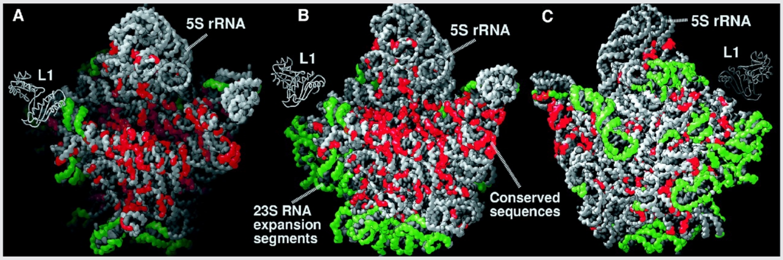
[3] N. Ban, P. Nissen, J. Hansen, P. B. Moore, and T. A. Steitz, *Science*, 289, 905, 2000; P. Nissen, J. Hansen, N. Ban, P. B. Moore, and T. A. Steitz, *Science*, 289, 920, 2000.



The large ribosomal subunit at 2.4 Å resolution. (A) The particle rotated with respect to the crown view so that its active site cleft can be seen. (B) The crown view. (C) The back view of the particle, i.e., the crown view rotated 180° about its vertical axis. Reprinted with permission from Ban et al., *Science* 289, 905 (2000). Copyright 2000 American Association for the Advancement of Science.

proteins present help organize the structure, but they do not play a catalytic role. This is in line with the idea that the original process in early life forms used RNA alone. As proteins were created in processes guided and catalyzed by RNA, some proteins were incorporated into the RNA catalytic unit during evolution and improved the ribosome's function. A follow-up paper[4] indicates a way in which the RNA could carry out the catalyzed synthesis of proteins. A particular adenosine unit in the catalytic RNA has the correct properties to be able to assist the formation of peptide bonds, which are the links in proteins.

All this is basic chemical research that has wide importance, determining the molecular structure of a component of living cells. Simply, it tells us the details of how proteins are now made, but more generally it strengthens the picture of how life may have started in a world where RNA was both information molecule and catalyst. It is a major advance in scientific understanding.

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[4] G. W. Muth, L. Ortoleva-Donnelly, and S. A. Strobel, *Science,* 289, 947, 2000.

One driver for new discovery will be the completion of the human genome project. As a result of this project, the locations and sequences associated with the tens of thousands of genes of the human genome will have been determined. In the post-genomic era, then, we will know the DNA sequences and genes of a human being, but that is only the start. What are the functions associated with these sequences? We will need to isolate the proteins that are the gene products, determine their structures, characterize their reactions and their partners in reactivity. To perturb the actions of these proteins, we will need to develop diverse arrays of small-molecule inhibitors and activators. While the human genome project gives us access to the library of the cell, we will need to learn much to exploit the information that we will have.

For example, although we designate gene sequences by a one-dimensional string of letters, the protein gene products they encode have three-dimensional architectures, and when properly folded they carry out biological function. A critical challenge in this post-genomic era will be to make the connections between protein sequence and architecture, and between protein architecture and function. We need to learn to predict how a protein folds and the relationships between a folded structure of a protein and its function. Indeed, in reaching that level of chemical understanding, we can then seek to design new functions for proteins. Both combinatorial and rational design strategies may be applied in the construction of novel biologically based catalysts.

Genomics and gene arrays will become increasingly important in strategies to prevent disease. Today, for example, we make use of simple assays such as the PSA (prostate screening antigen) test in the early detection of prostate cancer. Transcriptional profiling using gene chip technology will likely facilitate analogous tests for all cancers by simultaneously measuring all relevant mRNA levels. We will be able to determine what mRNAs or small natural products rise in concentration in association with cancers, and hence use detection methods for these molecules in cancer prevention. A challenge resulting from the enormous amount of information associated with such transcriptional profiling will be the determination of causal relationships, and of the partners and pathways associated with cellular transformation. Indeed, a major intellectual challenge to the chemical sciences is developing a systematic framework and computational tools to relate microarray data, as well as data on protein levels, to a description of the dynamic regulatory networks controlling cellular functions.

Proteomics is a combination of experimental and analytical tools to determine the total protein content of a cell or tissue. While genomics identifies the potential proteins in an organism, proteomics provides information on which proteins are actually present in a tissue under specific environmental conditions and accounts for the physiologic history of the tissue. Proteomic information is difficult to obtain due to the large amount of chemical heterogeneity displayed by proteins and our inability to amplify the amount of proteins in a sample. In contrast, polymers of nucleic acids are rather more chemically homogeneous and can be amplified using the chemical technique of polymerase chain reaction (PCR). Currently much proteomics work is accomplished using a technique called two-dimensional gel electrophoresis. This technique is slow, requires highly skilled technicians, and many proteins in a cell are too rare or too hydrophobic (water hating) to be resolved by this technique. Nonetheless, 2-D gel electrophoresis has been used successfully to monitor prion diseases (e.g., mad cow disease) and shows promise in the diagnosis of neurodegenerative disorders such as Alzheimer's disease. A major opportunity in the chemical sciences is the development of microarray technologies that can provide more rapid and complete proteomic information. The techniques of biotechnology applied on the nanoscale may result in miniature devices that can be used in a massively parallel fashion to do rapid separation and analysis of DNA, RNAs, or protein solutions.

Progress in genomics and proteomics offers opportunities also in the diagnosis and treatment of disease. We will soon be able to develop the chemistry necessary to routinely detect genetic variations in individuals, and to do so for a full range of genes. In fact, some pharmaceuticals that are largely effective and might represent medical advances currently fail during clinical trials as a result of an adverse reaction within a genetic subpopulation. With genetic screening, and a better understanding of the underlying biochemistry, we will be able to tailor-make therapies for patients based on their genetic dispositions.

More generally, as described earlier, medicinal chemistry has greatly contributed to the fight against disease, but there are still major challenges ahead. For example, we don't yet have generally effective drugs to treat viral diseases, such as influenza or Ebola (although some trials of a new drug for the treatment of influenza indicate that it decreases the length of the infection). This is critical. Imagine the problem if the HIV virus that causes AIDS, or the Ebola virus that kills quickly, were able to be transmitted by the bite of a mosquito, as some other less lethal viruses can be. Until we have effective medicines to cure such viral infections, humanity is at great risk.

Another problem is bacterial resistance to antibiotics. As doctors have treated people with the available antibiotics that medicinal chemistry devised in the past, they have selected for strains of bacteria that are resistant to those antibiotics. There is now a race against time by medicinal chemists to devise new antibiotics that will work against the resistant organisms. If we do not succeed, many bacterial infections that we thought had been cured will emerge again as major threats to our health and life.

We still need much better medicines to cure cancer, heart disease, stroke, and Alzheimer's disease. We need better drugs to deal with obesity, diabetes, arthritis, and schizophrenia. The treatments of diabetes, arthritis, and mental defects such as schizophrenia or manic depression are not yet cures, just ways to keep the symptoms under control. Cures are needed. Insights from genetics may help guide us toward elegant and rational cures, but we will also make use of screens to identify natural products and libraries of randomly generated synthetic compounds (combinatorial chemistry). A semi-empirical approach may be the best hope over the next two decades to yield drugs to alleviate these diseases.

Many of the natural products may come from "unusual" organisms and may be difficult to synthesize. In those cases, it will be necessary to develop appropriate bioprocesses to produce, recover, and purify these compounds. Both chemists and biochemical engineers will be involved in creating such processes.

But medicinal chemistry will also change in basic ways. Indeed, we are entering a completely new era of **molecular medicine**. We will develop technologies to screen the effects of small molecules on large arrays of gene products, from enzymes to receptors, and doing so will require advances in fields ranging from biochemistry to material design. We will develop the tools to create genomic maps of protein-protein contacts and chemical tools to decipher the hierarchy of those contacts. Our ability to digest and exploit the enormous information we obtain will also provide challenges in computation, in structure prediction, and in our quantitative understanding of molecular recognition. As a result, fundamentally new strategies will be developed to attack disease on a molecular level. For example, it is already clear that strategies to fight cancer are shifting, from those centered on maximizing toxicity in cancerous cells to those where we activate or harness different signaling pathways of the cell, depending on whether the cell has undergone transformation from normal to cancerous.

Among the fundamental new strategies, and certainly an important step to be taken by chemists in this new era of molecular medicine, will be developing a general understanding of how small molecules can be utilized to regulate gene expression and signal transduction. The goal is the design of small molecules not simply as general poisons to the cell or to some cellular function, but instead as reagents that turn off or turn on critical pathways. This challenge depends upon advances also in our understanding of **molecular recognition**. When a protein or small molecule binds to a particular receptor, an ensemble of weak noncovalent contacts are specifically arrayed in three-dimensional space to facilitate this recognition of one molecule by another. Chemists are now working on general strategies to achieve highly specific molecular recognition, and doing so is a first step in the rational design of new drugs as regulators of cellular processes.

Associated with this question is how to target these small molecules to sites of specific action in the cell or tissue. We have, for example, made substantial progress in delineating how some small molecules and metal ions are trafficked through the cell. Can we apply this knowledge to invent strategies for targeting small molecules to specific organelles within the cell? Our current understanding of what controls cell permeability and bioavailability is primitive, often not appreciably more advanced than "oil versus water." As we develop a molecular perspective concerning the trafficking of molecules into and through the cell—as well as the chemistry underlying what distinguishes the surfaces of different cells—we will establish a more rational approach to targeting molecules more powerfully, and even with tissue specificity.

Because cells and the body respond not only to genetic information but also to environmental cues, any analysis must take into account the time and environment-dependent nature of the biological system. Because of their training in analysis of integrated systems, biochemical engineers should be able to contribute integrated, quantitative models of these biological systems to guide the selection of targets for intervention and the synthesis of a precise delivery system. In some cases these devices will need to be "smart" devices to respond to a current physiological state. An example of such a device, already in research and development, is one to monitor blood glucose levels and to release insulin in response to changes in blood glucose level. This device would effectively mimic the responses of the natural pancreas. Other delivery systems may mimic viruses for DNA delivery to specific target cells as a more controllable method for gene therapy. Indeed, the controlled delivery of macromolecular therapeutics with temporal and spatial control of therapeutic distribution is an important goal for chemists and chemical engineers.

Controlled Delivery of Therapeutics

Many pharmaceuticals are designed to effect change in a single organ or tissue. Traditional methods of drug delivery using pills or injections require the pharmaceutical to enter the blood stream and to be dispersed throughout the body (systemic delivery). Often undesirable side effects occur in nontarget organs before a therapeutically useful level of the agent is achieved at the target organ or tissue. Alternative methods of drug delivery are needed to deliver the drug to the right tissue, at the right time, and at the right amount.

As an example, consider treatment of a brain tumor. The brain protects itself from the entry of potentially toxic substances through a blood-brain barrier, which is a highly organized cellular barrier to the transport of such compounds from the blood into the brain. To administer a chemotherapeutic agent to the brain through injection into the blood stream may be impractical since a very high concentration of the drug may be necessary for the drug to cross the blood-brain barrier, and the side effects of the drug on other organs in the body may be toxic. Robert Langer developed a solution to this problem and related ones through the construction of polymeric devices to release drugs at a predetermined rate for extended periods. In this particular disease, the brain tumor is removed and polymeric disks filled with a chemotherapeutic drug are inserted. The polymers have been carefully synthesized to be biocompatible and to break down at a known rate in bodily fluids. As the polymer matrix is dissolved, the drug is released slowly at high local concentrations for many weeks, killing residual cancer cells. Since the polymer disks are in the brain, the drug does not have to diffuse across the blood-brain barrier. Thus, the target, the brain, receives a high dose of drug in the area near the tumor, and the rest of the body experiences only low levels of the drug. This therapy is currently in use and can significantly extend the symptom-free lives of patients.

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Langer received the Draper Prize from the National Academy of Engineering in 2002 in recognition of his work on development of modern biomaterials. The polymer used for controlled release of chemotherapeutic agents in the brain is only one example. Other examples include the use of such biomaterials for controlled release of large molecules (proteins or DNA for gene therapy), as scaffolds for tissue engineering where they release growth-promoting signals, and porous aerosol particles for inhalation drug delivery. The controlled-release drug delivery industry is estimated to have revenues of $20 billion a year with excellent prospects for continued growth. This industry is based on combining a knowledge of polymer synthesis, polymer interaction with biological molecules, the kinetics of the reaction of specific chemical bonds in the polymer with water or biological fluids, and the rate of mass transfer of molecules in a polymer matrix and in tissue.

We will also look to the chemical details of biology for lessons in how to carry out complex and important reactions under mild conditions. Today, the chemical industry produces ammonia from nitrogen through a high-temperature, high-pressure reaction that consumes lots of energy, yet microorganisms are capable of carrying out the same reaction at normal pressures and temperatures within the environment of the cell, using a metalloprotein catalyst called nitrogenase. Structural insights into this and other remarkable metalloprotein catalysts have recently become available. But can we now harness that understanding to develop new methods and new small molecular catalysts that incorporate the key attributes of the natural enzymes? Many of these enzymes, nitrogenase in particular, are capable of activating small, abundant, basically inert molecules through multielectron reactions. A tremendous challenge to the chemist lies in the design and application of catalysts, whether small molecules or materials, that can carry out such multielectron transfers to activate small molecules such as nitrogen, oxygen, and methane. Imitating some aspects of life, **biomimetic** chemistry is not the only way to invent new things, but it is one of the ways.

We will look to chemical biology for guidance not only in designing new smaller catalysts but also in devising methods to assemble large molecular machines. Replication, transcription, and translation, as well as other critical cellular functions, appear to be carried out through the function of multiprotein/nucleic acid particles. Advances in x-ray crystallography coupled with other imaging methods such as NMR and electron microscopy are now providing our first snapshots of these macromolecular machines, such as the ribosome in which proteins are synthesized in the cell. A spectacular recent advance is the determination of the three-dimensional chemical structure of the multimolecular photosynthetic reaction center, for which Johann Deisenhofer, Robert Huber, and Hartmut Michel received the Nobel prize in 1988. New advances in imaging will be needed to delineate these and still larger macromolecular assemblies at atomic resolution. These structural pictures provide a critical foundation for understanding how they function. But how do these machines assemble? Are they remarkable examples of spontaneous supramolecular assembly or are they guided in some way in coming together? How do the parts of these assemblies function in concert? Are macromolecular assemblies of such complexity required to carry out these functions? Indeed, can we next begin to design novel macromolecular machines to carry out new, still more complex functions? The construction and assembly of such machines would represent the first step in compartmentalizing chemical reactions. As such, it would represent the very first steps in a tremendous challenge to the chemist and chemical engineer, the design of a synthetic cell.

Sequencing the Human Genome

The year 2000 marked the completion of the Human Genome Project's primary goal. Through intensive efforts of both private and public agencies, the sequence for the three billion base pairs that encodes the instructions for being human has now been determined.[5] As a result of the Human Genome Project, we have determined the complete chemical structure, nucleotide by nucleotide, of the DNA within each of these chromosomes, the chemical structures that encode our lives. It is an extraordinary accomplishment in chemistry.

Completing this sequencing of the human genome could only be accomplished by building upon discoveries in chemistry made over the past 30 years. It was about 20 years ago that W. Gilbert and F. Sanger showed that small segments of DNA could be sequenced directly using chemical methods. About 10 years ago, instrumentation for automated sequencing was engineered. And building upon all the advances in biotechnology of the last decades, from oligonucleotide synthesis to the polymerase chain reaction and shot-gun sequencing, biochemists in the last 2 years have been able to increase the pace of analysis, so that full genomic maps can be deciphered in months.

In this post-genomic era, what can we expect? Mapping the human genome brings not only a high-resolution picture of the DNA within our

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[5] J. D. McPherson, et al., *Nature,* 409, 934, 2001; J. C. Venter, et al., *Science,* 291, 1304, 2001.

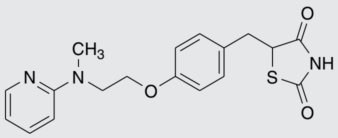
continues

cells but also the promise of molecular-based diagnosis and treatment of disease. Therapeutics could be tailor-made to take into account our individual genetic propensities. The cost of such pharmaceuticals will surely decline as clinical trials take such genetic information into account. And preventive medicine will certainly flourish as we begin to catalogue and diagnose our individual genetic predispositions to disease. But none of this is likely to happen tomorrow or even next year. There are many more conceptual advances in the chemistry of life that we need to achieve. At the start of the 21st century, we may know the sequence of bases of the human genome, but we can't yet read this sequence to know what reactions, what chemical functions, actually make us human.

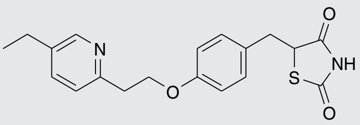
Post-Genomic Therapies

We have already had a glimpse into the future with the recent approval of a new approach for the treatment of adult onset, noninsulin dependent diabetes (NIDD). In this disease, also known as Type 2 diabetes, the body becomes increasingly resistant to insulin and loses its ability to control sugar levels.

The glitazone family of drugs acts to increase insulin sensitivity and thus increase glycemic control. They do this by acting upstream of a *gene*! As selective activators (agonists) of a nuclear receptor called PPAR-gamma (found in key tissues like fat and liver) they regulate transcription of the insulin responsive genes involved in the control of glucose production, transport, and utilization. Using the cell's signaling machinery, the drugs help the body compensate by getting the cells back to where they should be: sensitive to insulin.



Rosiglitazone



Pioglitazone

The explosive growth in our understanding of the chemical basis of life and its processes couldn't come at a better time. The demographic shift of an aging generation of baby boomers will sorely challenge the nation's resources (both financial and human capital). The need for more effective and cost-efficient therapies will become paramount. As our understanding of the chemistry of the brain grows, intervention will be based on new insights at the molecular level. Selective therapies for problems of memory and cognition, vision and hearing, pain, addiction, and sleep disorders will be designed. The subtle control needed to balance metabolic processes—like weight gain or loss and even aging—is already on the horizon. At the same time the revolution in microprocessors, telecommunications, and materials will enable the production of human "spare parts": joints and valves, eyes and ears linked to the brain. Even implantable endocrine systems—miniature chemical factories that combine real-time analysis with the synthesis or release of therapeutic agents—are becoming a reality.

WHY ALL THIS IS IMPORTANT

What are the details of all the chemical transformations that occur in a living cell? How are these details affected by the physical organization of the cell, with various components such as membranes and ribosomes. How do these details differ among cells of different types (liver versus brain, human versus bacterial)? We can also begin to ask what chemical signals direct the development of a single fertilized egg into the different organized tissues in a human being, and how such signals work. What is the chemistry of aging? What special chemistry operates in the brain to store memories? Underlying these functions—functions that make humans what they are—are chemical processes that remain to be discovered and harnessed.

Other opportunities will drive both basic discovery and invention. New and improved drugs will be needed to fight disease and improve quality of life. At the same time, better methods will be needed for delivery of these drugs, and a variety of new medical devices will depend on the work of chemists and chemical engineers. While the engineering of tissue constructs has had commercial success, highly perfused or vascularized tissue remains problematic. Artificial organs, such as an artificial liver, remain objects of intense research. Commercially viable replacement organs are certainly more than a decade away. The primary challenges are understanding the signals that tissues need to control proliferation and differentiation and constructing bioreactors and scaffolds that will provide signals in appropriate sequences.

A closely related challenge is the design of materials that interact with cells or living tissues to promote desired biological responses. Such responses might be cell attachment, cellular differentiation and organization into functional tissue, or promotion of in-growth of bone into an artificial prosthesis such as an artificial hip.

The coupling of the techniques of microfabrication on silicon with cells or biological molecules also offers great promise. Devices at the natural length scales of biological systems will facilitate the use of biosensors that can be implanted. They will also aid the development of models having biological components that can be used to gain predictive insight into *in vivo* systems. Such nanoscale devices may mimic the biochemical interactions in the body by connecting "tissue" compartments in ways that mimic the body's circulatory system. A particular model that would be useful would be of the blood-brain barrier, to predict which drugs or chemicals may enter the brain.

While we have very functional processes for manufacture of therapeutics, there are significant challenges left to the process chemical sciences. The United States faces a near-term crisis in the production of therapeutic proteins from mammalian cell culture due to the absence of sufficient facilities. Mammalian cell culture is both expensive and has low yields; it is used to ensure that all of the post-translational protein-processing steps (e.g., glycosylation or specific addition of certain sugar complexes to predetermined sites on the protein) are humanlike. Can we find ways to alter cellular machinery in other, more productive host cells, to produce large amounts of proteins with humanlike post-translational processing? Another challenge comes from the need to respond to bioterrorism (Chapter 11). We need new methods to produce large amounts of protective antibodies or vaccines in a matter of weeks rather than years. In addition, ways are needed to integrate better genomic, proteomic, and advanced computational methods with metabolic engineering to inexpensively produce large amounts of nonprotein products.

This listing of challenges for the future is not exhaustive, but it should provide the reader with a sense of vast possibilities for the interface of the chemical sciences and engineering with biology. These are complex scientific problems requiring multidisciplinary research. Research at the interfaces of many disciplines requires greater understanding of neighboring fields. We are left with a training paradox—we need highly skilled specialists who are also generalists. In addition, we have a funding paradox—success requires support of both fundamental research and cross-disciplinary research. With collaborative efforts these paradoxes will disappear, and we will realize the incredible potential that lies before us. The early part of the 21st century will be known as the Golden Age of the Chemistry of Life.

8

Materials by Design[1]

Some Challenges for Chemists and Chemical Engineers

- Invent improved structural materials that are stable at high temperatures and easily machined.
- Invent materials with useful electrical and optical properties, including high-temperature superconductivity.
- Invent materials that are lighter, stronger, and more easily recycled.
- Invent materials for surface protection (paints and coatings) that are truly long-lasting and rugged.
- Understand and utilize the properties of nanoscale materials and materials that are not homogeneous.
- Build materials with the kind of actuating response found in physiological systems such as muscle.
- Develop and process materials in which complex structural assembly occurs spontaneously or with minimal guidance and in useful timescales to produce durable systems with diverse utility.
- Create nanomaterials technology from nanoscale chemical science.

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[1] As part of the overall project on Challenges for the Chemical Sciences in the 21st Century, a workshop on Materials and Manufacturing will lead to a separate report. The reader is urged to consult that report for further information.

GOALS

A material is defined as "the substance or substances out of which a thing is made or composed."[2] Understanding materials therefore necessitates a marriage between understanding *substances* and knowing how to assemble them into useful *structures*. Materials with specially tailored properties are at the core of nearly all interesting assemblies that are not living, and many that are. Chemical scientists synthesize, characterize, produce, and construct with materials. Moreover, they do this at length scales from molecules at the nanometer level, to polymers and electronic devices at the submicron scale, and to ceramics and cement in large-scale structures. Revolutionary developments are being made in all aspects of materials science. The materials sector of the chemical sciences is vital, both fundamentally and pragmatically, for all areas of science and technology—as well as for the societal needs in energy, transportation, national defense, and medicine.

The overall goal of materials research within the chemical sciences is to explore, design, and control—through synthesis and processing—the relationships among structure, properties, composition, and processing that determine the useful behavior of all materials. The chemical sciences are especially powerful (as they are in all areas of synthesis and manufacturing) in molecular-level construction of material structures. Though the domain of materials chemistry is rapidly expanding, it remains underdeveloped.

A frontier challenge in the chemical sciences is to investigate the chemistry and properties of single isolated molecules and compare that behavior with the average molecular behavior in an assembly, solution, or condensed phase of molecules. Many parts of the chemical sciences are concerned with the collective properties of materials in condensed phases, which have a variety of intriguing and controllable properties. Today, we recognize fully that the most interesting materials are *functional* systems, derived from our evolving knowledge of structure-function relationships. Catalysts are superb examples of chemically functional materials, and the area of catalytic materials is an exemplary branch of modern functional materials science. Responsive materials, often consisting of softer materials, give rise to many kinds of functionality, such as sensing and actuation.

Composites are an important class of solid materials, whose history goes back to ancient times. For example, bricks made only of clay were not as strong as those in which straw was mixed with the clay. Now we use clay as the filler in new polymeric composites to enhance their mechanical properties. The ionic con-

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[2] *Random House Webster's Unabridged Dictionary,* V2.2 for 16-bit Windows systems, copyright 1999, Random House, Inc.

ductivity of the polymer electrolytes used in energy storage systems also can be enhanced by addition of tiny clay particles. Another example is found in building construction, where concrete is reinforced with steel rods to producing a composite in which the components mutually reinforce the overall strength. Other recent examples are the graphitic materials used in tennis rackets and golf clubs, where long strands of carbon fibers are combined with resins. The science of the boundaries or interfaces between phases, and aggregates of matter with sizes between the molecular and the macroscopic, has become a vigorous part of the chemical sciences. Constructing nano- and microstructures of any complexity requires joint modules or elements through interfaces.

The goals of molecular understanding, synthetic control, and novel fabrication of various materials are inherently based in the chemical sciences and technology. The goal of applied chemistry and chemical engineering is to convert available substances into useful materials, normally by changing their molecular composition and arrangement, through controlled synthesis, processing, and manufacturing methods.

Chemical scientists seek to understand the properties of materials in which there is organization of the components. *Chemistry is the original synthetic nanotechnology (as biology is the original natural nanotechnology); chemists have been designing and executing constructions requiring placements of atoms with subnanometer precision for most of the last century.* Chemical engineers are now aiming to do this on larger scales. As self-assembly and nanotechnology move from laboratory demonstrations to more widespread means of fabrication and manufacturing, the variety of materials available to technology and society will grow enormously. New catalytic chemistry and processes, such as the revolution in metallocene catalysts, is an area where chemists and chemical engineers are creating new routes to macromolecular structural control at the nanometer scale.

Methodologies of synthetic chemistry (Chapter 3) must be adapted to achieve the full potential of chemical materials science and technology. This in turn will allow chemists and chemical engineers to characterize the synthesis of supramolecular entities and the three-dimensional character of materials. Our abilities to achieve these goals in new materials synthesis are enhanced by intricate optical, micromechanical, and spectroscopic probes, just as they are by the use of noncovalent bonding, self-assembly, and assembly directed by forces such as fluid mechanical or electric fields. The miniaturization and diversification of synthesis through biological or combinatorial approaches provide unprecedented opportunities. Chemical science should take better and broader advantage of naturally abundant substances to produce building blocks for molecular (or larger) assemblies. Surface science applied to materials—particularly to organic materials—is of growing importance and will expand significantly with the development of new materials for biotechnology, medicine, information technology, and nanotechnology.

To achieve these goals will require, among many other things, a dramatic increase in the interactions among chemists, engineers, biologists, and physicists.

PROGRESS TO DATE

Since early civilization humans have been interested in the properties of the various minerals found in the earth. The discovery that materials we now recognize as iron oxides could be heated with charcoal to produce iron led to wonderful new tools in the Iron Age, while similar transformation of other minerals led to copper, tin, and other metals. Although we think of them as common, few metals are naturally occurring; they are produced by chemical reactions of their naturally occurring compounds. One of the earliest synthetic materials is glass, produced over 5,000 years ago by heating various natural minerals together. Clearly, the discovery, refinement, and creation of materials has arisen from the chemical sciences and processing technology (and sometimes vice versa).

Synthetic Polymers and Self-Assembly

The story of polymers is one that shows enormous effects on human life. Though polymer science revolutionized 20th century life and is now a well-developed academic field, polymer synthesis is still progressing rapidly. Synthetic polymers have often consisted of long chains of identical subunits. Sometimes the synthetic polymer chains have cross-links between the chains (in proteins, cross-links within a chain help determine a specific folded geometry). For many years, copolymers have also been produced to gain the beneficial properties from more than one monomer. Glassy polymers can be blended with rubbery ones to generate desirable mechanical properties. Block copolymers—produced with long runs of one or the other monomer—phase separate on a nanoscopic scale (typically 10 to 50 nm) that is determined by the block molecular weight. These microphase-separated polymers often have remarkably better properties than blends of the two components, and are an early example of using self-assembly to produce new materials.

The architecture of macromolecules is another important synthetic variable. New materials with controlled branching sequences or stereoregularity provide tremendous opportunity for development. New polymerization catalysts and initiators for controlled free-radical polymerization are driving many new materials design, synthesis, and production capabilities. Combined with state-of-the-art characterization by probe microscopy, radiation scattering, and spectroscopy, the field of polymer science is poised for explosive development of novel and important materials. New classes of nonlinear structured polymeric materials have been invented, such as dendrimers. These structures have regularly spaced branch points beginning from a central point—like branches from a tree trunk. New structures create new possibilities for applications, a direction that will continue to drive materials chemistry.

High-molecular-weight polymers can be useful as solid materials and in solution, and lower molecular weight polymers can make liquids that are unusual in character. Synthetic adhesives illustrate liquid-phase materials that cross-link or polymerize when they set. Water-based paints are another example, liquids with suspended solid polymer particles that form uniform solid films during drying. So-called liquid crystals illustrate another exciting example of complex fluid materials; these are liquid-phase materials made up of anisotropic, usually fairly rigid, molecules of high aspect ratio that have strong electric dipole moments. Such molecules are prone to adopt preferred orientations, especially under the influence of surfaces, electric fields, and flow processes. Control over preferred orientations gives high anisotropic strength of materials and switchable optical properties, making them useful in displays such as those on digital watches and laptop computers.

Multicomponent systems having molecules of macromolecular size and heterogeneous composition can be exquisitely sensitive to the delicate balance of intermolecular forces. The fine interplay among a suite of noncovalent interactions (e.g., steric, electrostatic, electrodynamic, and solvation forces) dictates microstructure and dynamics. Molecular organization and interaction cause collective and cooperative behavior to dictate macroscopic properties. Often the balance of forces is such that self-assembly occurs to generate aggregates, arrays, or other supramolecular structures. Large molecular size enables amplification of a small segmental effect into a large intermolecular effect. Self-assembly can amplify the small forces between small objects to produce large-scale structures useful for macroscopic creations for patterning, sieving, sorting, detecting, or growing materials, biological molecules, or chemicals. Learning to understand and harness intermolecular interactions in multicomponent polymer and composite systems offers huge challenges, as well as opportunities to mimic nature, which has learned to do this in many instances.

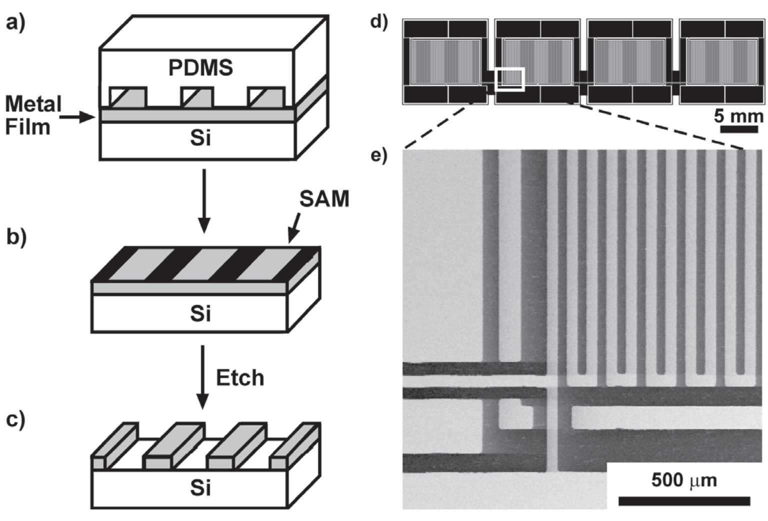
Self-assembled monolayers (SAMs) are ordered, two-dimensional crystals or quasi-crystals formed by adsorption and ordering of organic molecules or metal complexes on planar substrates. Development of these monolayers is based on early studies in which chemists learned to attach chemicals to surfaces—for purposes ranging from adhesion to chromatography to electrochemistry—but often without strong ordering in the monolayers. The ordered structures have made it possible to develop a rational surface science of organic materials. They provide the best current example of the power of self-assembly to make possible the design of the properties of materials. They have made routine the control of wetting, adhesion, and corrosion in certain systems, and—through soft lithography—they have provided a new approach to microfabrication that is uniquely chemical in its versatility. They have also greatly advanced the field of biomaterials by making it possible to control the interface between cells and synthetic materials at the molecular level.

Soft Lithography

Building ever smaller devices has been a dominant trend in microelectronics technology for 50 years. The technology used for this type of fabrication is photolithography. This astonishingly sophisticated technology is a kind of photography: The pattern that is to be a part of the circuit is formed by shining ultraviolet light through a mask (a pattern of chromium on silica), through a reducing lens, onto a thin film of photosensitive polymer (a photoresist) covering the surface of a silicon wafer. After exposure, the exposed polymer differs in its solubility from unexposed material, and a suitable solvent allows the selective dissolution of either exposed or unexposed regions. The exposed regions are then treated (by deposition of metal, etching, or implantation of ions) to make a part of the final device.

Photolithography is the basis of one of the technologies that has genuinely changed the world—it has made possible the computing and information revolution. But it is not suited for making every possible type of small structure. As the advantages of "small" have become obvious in microelectronics, researchers have searched for ways to make small channels (for analysis of fluids or for synthesis), small machines (so-called microelectromechanical systems, or MEMS, for accelerometers and display projectors), and small optical systems (for optical communications). Such targets for fabrication all have different requirements in materials and costs, and photolithography is not a "one size fits all" technology.

An alternative to photolithography has been developed that is—for many applications in chemistry and biology—more versatile and much less expensive. This technology depends on a "back to the future" strategy that produces micron- and nanometer-scale patterns by stamping, printing, and molding. The element in these methods is a stamp or mold that is fabricated in a transparent, chemically inert elastomer, poly(dimethyl siloxane) (PDMS). Because the stamp can deform, it is called soft; the organic materials that are printed and molded are also called soft matter by physicists—hence the name soft lithography. Patterns of small features are embossed in the surface of the element; when it is "inked" with a suitable ink, it can print lines that are <100 nm in width (that is, the size of a line of 200 gold atoms). As illustrated here, when the recessed regions are filled with a polymer, and the pattern is transferred to a surface, the resolution is <10 nm. If the stamp is sealed to another surface, the patterns become microchannels for analysis of nucleic acids, proteins, or cells.



Soft Lithography. Figures a-c illustrate a soft-lithographic technique called microcontact printing. A PDMS stamp with features in bas-relief is coated with an ethanolic solution of octadecanethiol, and placed in contact with the surface of a thin metallic film (30-50 nm) of gold, silver, or palladium. A self-assembled monolayer (SAM) of octadecanethiolate forms on the surface of the metal in the regions where it contacts the PDMS stamp. The stamp is removed and the regions of the metallic film without a SAM are dissolved by wet-chemical etching. Figure d is a schematic diagram of a long, serpentine, palladium wire (2 m) with contact pads that are connected to the wire at every 0.25 m along the length of the wire; it is a part of a sensor for hydrogen. Figure e is a SEM image of a section of the pattern. Drawings a-c courtesy of George M. Whitesides; d-e reprinted with permission from D. B. Wolfe et al., *Applied Physics Letters* 80, 12, 2222 (2002).

Soft lithography is very simple, and it does not require expensive instrumentation or access to clean rooms. It does not give the lateral accuracy of photolithography, but it is much less expensive. The size of the features it can make is not limited by optical diffraction, but rather by van der Waals contacts and by deformations in the polymer used. It has become a tool that is widely used in chemistry to make micro- and nanostructures. It also has helped to open doors to chemists wishing to play an active role in many areas of cell biology, bioanalytical chemistry, microfluidics, optics, and new forms of electronics such as “all-organic” electronics: that is, electronics that does not rely on silicon, but instead uses organic or organometallic compounds as conductors, semiconductors, and insulators.

Micelles, liposomes, shell-linked particles, and vesicles are all results of the spontaneous self-assembly of amphiphilic molecules to form enclosed or aggregate structures that contain solvophobic regions surrounded by solvent-loving moieties. In all of these structures, opportunities abound to exploit them for chemical separations, controlled release, directed transport, and synthesis. Fundamental studies of these organized systems have increased in the recent decade. The pursuit is often biologically inspired, but in creating mimics we still fall short of the natural systems. Combining this activity with concerted synthetic chemistry and biochemistry provides great potential for the future.

Electronic, Optoelectronic, Photonic, Magnetic, and Superconducting Materials

The properties of modern electronic, optoelectronic, photonic, and magnetic devices provide another story of great science that has affected most of humankind. Electronic devices require special materials: materials that emit light when struck by a beam of electrons for use in television screens and computer monitors, materials to make the semiconductors that are the heart of electronic and microelectronic circuits, and materials that are used in magnetic memory storage devices for computers.

Classical electronic circuits and communication lines are made of metal to conduct electricity. Now we have the prospect of massively communicating by optical signals. The great progress in the use of optical fibers to permit light to travel in and between devices results from major achievements in materials processing. Special surface coatings on the fibers reduce signal degradation; optical switches allow connections with devices communicating through optical fibers. The optical fiber revolution provides very high speed plus the ability to pack much more information into a given transmission.

There is considerable interest in developing new types of magnetic materials, with a particular hope that ferroelectric solids and polymers can be constructed—materials having spontaneous electric polarization that can be reversed by an electric field. Such materials could lead to new low-cost memory devices for computers. The fine control of dispersed magnetic nanostructures will take the storage and tunability of magnetic media to new levels, and novel tunneling microscopy approaches allow measurement of microscopic hysteresis effects in iron nanowires.

One of the most exciting properties of some materials is superconductivity. Some complex metal oxides have the ability to conduct electricity free of any resistance, and thus free of power loss. Many materials are superconducting at very low temperatures (close to absolute zero), but recent work has moved the so-called transition temperature (where superconducting properties appear) to higher and higher values. There are still no superconductors that can operate at room temperature, but this goal is actively pursued. As more current is passed through a superconductor the transition temperature moves lower; consequently, high electrical current tends to make the materials lose their superconducting ability. The development of a full, predictive theory of high-temperature superconductivity would be a major asset to the realization of practical materials in this area. The materials studied to date are also difficult to process—they are easily corroded or brittle—thus motivating further study of novel processing or assembly techniques. If practical superconductors can be made that will conduct appreciable currents at reasonable temperatures—perhaps even from organic materials—it may become possible to transfer electric power over long distances with high efficiency, and to exploit magnetic levitation for transportation systems.

Quantum Computation

The first demonstration of continuous electrical tunability of spin coherence (the state and degree of alignment of electronic spins) in semiconductor nanostructures has recently been made. This opens possibilities for the field of quantum computation by permitting properties other than electronic charge—and particularly the quantum property of spin—to be manipulated for computing purposes. Spin, often described by analogy with rotation of the earth, is a quantum property of electrons (and some atomic nuclei) that must have one of two possible values analogous to clockwise or counter-clockwise rotation of a rotating body.

While magnetic fields are conventionally used to manipulate spins in familiar magnetic devices like hard-disk drives, this demonstration of electrical control of aligned spins represents a significant step toward making new spin-based technologies. One future technology is quantum computing, where many schemes make use of electron spin states as bits of information analogous to the 0 and 1 of binary computing. Unlike ordinary bits, *quantum bits* can be any combination of both 0 and 1 simultaneously, corresponding to a continuous range of possible directions.

By classical mechanics, magnetic fields can modify the behavior of spins by inducing precession, which is an additional rotation of the spin axis with respect to the magnetic field. While the speed of electron spin precession in a magnetic field is generally fixed by the particular materials used, recent research has shown that both the speed and direction of precession can be continuously adjusted by applying electric fields in specially engineered quantum structures.[3] It is more fitting to refer to

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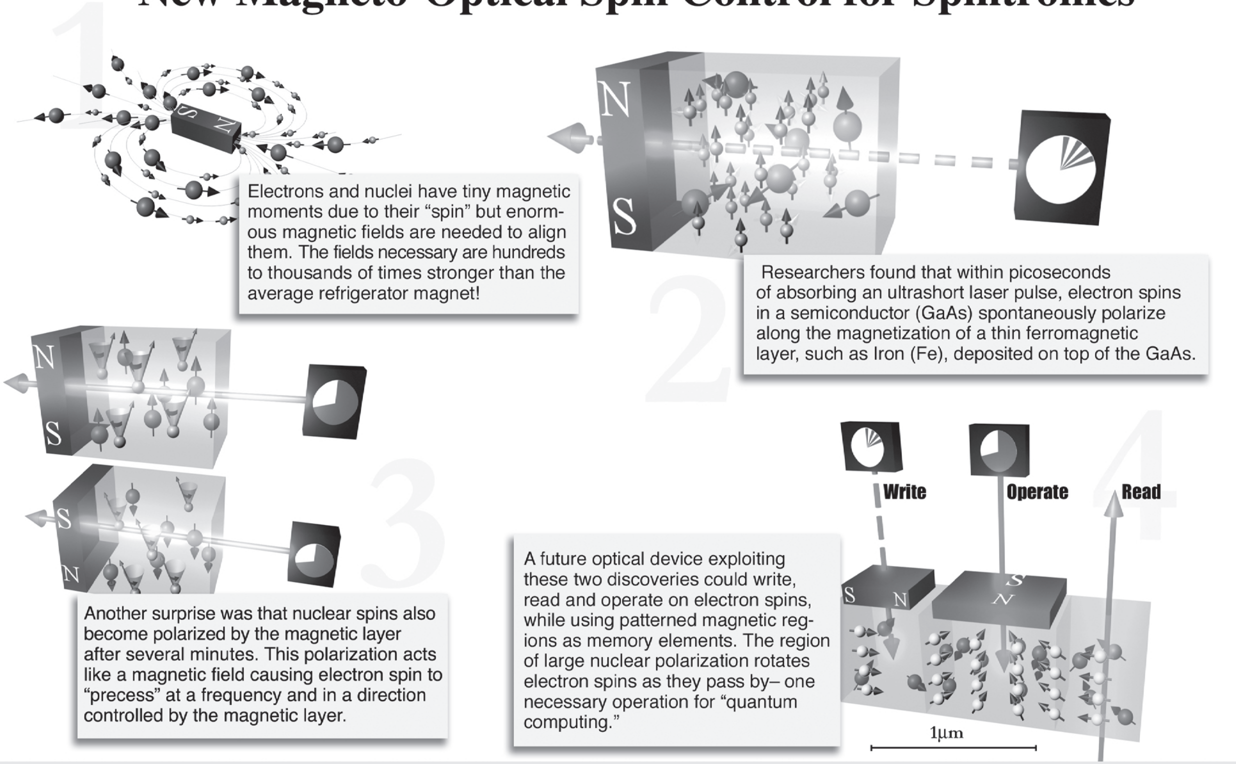
[3] G. Salis, Y. Kato, K. Ensslin, D. C. Driscoll, A. C. Gossard, D. D. Awschalom, *Nature*, 414, 619, 2001

continues

New Magneto-Optical Spin Control for Spintronics



Electrons and nuclei have tiny magnetic moments due to their “spin” but enormous magnetic fields are needed to align them. The fields necessary are hundreds to thousands of times stronger than the average refrigerator magnet!

Researchers found that within picoseconds of absorbing an ultrashort laser pulse, electron spins in a semiconductor (GaAs) spontaneously polarize along the magnetization of a thin ferromagnetic layer, such as Iron (Fe), deposited on top of the GaAs.

Another surprise was that nuclear spins also become polarized by the magnetic layer after several minutes. This polarization acts like a magnetic field causing electron spin to “precess” at a frequency and in a direction controlled by the magnetic layer.

A future optical device exploiting these two discoveries could write, read and operate on electron spins, while using patterned magnetic regions as memory elements. The region of large nuclear polarization rotates electron spins as they pass by– one necessary operation for “quantum computing.”

these devices as gates rather than switches because they perform continuous tuning of electron spin. Instead of the "off" and "on" options for a switch, a gate operates across a continuum in the same way that lights can be dimmed by a rheostat.

Such spin gates are an example of the rapidly developing field of spintronics, which studies electronic devices that are based on electron spin. *Spintronics* uses magnetic fields to manipulate the distribution of spin coherence, whereas *electronics* uses electric fields to manipulate charge distribution. This raises the question, What might spintronics do that electronics cannot? In addition to the longer-term goal of quantum computing, spintronics offers the near-term possibility of revolutionizing the way we think about piecing together different technologies.

The creation of nanoscale sandwiches of compound semiconductor heterostructures, with gradients of chemical composition that are precisely sculpted, could produce quantum wells with appropriate properties. One can eventually think of a combined device that incorporates logic, storage, and communication for computing—based on a combination of electronic, spintronic, photonic, and optical technologies. Precise production and integrated use of many different materials will be a hallmark of future advanced device technology.

The opportunities to develop new structures for computing, quantum computation, and spintronics—together with other areas in molecular electronics—raise important issues about the role of computation in the chemical sciences (Chapter 6). In order for chemical scientists to play a major role in converting clever new ideas for computational devices into full-fledged computers, they will have to become increasingly competent in the architectures, algorithms, and protocols that are necessary for reliable computation.

Ceramics, Carbon Structures, and Crystal Engineering

Inorganic substances are the components of ceramics, such as those in dinner plates. Ceramics have important industrial uses as well; a typical example is the ceramic insulating materials that are used to suspend power lines. Ceramics are typically poor conductors of heat and electricity, and they perform well at high temperatures. Consequently, they find applications that take advantage of these properties. Some use of ceramics in automobile engines is being developed to achieve improved fuel efficiency at higher-temperature operation. The fragility of current ceramics and the difficulty in machining them (relative to machining metals) are still problems for such uses. One approach to ceramics with better properties is to overcome their fragility by incorporating them into composites. As chemistry moves from pure materials to organized systems of different materials, composites are leading the way. A challenge for the future is to invent improved structural materials, probably composites based on resins or on ceramics, that are stable at high temperatures and easily machined.

Carbon atoms in pure form can be obtained as materials having two classic types of molecular structure: diamond and graphite. In diamond each carbon atom is linked by equivalent single bonds to four neighboring carbons. The result is a clear very hard material that is used for cutting, in saws with tiny diamonds imbedded in the blades, as tough coatings for metals, and in other industrial uses as well as in jewelry. By contrast, each carbon atom in graphite is linked to only three neighboring carbons, in a sheet, and some of the electrons are in delocalized pi orbitals that permit them to move easily along the sheets. The extensive aromaticity of carbon sheets leads to electronic transitions with energies in the visible light region, so that graphite absorbs throughout the visible region and is a black material. In addition, the mobility of the pi electrons in graphite makes it an electrical conductor, in stark contrast to the insulating properties of diamond.

A new type of structure has recently been discovered in which the sheets of graphite-like carbons are curved. The first example, called fullerene (after the geodesic domes of Buckminster Fuller), has 60 carbons in a sphere. It resembles a soccer ball with its five- and six-sided polygons (in contrast to graphite, which resembles a floor tile pattern, with hexagons only). A Nobel prize was awarded in 1996 to Robert F. Curl, Jr., Harold W. Kroto, and Richard E. Smalley for their discovery of fullerenes. Instead of curling into a sphere, the sheets of carbon with hexagons can also curve into tubes with diameters on the order of 1 nm (often called nanotubes), tiny whiskers that are sometimes quite long. Because of the electrical conductivity of pi electrons, these tubes are also electrically conducting, somewhat like graphite. While they are already used in research instruments to probe microscopic structures, one of the challenges is to use these new structures in miniature devices, or as building blocks for organized chemical structures.

The importance of crystal form often is underappreciated. In many applications—from drugs (in which bioavailability may be determined by crystal form) to explosives (where crystals may differ in stability) and optical devices (where the nonlinear optical properties required for the device are based on a particular crystalline architecture)—the correct crystalline form is essential to obtaining the desired chemical and physical properties of a material. Crystallization has long been an art rather than a science; sometimes the same substances will exhibit polymorphism and adopt different crystalline forms depending on the crystallization conditions. Crystal engineering—the prediction and control of molecular crystal structures based on the constituent molecular structures—is on the verge of becoming a science. The current generation of computers is finally powerful enough to rationalize the crystal structures of simple, relatively rigid, organic molecules. As computer capability increases, and as the sophistication of the programs used increases, it seems very probable that it will soon be possible to predict the structures of crystals. Learning to template or guide desired organization of molecules will have great utility.

Layered Materials and Surface Modification

The scale of components in complex condensed matter often results in structures having a high surface-area-to-volume ratio. In these systems, interfacial effects can be very important. The interfaces between vapor and condensed phases and between two condensed phases have been well studied over the past four decades. These studies have contributed to technologies from electronic materials and devices, to corrosion passivation, to heterogeneous catalysis. In recent years, the focus has broadened to include the interfaces between vapors, liquids, or solids and self-assembled structures of organic, biological, and polymeric nature.

In a simple material, its surface properties are dictated by the properties of the bulk, which are not necessarily desirable. For example, we may need a bulk material for its strength but want to make a medical device—such as an artificial heart—where the surface must not cause a reaction leading to rejection or blood clotting. This leads to the challenge of learning how to add biocompatible surface layers to materials. This challenge is not yet fully met, but interesting approaches to creating biomimetic functionality on surfaces are rapidly emerging. This field is an example of the transition of chemistry from pure materials to organized systems and materials, in this case the organization being the modification of the surface with a different material for a biofunctional purpose.

The ability to modify surfaces by attaching chemicals to them has for years encouraged scientists to attempt to design surface adhesive and wetting properties. The advent of self-assembled monolayers, including mixtures of molecules in a monolayer, has led to more detailed control and understanding of surface adhesion and wetting. This capability has been extended with the use of novel monolayers to alter liquid-crystalline anchoring processes, surface friction, and biocompatibility. Important applications of this approach have arisen in microfluidics and liquid crystalline displays. Work pioneered by Nuzzo and Allara at Bell Laboratories in the early 1980s with thiol self-assembled monolayers on gold has led to a great deal of research, much of which has been revolutionary.

Thus the study of surfaces has emerged as an important focus in the chemical sciences, and the relationship between surfaces of small systems and their performance has emerged as a major technological issue. Flow in microfluidic systems—for example, in micromechanical systems with potential problems of stiction (sticking and adhesion) and for chemistry on gene chips—depends on the properties of system surfaces. Complex heterogeneous phases with high surface areas—suspensions of colloids and liquid crystals—have developed substantial technological importance. In certain size ranges, we have seen new and scientifically engaging phenomena, such as electron tunneling through nanometer-thick insulators and diffraction of light in photonic band-gap crystals. New tools and systems—from scanning tunneling microscope and atomic force microscope (STM and AFM) to self-assembled monolayers and carbon nanotubes—have fundamentally changed our ability to characterize and prepare these complex systems. Finally, microelectronics—complex systems of small functional components fabricated in silicon and silicon dioxide, and other materials—have become so important that we must develop the science and technology relevant to future systems of small components, whether based on microelectronics or other technologies. The microelectronics industry is entirely based on chemical processing, using such techniques as chemical vapor deposition (CVD), plasma processing, etching, and electroless deposition.

Nanomaterials

As the analytical, synthetic, and physical characterization techniques of the chemical sciences have advanced, the scale of material control moves to smaller sizes. Nanoscience is the examination of objects—particles, liquid droplets, crystals, fibers—with sizes that are larger than molecules but smaller than structures commonly prepared by photolithographic microfabrication. The definition of nanomaterials is neither sharp nor easy, nor need it be. Single molecules can be considered components of nanosystems (and are considered as such in fields such as molecular electronics and molecular motors). So can objects that have dimensions of >100 nm, even though such objects can be fabricated—albeit with substantial technical difficulty—by photolithography. We will define (somewhat arbitrarily) nanoscience as the study of the preparation, characterization, and use of substances having dimensions in the range of 1 to 100 nm. Many types of chemical systems, such as self-assembled monolayers (with only one dimension small) or carbon nanotubes (*buckytubes*) (with two dimensions small), are considered nanosystems.

Whether there is currently a *nanotechnology* is a question of definition. If one asks whether there are (or are soon likely to be) commercial electronic fluidic, photonic, or mechanical devices with critical lateral dimensions less than 20 nm, the answer is “no,” although there may be in 10 to 20 years. There is, however, a range of important technologies—especially involving colloids, emulsions, polymers, ceramic and semiconductor particles, and metallic alloys—that currently exist. But there is no question that the field of *nanoscience* already exists.

The current, intense interest in “nano” is based on the (correct) perception that the study of nanoscience has exploded. As new tools have become available for the preparation and characterization of systems with these dimensions, the opportunities in the chemical sciences have grown enormously. The attention also results from the as yet untested proposition that nanoscience will eventually revolutionize existing areas of important technology, especially microelectronics.

There is great interest in the electrical and optical properties of materials confined within small particles known as nanoparticles. These are materials made up of clusters (of atoms or molecules) that are small enough to have material properties very different from the bulk. Most of the atoms or molecules are near the surface and have different environments from those in the interior—indeed, the properties vary with the nanoparticle's actual size. These are key players in what is hoped to be the nanoscience revolution. There is still very active work to learn how to make nanoscale particles of defined size and composition, to measure their properties, and to understand how their special properties depend on particle size. One vision of this revolution includes the possibility of making tiny machines that can imitate many of the processes we see in single-cell organisms, that possess much of the information content of biological systems, and that have the ability to form tiny computer components and enable the design of much faster computers. However, like truisms of the past, nanoparticles are such an unknown area of chemical materials that predictions of their possible uses will evolve and expand rapidly in the future.

Several techniques are now available for the fabrication of nanostructures. These techniques arise from four approaches, and their simultaneous applicability to a common set of targets is one of the reasons for the excitement in the field. The first set includes the classical techniques developed from microfabrication:

- electron beam writing, which is the most important, although x-ray and deep UV photolithographies may also contribute;
- use of scanning probe devices to move individual atoms or to write patterns;
- preparation of colloids, vesicles, emulsions, buckytubes, and self-assembled monolayers using chemical self-assembly methods (some with histories that date back to the beginning of chemistry);
- soft lithography and nanoimprint lithography, which use printing, molding, and embossing technologies developed on the macroscopic scale to replicate structures at the nanoscale.

The characterization of simple nanostructures is now possible with remarkable detail, but is highly dependent on access to the tools of measurement science and to scanning probe microscopies.

These methods have made available a set of nanostructured systems that have begun to reveal the characteristics of nanoscale matter. The long list of discoveries in the last decade includes:

- "quantum box" behavior in colloids of semiconductors precipitated from solution;

- quantized capacitive charging of metal nanoparticles coated with low dielectric monolayers;
- a range of electrical properties in carbon nanotubes grown from vapor-phase precursors using metallic catalysts (with the highest observed conductivities comparable to those observed in graphite);
- high mechanical strength of buckytubes (combined with the above-mentioned electrical properties) that makes them possible candidates for "nanowires";
- remarkably regular nanostructures in phase-separated block copolymers;
- functional transistors prepared in organic semiconductors with 100-nanometer gate widths;
- membranes containing nanopores with controlled interior functionality;
- versatile methods of preparing nanostructures that are based on simple ideas taken from printing, writing, molding, and embossing, and that have made it possible to prepare certain nanostructures without use of expensive apparatus.

Two important conclusions have emerged in this field. First, the methods employed for microelectronics—photolithography using UV wavelengths—are unlikely to provide inexpensive access to nanostructures. Second, the techniques of chemistry and chemical engineering—although very early in their development—will be able to provide nanostructures with a wide range of compositions and properties, and at costs that are very low compared to those prepared by e-beam or other "conventional" techniques for fabrication at small dimensions. In particular, chemical affinities should make it possible for tiny structures and devices to self-assemble spontaneously, an appealing idea for large-scale manufacturing.

CHALLENGES AND OPPORTUNITIES FOR THE FUTURE

Many of the challenges of the formation and processing of new materials will be met with advances in the chemical sciences. There are some revolutionary things happening in materials: organic electronics and spintronics, attempting to replace classical silicon electronics, the exploration of single-molecule electronics to achieve the ultimate in size reduction, sophisticated biocompatible materials for tissue engineering, implants, man-machine hybrids, ferromagnetic organic materials, materials with negative index of refraction, nanoelectronics, and functional colloids.

Self-assembly and nanotechnology are advancing rapidly, but the challenge still remains to develop a means of fabrication and manufacturing. The rapid developments in synthetic chemistry produce myriad new polymeric and composite materials. These advances are enhanced by progress in optical, micromechanical, and spectroscopic probes. The miniaturization and diversification of synthesis through biological or combinatorial approaches provide unprecedented opportunities. The approach to the future should be a holistic one, with synthetic advances moving in concert with assembly and microstructural control. Summarized below are a few of the leaps that can be viewed as important aspirations for the chemical science community.

Templating

The development of templated syntheses—of metallic, ceramic or semiconductor particles, wires using novel synthetic and self-assembling structures such as dendrimers, micelles, and nanotubes—is in its infancy. This is a prime example where synthetic advances in the creation of new lipids, surfactants, and amphiphilic polymers work together with probes of structure and function of infinitesimal wires or particles. New techniques such as scanning microscopy must be developed to follow the electronic and magnetic processes occurring in the small systems. Spectroscopists, microscopists, engineers, and chemists must work together at the frontiers involving techniques developed by those from disparate fields of electronics and biology.

Higher Order Structures

The ability to program synthetic polymers with the correct information to self-assemble, recognize analytes, or provide biological function seems fairly futuristic. However, the close interplay between chemical composition and physical interactions makes this a possibility; new synthetic approaches involving controlled living polymerizations and biological synthetic pathways allow control of molecular composition. Additional research on the balance of physical forces driving self-assembly, recognition, field responsive behavior, and biological compatibility should be closely tied to the synthetic efforts.

New approaches in synthetic chemistry and biochemistry pave the way for tremendous advances in self-assembly. Highly controlled living polymerizations will allow the creation of ever more complex macromolecules having prescribed architectures (branching, stereoregularity) and chemical specificity. The future will hold the opportunity for chemists to make molecules of size and complexity approaching protein structures—and to fold and assemble them. Then, mimicking nature becomes a question of choosing important problems and technologies needing improvement or intervention. By creating the appropriate molecules, patterning them on the appropriate surfaces, and providing them with the appropriate functions, we can think of mimicking the most chemical of senses: taste and smell. These analytic advances, when taken in parallel with the computational and electronics revolution, suggest the possible creation of the robots and gadgets that were previously envisioned only in science fiction.

Semiconductor Processing

We need novel materials to maintain the computer revolution, since we may be reaching the limits of “top down” miniaturization. Instead of etching pieces of silicon to produce electronic circuits that are smaller and smaller, there is the hope that “bottom up” design will work. In other words, self-assembly of molecules or nanoparticles offers the potential for construction of miniature electronic circuits that will be faster and will permit more computer power in a given space. Promising physical approaches involve soft-lithography or crystal or nanoparticle growth, but other processes doubtless will emerge as the field of nanoparticle science evolves.

Chemical scientists will seek new methods of generating nanostructures with a range of materials and processes that rely on ideas common in chemistry—self-assembly, diffusion, phase-separation, catalysis, wetting—to make these structures accessible and inexpensive.

In terms of technology, it is too early to predict what will emerge from nanoscience, although it is clear—for a field as fundamental as this one—that technologies will surely emerge. Candidates for early success include systems of photoluminescent colloids in which the same materials base provides any desired color simply by tailoring the size (for displays); compact disks with <50-nanometer pits (for very dense memory devices that will require near field recording technology); and optical elements for manipulating extreme UV and x-ray light. In the longer term, there will be, at minimum, demonstrations of information processors having key components with nanometer dimensions (perhaps made of organic or organometallic materials) and probes for exploring the interior of the cell.

As self-assembly and nanotechnology move from curiosities and demonstrations to more serious means of fabrication and manufacturing, the need for characterization tools, especially those that can meet the time scales for real-time processing, will grow enormously.

Molecular Electronic Materials

Improving the molecular control of addressable, switchable, or conducting molecules that have extremely high purity, selectivity, or specificity is a goal within reach in the coming decades. This will require the combination of synthetic and processing strategies, such as recognition and controlled binding, to tailor oligomeric materials with finely tuned properties. In this field, the chemical sciences will have to interact creatively with computer science and engineering in order to turn promising molecular switching ideas into practical computer architectures.

Composite and Hybrid Materials

As the ability to control materials moves to molecular dimensions, the expectations for composite materials will grow. Rather than relying on incorporation of macroscopic particles or fibers as discussed above, one can hope to create important marriages between disparate materials that will allow the development of new material properties. Combining this synthetic expertise with physical patterning, self-assembly, deposition, or quenching techniques will lead to the creation of new materials with optimal properties. Organized nanocomposite materials can be important for photonic band gap materials as well as membranes and catalysts with high selectivity.

Surface Modification and Interfaces with Biology and Electronics

The connection between biological function and a useful electrical signal is the capstone of sensor technology that will change medical, environmental, and personal-protection strategies in the coming decades. The link between biology and electronics is through the chemical sciences. The ability to mimic nature and reliably anchor biologically active moieties to a surface is in its infancy. Here another level of complexity and functional integration are possible. Coupling the physical chemical means to manipulate interfaces with synthetic strategies inspired by nature provides powerful opportunities for gains in environmental and medical devices. As an example, the recent understanding of virus phage packaging, combined with the ability to inject DNA into a host or a host mimic, opens the way for molecular scientists to develop new therapies and delivery strategies. Another challenge is the construction of materials with the kind of actuating response found in physiological systems such as muscle—soft materials in which a large-amplitude mechanical response could be produced in response to a small-amplitude stimulus.

Capitalizing on self-assembly and nanoscience will enhance the ability to screen drugs for individual sensitivities. Advances in drug discovery, combinatorial synthesis, and screening with sensors that have the ability to detect multitudes of specific genetic matches—marrying microelectronics and self-assembly—are expected to be near-term breakthroughs. Then the creation of advanced forms of "in the field" or "in the office" tests for chemical risks, pharmaceutical compatibility, or environmental hazards will be possible.

The processing of materials through self-assembly will also have to meet several kinds of challenges that arise from scaling up in physical size and speed, and in complex shapes. Little has been done with complex shapes and nonplanar surfaces. Can processes that work on glass slides or mica or 4-inch silicon wafers be scaled up to very large surface areas, such as continuously moving webs of paper, film, or tape, or surfaces of tubular biomaterials? Building large volumes of nanostructured, self-assembled materials in three dimensions may be even more challenging than scaling up to large surfaces.

Processing speed presents different challenges. Since self-assembly is a process that moves down a free energy gradient, there is a predetermined end point; but it is not known how to anticipate its speed. Study of the kinetics and dynamics of self-assembly processes will be necessary to bring this field to a level comparable to traditional methods of synthetic chemistry and chemical engineering. Few studies of kinetics of assembly processes have been pursued, in part because following the assembly process presents analytical difficulties. Practical processing rates will certainly have to be much faster than those of typical current research laboratory practice. The free energy landscapes along the paths toward self-assembled products are not fully explored. Local minima and metastable states lurk but are uncharted, and it is often not appreciated when they are occupied or when they are trapping the process far from the desired equilibrium state. The challenges of kinetics and of metastable states raise the question of catalysis and whether routes to assist, accelerate, and guide self-assembly processes can be developed.

Self-assembly processes in nature are sometimes catalyzed by enzymes. Zeolites are, in many ways, the inorganic counterparts of enzymes, with their ability to selectively bind other substances and perform catalysis. Can templates or catalysts be effective in increasing rates and reducing defects in a wide range of nanostructured materials?

One of the most general forms of the surface modification of materials is *painting*. We have become used to the idea that paints, while serving their important function of preventing corrosion and water damage, need to be renewed on a regular basis, with a significant cost in labor and materials. One less glamorous challenge that could make a significant contribution to modern life is the invention of long-lasting paint, perhaps 100-year paint. In addition, it would also be desirable that this long-lasting paint be easily cleaned, perhaps simply by natural rain, and that it have a mechanism to repair damage to itself. We are used to the idea that our body can repair wounds; it is an important challenge to devise methods by which synthetic materials would also have this wound-healing ability. As one approach, the wound might expose pools of monomer that could spontaneously fill the void and solidify.

Green Materials and Eco-Technology

Other challenges facing materials scientists have to do with the environment. We have traditionally made materials that are as stable as possible, so they will last a long time and not need to be replaced. This longevity has the undesirable consequences of creating waste that requires significant energy to process, or else it clutters the landscape when discarded. As one approach, chemical scientists and engineers need to focus on recycling and materials that can be easily recycled. Another approach is to produce materials that undergo rapid degradation into invisible and harmless substances. Some progress has been made by incorporating ketone groups into polyethylene so that sunlight will break chemical bonds and cause the polymer to disintegrate into tiny particles. However, these materials are not yet economically attractive, and more efforts of this kind are needed.

This is part of the general need, discussed in Chapter 9, to make materials such as insecticides or refrigerants that will degrade in the environment rather than cause problems with bird life or with the ozone layer in the stratosphere. In addition, as the world demand for synthetic materials grows, new renewable resources for chemical feed stocks must be sought, and we must reconsider our current infatuation with burning the petroleum reserves that are important feedstocks (as discussed also in Chapter 10). Zero-effluent processing plants also need to be developed. There are innumerable opportunities for advanced chemical processing of materials to create micro- and nanodevices for environmental and ecological monitoring.

Another challenge is to develop methods to replace the volatile organic solvents that are used in many industrial procedures. One choice is water as a solvent; it is easily repurified, and has a harmless vapor. Another choice is supercritical carbon dioxide, a good solvent for many organic substances. It is not as innocuous as is water, but carbon dioxide can be easily recovered and reused. It is currently used to remove caffeine from coffee, and is being developed as a dry-cleaning solvent to replace organic solvents (Chapter 9).

Analysis and Simulation

Advances in computational capability have raised our ability to model and simulate materials structure and properties to the level at which computer “experiments” can sometimes offer significant guidance to experimentation, or at least provide significant insights into experimental design and interpretation. For self-assembled macromolecular structures, these simulations can be approached from the atomic-molecular scale through the use of molecular dynamics or finite element analysis. Chapter 6 discusses opportunities in computational chemical science and computational materials science.

Molecular dynamics simulations are capable of addressing the self-assembly process at a rudimentary, but often impressive, level. These calculations can be used to study the secondary structure (and some tertiary structure) of large complex molecules. Present computers and codes can handle massive calculations but cannot eliminate concerns that boundary conditions may affect the result. Eventually, continued improvements in computer hardware will provide this added capacity in serial computers; development of parallel computer codes is likely to accomplish the goal more quickly. In addition, the development of realistic, time-efficient potentials will accelerate the useful application of dynamic simulation to the self-assembly process. In addition, principles are needed to guide the selection of initial configurations; the proper initial conditions accelerate convergence and minimize problems associated with metastable configurations.

Molecular calculations provide approaches to supramolecular structure and to the dynamics of self-assembly by extending atomic-molecular physics. Alternatively, the tools of finite element analysis can be used to approach the simulation of self-assembled film properties. The voxel[4] size in finite element analysis needs be small compared to significant variation in structure-property relationships; for self-assembled structures, this implies use of voxels of nanometer dimensions. However, the continuum constitutive relationships utilized for macroscopic-system calculations will be difficult to extend at this scale because nanostructure properties are expected to differ from microstructural properties. In addition, in structures with a high density of boundaries (such as thin multilayer films), poorly understood boundary conditions may contribute to inaccuracies.

Image analysis is an important aspect of many areas of science and engineering, and imaging will play an important role in characterizing self-assembled structures as well as in on-line process control. Development of effective noise identification and suppression, contrast enhancements, visualization, pattern recognition, and correlation algorithms should be co-opted where possible and adapted to the analysis of self-assembled structures.

Models of the self-assembly process also will be important. Because self-assembled structures can be diverse, those models are likely to be highly complex. Sensitivity analysis can be an important approach to the identification and control of critical parameters.

Adaptive and Responsive Materials

An area of great promise for the future is that of materials for which properties change in response to external influences. The most prominent is giant magnetoresistive (GMR) materials—materials for which the electrical conductivity can change by a few percent under the application of an external magnetic field. GMR materials moved from a laboratory curiosity to the dominant technology in computer memories within a decade—a startling example of how a new material can completely change a major industry. The invention of new materials has been an area in which the United States has played a central role; the current emphasis on focused, shorter-term projects has, however, made it very difficult to support a lively activity in new materials, which by definition are far from a final product.

Among the adaptive materials currently on the forefront are liquid crystals, electro- and magneto-rheological (ER/MR) fluids, thermo- and physioreponsive gels, and shape memory alloys. In all but the last case, these systems involve

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[4] A *voxel* is a volume-pixel. While a pixel is a two-dimensional point that has the attributes of height and width, a voxel is a three-dimensional point with the attributes of height, width, and depth.

fluid-solid interfaces, complex or dispersed suspensions, and external fields. Thus, all of the directions outlined above for self-assembly and interfaces come into play when pursuing these "smart fluids." Improvements in synthesis and spatial resolution of the external fields through soft-lithography (self-assembled monolayers, etc.) will provide new capabilities of control and tuning of these complex fluids.

Tools, Resources, and Infrastructures

The area of complex condensed matter depends crucially on the availability of appropriate tools for both fabrication and characterization. These tools are of "intermediate" size: they are neither a test tube nor a synchrotron. Typical tools—scanning probe microscopes, x-ray photoelectron spectrometers, electron microscopes, clean rooms—cost from $0.1 million to $5 million. They are shared-use facilities, but they must be local to the user group—travel to distance facilities for routine measurements is not practical.

Simulations in this area also require access to high-level computational capabilities. By definition, simulations involve both large numbers of atoms and dynamic behavior; both consume large numbers of CPU cycles. Because the field is so demanding on computer time, analytical theory is very important, even if it yields only approximate solutions.

Many of the tools required for the nanoscience revolution in materials involve sophisticated experiments requiring leadership, training, and infrastructure. User facilities such as high-resolution electron microscopes, synchrotrons and NMR facilities need to be easily accessible and provide adequate support for efficient experimentation.

The nanometer- to micrometer-scale dimensions of supramolecular assemblies present many challenges to rigorous compositional and structural characterization. Development of adequate structure-property relationships for these complex hierarchical systems will require improved measurement methods and techniques. The following areas constitute critical thrusts in instrument development.

- Many techniques ideally suited for nanostructure characterization unfortunately depend also on the substrate properties. For example, the reflectivity and conductivity of a substrate play an important role in the successful execution of the instrumental method. Hence, substrate-independent techniques are needed so that structure and/or behavior of the material can be investigated in a confined geometry, decoupled from the potentially invasive effect of the substrate-material interface.
- Feedback provided by on-line monitoring of self-assembling processes will play an increasingly important role in controlling the microscopic and macroscopic architecture of molecular assemblies. Successful adaptation of char-

acterization methods for noninvasive in situ monitoring will require miniaturization of many of the analytical devices commonly used for interrogating self-assembled structures. The revolution in microscopic identification and control provides new opportunities for chemists and chemical engineers. Promising routes to achieve this goal include the use of optical fibers in spectroscopic methods and the development of MEMS-based analytical instrumentation.

- Order and polydispersity are key parameters that characterize many self-assembled systems. However, accurate measurement of particle sizes in concentrated solution-phase systems, and determination of crystallinity for thin-film systems, remain problematic. While inverse methods such as scattering and diffraction provide measures of these properties, often the physical information derived from such data is ambiguous and model dependent. Hence development of improved theory and data analysis methods for extracting real-space information from inverse methods is a priority.
- Use of diverse techniques provides significant structural information in dispersed and thin-film systems. If significant advances in source intensities (e.g., higher neutron and x-ray fluxes, higher power diode lasers) and photon detector technology (e.g., high quantum efficiency, large bandwidth charge-coupled devices, CCDs) are achieved in the near term, these methods could be extended readily to studies of nanoscale features. Since the experimental and theoretical frameworks for these techniques are well established, extension to smaller length scales should be straightforward.
- The already critical need for molecular-scale compositional mapping will increase as more complex structures are assembled. Currently, electron microscopy, scanning probe microscopy (SPM) and fluorescence resonance energy transfer (FRET) are the only methods that routinely provide nanometer resolution.

In contrast to the mature instrumental techniques discussed above, a hitherto nonexistent class of techniques will require substantial development effort. The new instruments will be capable of measuring the thermal (e.g., glass transition temperatures for amorphous or semicrystalline polymers and melting temperatures for materials in the crystalline phase), chemical, and mechanical (e.g., viscoelastic) properties of nanoscale films in confined geometries, and their creation will require rethinking of conventional methods that are used for bulk measurements.

WHY ALL THIS IS IMPORTANT

Materials science and engineering is inseparable from chemistry and chemical engineering. The importance of materials is illustrated by the effects they have on the quality of human life—underscored by the way our society uses new materials and the technology they spawn to define epochs in history. The list of the 20 greatest engineering achievements of the 20th century, compiled in 2000 by the National Academy of Engineering,[5] contains many entries (for example, high-performance materials, automobiles, airplanes, electronics, computers, telephones, and fiber optics) that depend essentially on advances in materials science and engineering. From synthesis to processing to commodity manufacturing of materials, the tools of chemical science and engineering will be essential to defining the next century in these terms. New materials with predictable properties will provide worthy and formidable targets for design and synthesis, while processing and manufacturing these new materials will present significant challenging new objectives for chemical process-systems engineering.

The science of materials reflects the way that chemistry has changed—from a field concerned only with atoms and molecules and their properties in isolation, to a field increasingly concerned with organized interactive systems. This change opens opportunities and challenges in fundamental science that will let us ask not just: What are the chemical components of that stuff? We will be asking as well: How do those components interact to produce the properties of that stuff? The answers to such questions will greatly add to our understanding of the chemical universe.

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[5] *http://www.greatachievements.org/*

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Atmospheric and Environmental Chemistry[1]

Some Challenges for Chemists and Chemical Engineers

- Elucidate the entire complex interactive chemistry of our biosphere—the atmosphere, the earth, and its lakes, rivers, and oceans—and provide the scientific basis for policies that preserve our environment.
- Ensure that chemical manufacturing and chemical products are environmentally and biologically benign, never harmful.
- Learn how to make products that are stable over their necessary life but then undergo degradation so they do not persist in the environment or in living creatures.
- Invent agricultural chemicals that do not harm unintended targets in any way and are not overly persistent.
- Develop selective catalysts that enable the manufacture of useful products without producing unwanted waste products and without using excessive energy.
- Invent processes for the generation and distribution of energy that do not release greenhouse gases or toxic contaminants into the atmosphere.
- Help humans control their population growth by inventing birth control methods that are safe and effective, inexpensive, and widely available and accepted.

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[1] As part of the overall project on Challenges for the Chemical Sciences in the 21st Century, a workshop on The Environment will lead to a separate report. The reader is urged to consult that report for further information.

GOALS

Chemists and chemical engineers want to understand the chemical composition and behavior of the earth, its rivers, lakes, and oceans, and its atmosphere. What are the complex interactions among these systems that occur naturally, how are they influenced by human activity, and what will be the chemical and physical consequences that affect our environment? To what extent can the knowledge and capabilities of chemists and chemical engineers be used to understand and prevent or correct problems, either by direct chemical intervention or by guiding changes in human behavior? As a society, we want to be assured that the products we use are safe for us and our environment—and to be sure that the methods of their production do not harm us, our children, or our environment. The safety of our environment is not a local issue. Concerns about global climate change make it clear that chemists and chemical engineers will want to help—and will need to help—in addressing these important scientific issues on a worldwide basis.

Systems in place—ranging from laws and policies of government regulatory bodies to voluntary programs of the industry—are intended to anticipate, detect, and prevent unacceptable risks to the public, both now and in the future. The ability of chemists and chemical engineers to meet these challenges, as contributors to and beneficiaries of the chemical enterprise, requires that they utilize the best science available today and aggressively advance that science in the future. This ability will also be enhanced by educational efforts—not only efforts by the scientific community to increase public understanding of science and technology, but also changes in the ways that engineers and scientists are educated. Greater understanding of the societal implications of their work by scientists and engineers will enhance our stewardship of this planet.

PROGRESS TO DATE

Geochemists have made major progress in learning about the chemistry of the earth and its components, including rivers, lakes, and oceans. Much of this involves such fundamental theories as thermodynamics, but on a scale much larger than the molecular level that has been the past focus of the chemical sciences. In the last decade, the chemistry of the atmosphere has also been elucidated in much more detail. A field called earth systems engineering is emerging, and it will require further development, with the chemical sciences and engineering as a crucial component. This field will address matters such as global warming, carbon sequestration, and environmentally benign manufacturing. It will also address new analytical, computational, and assessment techniques through which global-scale interactions in complex systems can be better understood and optimized. Earth systems engineering is made even more intricate and involved by its international character. The factual, quantitative, and analytical input that can be supplied by chemical scientists will be of great value in this endeavor.

Chemists and chemical engineers have identified the processes that convert ordinary oxygen molecules (O_2) into ozone (O_3) in the high altitude ozone layer of the stratosphere, under the influence of ultraviolet light from the sun. Furthermore, chemists and chemical engineers have elucidated, through both experimentation and computational modeling, the processes by which extremely stable anthropogenic (human-generated) gases such as chlorofluorocarbon refrigerants cause degradation and depletion of the ozone layer. The ozone layer plays an important protective role for life on earth by blocking very-high-energy ultraviolet light; consequently, this fundamental atmospheric chemistry has important practical consequences. Similar understanding of the interaction of anthropogenic materials with water and with the minerals of the earth is also being developed by geochemists.

The chlorofluorocarbon effect on the ozone layer illustrates another chemical concern—the special problem that can arise when materials released into the environment are able to act as catalysts. If every chlorine atom generated in the upper atmosphere simply destroyed one ozone molecule, the effect would be minimal. But chemists have elucidated the catalytic cycle by which each chlorine atom destroys thousands of ozone molecules. It is particularly important for chemists to study and understand which substances can have such catalytic effects—and to learn how to prevent the release of such substances into the environment.

The interaction of gases such as carbon dioxide (CO_2) with earth and water has also been investigated. Carbon dioxide is in most respects a harmless molecule—the product of human, animal, and plant respiration and the starting material for the growth of plants by photosynthesis. It is also produced by burning carbonaceous fuels for energy, and in converting limestone to lime for cement production. It is now becoming clear that too much carbon dioxide in the atmosphere can contribute to what is called the greenhouse effect. The temperature of the earth's surface is governed by what happens to the energy in incident sunlight—how much of it is reflected back into space versus how much is retained by conversion into thermal energy, and how much of that is reemitted back into space as infrared radiation. There is a delicate balance among these processes, and a change in that balance can affect the overall temperature of the earth. Greenhouse gases absorb some of this infrared radiation and prevent its transmission back into space. Other gases, particularly water vapor, also contribute to the greenhouse effect, but carbon dioxide is of particular importance because CO_2 levels correlate with human activity. For this reason there has been extensive debate about the extent to which global climate change is anthropogenic.

Recent estimates indicate that the level of carbon dioxide in the atmosphere has increased by a third since the beginning of the industrial age, and that it contributes significantly to global warming. Other major contributors include methane, tropospheric ozone, and nitrous oxide. Methane is the principal component of natural gas, but it is also produced by other sources such as rice paddies and farm animals. Tropospheric ozone is generated naturally and by the sunlight-induced reactions of combustion by-products, and nitrous oxide is formed in microbial reactions, in part from nitrogen-containing fertilizers, and as a by-product of some chemical processes. Carbon dioxide and methane—generated by human activity—appear to be making the greatest contributions to global climate change. Both gases are more abundant in the atmosphere than at any time during the preceding 400,000 years.[2] Solution of this inherently chemical problem will require major contributions by chemists and chemical engineers.

At one point it was assumed that the earth, its oceans and rivers, and its atmosphere were so vast or self-cleansing that we could discharge anything into them without damage to our planet. We now know this is not true. Currently, we must deal with toxic waste dumps, with smog, with acid rain that kills forests, and with pollution of rivers and the ocean by chemical discharges. How did this happen?

Part of the problem is simply the slow accumulation of materials released into the environment. Any single activity may seem small and harmless, but all such activities add up. The combustion of fossil fuels has long been recognized as a major source of air pollution. For example, burning petroleum components in gasoline and diesel engines of vehicles can lead to air pollution by emission of unburned hydrocarbons and sulfur and nitrogen oxides produced during the combustion process. When this was realized, fuels were refined differently to reduce sulfur content and vehicles were fitted with catalytic converters, designed by chemists and chemical engineers, to remove the hydrocarbons and nitrogen oxides from vehicle exhaust. The catalytic converter was introduced in the U.S. automotive industry and is now used worldwide, an excellent example of the beneficial global effects of chemical science and technology. Fuel efficiency was also increased, so less fossil fuel had to be burned per mile traveled. This has provided major improvements, but the real solution may come from a change to other forms of energy production for transportation, as described in Chapter 10.

The chemical process industries make a huge contribution to civilization, but they have the potential for environmental pollution. During the early growth of the industry, many chemical companies built their plants in river valleys. The plants used the river water and subsequently returned it to the river with water-soluble by-products, while they discharged gaseous by-products into the air. Water and air pollution were serious problems near these plants. In recent decades, chemical manufacturing has undergone a revolution. Almost all chemical manufacturers in the United States, and increasingly worldwide, subscribe to a program called Responsible Care.[3] In brief, it involves a pledge by the manufacturers to make only products that are harmless to the environment and to its living occupants, and by processes that are also environmentally and biologically benign.

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[2] *Climate Change Science: An Analysis of Some Key Questions,* National Research Council, National Academy Press, Washington, D.C., 2001.

[3] *http://www.americanchemistry.com/*

Another important initiative is called green chemistry,[4] developed as part of efforts to reduce pollution at the source; it is defined as "the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances."[5] Originated in the United States (where prestigious awards for accomplishments in this area are given annually), it is increasingly becoming a worldwide program.

Benign processes help make chemical plants into good neighbors, and their operators into good citizens, but the products themselves are now being examined with a new perspective. For example, DDT (invented by Paul Müller, who received a Nobel Prize in 1948 for this invention) was an effective insecticide that greatly reduced the occurrence of insect-borne diseases such as malaria. However, its widespread use caused problems, because it is too stable. DDT persists in the environment and enters the food chain, a phenomenon that led to the nearly complete elimination of DDT use after it was shown to interfere with bird reproduction. At one point it was believed that persistence was a good thing, since the insecticide would keep on working, but it is now recognized that persistent chemicals can accumulate in the environment and lead to new or unexpected problems.

A similar situation is found with the herbicides that help make agriculture more productive by controlling weeds. Advantages are now recognized for herbicides having limited persistence, lasting long enough to do the job and then harmlessly disappearing.

Persistence was also the unforeseen problem with the role of chlorofluorocarbons (CFCs) in degrading the earth's ozone layer. CFCs were invented to replace toxic and dangerous gases (such as sulfur dioxide) that had been used as the working fluid for compressors in early refrigerators and air conditioners. Indeed, CFCs are so unreactive under normal conditions that they are quite harmless to humans and other living things. However, they are so stable that they diffuse throughout the atmosphere. When they reach the stratosphere—where the ozone layer is found—the greater intensity of high-energy radiation from the sun finally causes slow decomposition of the CFCs. This decomposition process produces chlorine atoms that catalyze the destruction of ozone in a chemical sequence that is now well understood. For elucidating these chemical processes in the stratosphere, Paul Crutzen, Mario Molina, and F. Sherwood Rowland received a Nobel Prize in 1995.

While the high stability and persistence of CFCs provided a major advantage for such applications as refrigeration and air conditioning, escape of the gases into the air has resulted in unacceptable changes in the upper atmosphere. The solution to the problem is to invent new relatives of CFCs that are adequate coolants but are less environmentally persistent. Chemists have indeed created such new substances, which are now replacing CFCs.

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[4] *http://www.epa.gov/greenchemistry/index.htm*

[5] *http://www.epa.gov/greenchemistry/whatis.htm*

Green Chemistry

A common definition of green chemistry, which clearly encompasses considerable chemical engineering as well, is “the design, development and implementation of chemical processes and products to reduce or eliminate substances hazardous to human health and the environment,” (P. T. Anastas and J. Warner, *Green Chemistry Theory and Practice,* Oxford University Press, Oxford, 1998). A more recent article expands this definition to twelve principles (M. Poliakoff, J. M. Fitzpatrick, T.R. Farren and P.T. Anastas, *Science*, 297, 807-810 (2002).

1. It is better to prevent waste than to treat or clean up waste after it is formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health or the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g., solvents, separation agents, and so forth) should be made unnecessary wherever possible, and innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. A raw material or feedstock should be renewable, rather than depleting, whenever technically and economically practicable.
8. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function, they do not persist in the environment, and they break down into innocuous degradation products.
11. Analytical methodologies need to be developed further to allow for real-time in-process monitoring and control before the formation of hazardous substances.
12. Substances, and the form of a substance used in a chemical process, should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

Many of the problems that affect our environment are the result of unexpected effects that accompany an entirely reasonable intention. The effect of CFCs on the ozone layer is such a case. Chlorofluorocarbons seemed to be perfect—they were chemically stable and noncorrosive, and they were not at all toxic—as replacements for the earlier toxic refrigerants. But then the ozone effect was discovered. Similarly, DDT seemed to be a perfect insecticide—controlling mosquitoes and other insects that transmit disease—until its effect on birds was discovered. A more recent example is methyl tertiary-butyl ether (MTBE), a fuel additive that improves the performance of gasoline in automotive engines. Unfortunately, spillage and leakage from underground gasoline tanks has allowed MTBE to enter the ground water. This has led to concern about the biological effects of MTBE and a probable end to its use.

To prevent or at least minimize such problems, we must better understand the environment at all levels, including the fundamental chemical processes that affect it. We have learned the lesson that when assessing the fate of new products in the environment, we should not underestimate the potential of these to appear in unexpected places. The recognition, avoidance, or solution of complex environmental problems requires the expertise of a variety of science and engineering disciplines. Only then will it be possible to produce realistic evaluations of how new compounds will be distributed and will act in the ecosystem. In addition to chemistry and biochemistry, fields such as solution thermodynamics and transport phenomena in which many chemical engineers work, as well as earth sciences and environmental engineering, have crucial contributions to make.

Another environmental problem is the contamination of soil by heavy metals or organics. These soil-based contaminants can produce health hazards by release of volatile substances, contamination of groundwater, or accumulation of heavy metals by plants growing in the soil. Incineration has been used to treat soils heavily contaminated by organic materials, but this approach is expensive and may result in other environmental problems. The potential toxicity of contaminated soils is governed by a variety of factors; the factors that affect bioavailability of soil-bound contaminants or the movement of contaminants in subsurface fluids are not well understood. Close cooperation of chemists and chemical engineers will be needed to gain the necessary understanding.

One promising form of treatment is bioremediation. Microbes in the soil are capable of converting organic chemicals to other compounds, and in the ideal case to CO_2 and H_2O, and some microbes have been found to convert heavy metals to complexes with reduced toxicity. Microbes can be harnessed through addition of nutrients, other chemicals, or specific microbes to enhance beneficial microbially mediated chemical reactions. However, the complex chemistry and biology of subsurface soil systems makes it difficult to achieve predictable responses. A much deeper knowledge of the interaction of the chemistry of the soil, fluid movement, and microbial physiology is an important challenge to making bioremediation a fully practical technology. (see Chapter 7 for discussion of related matters).

A half-century ago, people were only beginning to understand the extent to which human activity could affect the environment, often in very negative ways. Many of the early problems of pollution were the result of chemical processes, and "chemistry" received the blame. But "chemistry" has also provided solutions, and dramatic improvements have occurred. No longer do industrial plants belch foul smoke into the atmosphere, and no longer do chemical plants discharge brown or orange sludge into nearby streams and rivers. These improvements have been implemented by chemists and chemical engineers, and they have been implemented in ways that often have provided economic benefits to the United States.

This chapter has focused on the chemistry of the earth and its immediate atmosphere, but the concept of "environment" need not stop with the earth's atmosphere. Molecular chemistry also goes on in space, and it is an area of interesting chemical science. Large, although extremely diffuse, clouds of molecules exist between the stars, and such clouds are believed to be the origins of stars. So far, the chemistry in the clouds has been investigated not by direct sampling, but instead by observing the light that is emitted from them. Observations of such light in the microwave range have led to the identification of many remarkable substances—and of the likely transformations that they undergo. Chemists have synthesized some of these unusual substances here on earth so their microwave radiation can be compared with that from space, for identification of the space molecules. In addition, computational chemistry has reached the stage at which it is possible to predict the microwave radiation that some molecules would emit, again enabling earth-bound scientists to obtain evidence for the structures of materials that exist only in outer space.

CHALLENGES AND OPPORTUNITIES FOR THE FUTURE

Considerable progress has been made in understanding the environment and the chemical processes that affect the environment. However, the preceding discussion clearly shows that many challenges remain. Chemical scientists must learn how to make useful substances that have limited persistence—and will generate only completely harmless products when they degrade.

A full understanding will be needed of the complex chemistry by which the atmosphere and the earth interact, including the dependence of global climate on carbon dioxide concentrations in the atmosphere. Is there a way to deal with the carbon dioxide produced by burning coal and other hydrocarbon fuels so that it causes no problem? Chemical scientists will need to investigate effective ways to trap CO_2 that would otherwise build up in the atmosphere. Alternatively, it will be necessary to find ways to reduce the generation of carbon dioxide. As human activity continues to destroy forests, will this affect the carbon dioxide cycle and levels, and what can be done about that?

Supercritical Processing

Today we are witnessing a "green" revolution as it pertains to manufacturing industries' implementation of carbon dioxide as a replacement for their dependency on water and organic solvent usage. A major impetus for this conversion is driven by a concern for our environment—to reduce a company's footprint on our planet by reducing their usage of solvents and water. In addition, because of the low heat of vaporization of supercritical CO_2 (sCO_2) relative to water and organic solvents, corporate motivations also include the reduction of energy usage associated with using CO_2-based processes relative to conventional solvents and water. However, beyond pollution prevention and energy efficiency issues, sCO_2 is finding increasing appeal because of increased performance attributes associated with its inertness to many chemistries, to its exceedingly low surface tension and viscosity, and to its adjustable solvent quality due to its compressibility, especially in the supercritical state. Its critical temperature is conveniently located at 31°C, and it is both nontoxic and inexpensive. Recently, sCO_2 has been or is in the process of being commercialized in:

- Extraction processes for natural products including the decaffeination of coffee and tea and the isolation of nutraceuticals, flavors, and fragrances
- The production of melt processable plastics based on fluoroolefins
- The replacement of toxic solvents used in professional garment "dry" cleaning and critical/precision cleaning of manufactured goods
- Coating/encapsulation technologies for pharmaceuticals, textile apparel, and manufactured parts such as in the automotive industry
- Particle formation for use in drug delivery and xerography

These processes are enabled by breakthroughs in many areas. A fundamental understanding is emerging of the rational design of surfactants for sCO_2—molecules that reversibly self-assemble as the density of compressible sCO_2 is adjusted. Such surfactants enable the stabilization of polymer colloids in sCO_2 for heterogeneous polymerizations and for the emulsification of numerous sCO_2-insoluble substances including proteins, water, and catalysts to name a few. Creative engineering unit operations have been designed that allow for continuous reactions, automated reaction/separation schemes, and novel membrane-based separations. And finally, creative combinations of chemistry (novel compounds such as sCO_2-soluble functional polymers) with sCO_2-based applications have enabled entirely new processes.

Future commercial use of CO_2 will surely include such diverse applications as thin-film deposition for microelectronics using recently developed pressurized spin-coating and free meniscus coating instruments; in separations of value-added products from fermentation broths in biotechnology fields taking advantage of the immiscibility of CO_2 with water; and as the solvent in a broad range of synthesis including transition metal and enzymatic catalysis. All of these applications will lead to sustainable manufacturing methods that are not only ecologically preferable, but in themselves are enabled by working with a unique solvent that has the density of common liquids but the transport properties of a gas.

Humans affect the environment through simple living activities—they generate waste. Ordinary waste sites, in which people place trash and garbage, generate methane by microbiological action, and methane is one of the most potent greenhouse gases. Is this a significant problem, and if so, what can be done to prevent or solve it? Will it be possible to recycle waste that we currently bury, perhaps ameliorating the problem of waste sites? And if so, could we recover some of the chemicals and energy that were used to manufacture the discarded materials? Chemists and chemical engineers will need to devise the ways in which materials that are harvested from the earth can be recycled, not just discarded or burned. One of the approaches is bioremediation, in which microorganisms, perhaps genetically modified, are used to deal with the waste. This approach has already been used to some extent in dealing with oil spills. The ultimate goal is sustainability: using and recycling materials so that we do not simply exhaust the substances we have inherited, thus leaving less for our descendants.

The future production of chemicals will require continued awareness of possible unforeseen consequences, particularly with substances that persist in the environment. This will require investigation of how these substances interact with the environment, and it will necessitate the invention of new substances. As noted above, new and safe refrigerants will be needed that lack the persistence of CFCs. The world's food supply will depend on the discovery of new insecticides that do not harm unintended targets in any way and other agricultural chemicals such as herbicides and fertilizers that are neither harmful nor overly persistent. Other sectors of the chemical industry will rely on the invention of new and selective catalysts that enable the manufacture of useful products, including polymers, without producing unwanted waste products and without using excessive energy.

The existence of waste from past activities has created problems that will demand the attention of chemists and chemical engineers. Environmental cleanup —of toxic wastes, of contaminated groundwater, of radioactive waste—is a daunting challenge. Only by developing effective ways to clean up contaminated sites—and by developing processes by which such contamination can be prevented in the future—will it be possible to take full advantage of the technological opportunities that science has provided over the last century.

There are serious questions about the effect of continued growth of the human population. We often focus on the matter of adequate food production, but large populations also affect the environment and our need for energy. Chemists can furnish the tools to help deal with the political and social questions. Some population growth occurs not because it is intentional, but because adequate methods for birth control are unavailable to people in poor countries. Thus one challenge for chemists is to develop better methods that would be safe, effective, and inexpensive and would enable all people to pursue their own decisions regarding population growth.

Small amounts of some contaminants can be serious. When we burn coal, not only do we produce carbon dioxide, the major product, but we can liberate small amounts of mercury and larger amounts of sulfur dioxide. The mercury can form toxins that harm fish as well as humans, while sulfur dioxide can produce acid rain that destroys forests and water supplies. How can these contaminants be most effectively removed or dealt with? And how can we generate the energy that we need without releasing such by-products?

Environmentally responsible methods to manufacture useful products and to generate energy still need the largest contributions from chemists and chemical engineers. As we reexamine all human activities with a fresh eye, to see their environmental impact, the continuing challenge will be to invent new ways to achieve what society needs. Understanding the environmental effects of what we do is the first step, a job for basic chemical science. Inventing ways to improve what we do while still meeting human needs is a job for applied chemistry and chemical engineering. The opportunities for our science to improve the human condition will continue to pose exciting and important challenges.

Important educational challenges also confront the chemical sciences. Continuing emphasis on science education by government, foundations, industry, and educational institutions at all levels is essential. It is also essential to engage the professional practitioners in the chemical sciences—chemists and chemical engineers engaged in the broad spectrum of activities that characterize these fields—in education. Public outreach programs of professional societies like ACS and AIChE are important components, but more effort is needed both at the grassroots community level and in the improvement of the visibility of the chemical sciences through mass media. Greater emphasis in science and engineering education on the human aspects of the scientific endeavor is needed. Chemists and chemical engineers must also continue their own educations. This will improve their ability to contribute to a broader public understanding of science and technology, and it will enhance the contributions they can make to society.

We have come a long way. But there is still a long way to go. If we are to provide a favorable legacy for future generations, chemists and chemical engineers will need to develop effective ways to clean up existing waste and find ways to prevent the generation of waste in the future. And most importantly, they will need to develop a system that is fully sustainable—that will safely provide the energy, chemicals, materials, and manufactured products needed by society while neither irreversibly depleting the earth's scarce raw materials nor contaminating the earth with unhealthy by-products.

WHY ALL THIS IS IMPORTANT

Human activity, including manufacturing, can damage our environment if we are not thoughtful and careful. We do not want to live on a planet where the air and water are dangerous to health, or where life is not possible for various plants and animals. In the past society did not worry enough about such questions, but now we have learned to take them seriously. Fortunately, it has turned out that environmentally benign chemical manufacturing, using the principles of Responsible Care, is both environmentally useful and economically acceptable. In fact, many companies have discovered that good environmental practices are actually cost effective. In any case, the challenge is to learn how to continue to develop a modern civilization without causing environmental damage.

The consequences of human action on the environment are not always completely foreseeable, so there is also the challenge to recognize the likelihood and magnitude of those consequences that we can foresee, and to recognize patterns of particular vulnerability. To meet this challenge it is essential that we continue to cultivate a strong base of fundamental knowledge in the chemical and biological sciences—for we will need those tools not only to create new technologies, but also to anticipate their consequences. We must approach the creation of science and technology for human advancement with intelligence, knowledge, and reason. That is, after all, what makes the human animal special.

10

Energy: Providing for the Future[1]

Some Challenges for Chemists and Chemical Engineers

- Develop more stable and less expensive materials and methods for the capture of solar energy and its conversion to energy or to useful products.
- Design inexpensive, high-energy-density, and quickly rechargeable storage batteries that make electric vehicles truly practical.
- Develop practical, less expensive, more stable fuel cells with improved membranes, catalysts, electrodes, and electrolytes.
- Develop materials, processes, and infrastructure for hydrogen generation, distribution, storage, and delivery of energy for vehicles.
- Develop photocatalytic systems with efficiencies great enough to use for chemical processing on a significant scale.
- Learn how to concentrate and securely deal with the radioactive waste products from nuclear energy plants.
- Develop practical superconducting materials for energy distribution over long distances.

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[1] As part of the overall project on Challenges for the Chemical Sciences in the 21st Century, a workshop on Energy and Transportation will lead to a separate report. The reader is urged to consult that report for further information.

- Develop technologies and catalysts for the cleaner use of coal as a fuel and for the conversion of coal to other fuels.
- Develop methods to use biomass as a renewable fuel source.
- Develop technologies for the improved extraction of conventional fossil fuels, including unconventional sources such as oil shale, tar sands, and deep-sea methane hydrates.
- Develop practical and environmentally responsible methods of carbon dioxide capture and sequestration.
- Develop lower cost, lighter weight, more durable, more resilient, and recyclable materials for the construction of safer lighter-weight vehicles.
- Develop improved materials, processes, and practices that will allow reduced energy use per unit of gross domestic product.

Chemistry and chemical engineering are intimately concerned with the generation and use of energy. We need energy for manufacturing, for transportation, for heating and cooling our homes, for lighting, and for cooking. Currently about 85% of the world's energy is obtained by burning fossil fuels—petroleum, natural gas, and coal—but this must change soon. Affordable supplies will become scarcer, and burning fossil fuels produces carbon dioxide that contributes to the greenhouse effect by which solar energy is trapped within the atmosphere and warms the planet. Burning fossil fuels, at least with current technology, also produces oxides of nitrogen and sulfur and other pollutants that affect plants and animals.

The problem of having enough clean energy is related to population, standard of living, and the efficiency with which energy is used to provide a unit of economic output. Humans will always need energy, and chemists and chemical engineers will continue to play a central role in learning how to produce and use it.

GOALS

Chemists and chemical engineers will need to join with experts in other disciplines to invent new ways to generate and transport energy for human use and provide for the needs and aspirations of a growing population in a sustainable manner. New ways will also be needed to minimize the energy used for human activities, including manufacturing.

PROGRESS TO DATE

Generating Energy

Once petroleum is removed from the earth it is refined. It is separated into its various components by distillation, producing not only gasoline but also higher boiling materials such as diesel oil, kerosene, lubricating oil, and asphalt. Then part of it is *cracked*, converting some of the larger less volatile molecules to smaller ones more useful in gasoline, and it is *reformed*, transforming some of the molecules into others with smoother burning properties. Some of the products are also used as chemical raw materials, in addition to fuels.

Both cracking and reforming use special catalysts and processes. The overall process is highly efficient, so that essentially none of the components of petroleum are wasted. However, most agree that the supply of inexpensive petroleum will run out sometime, although there is disagreement as to exactly when. At current rates of consumption, we may still be using petroleum as a major source of energy 50 years from now. Natural gas may last 100 years, while coal reserves could last for perhaps four centuries. If population growth and standard of living improvement lead to increased energy consumption rates despite conservation efforts, the currently economically recoverable reserves will be depleted in a shorter period of time. In any event, development of more expensive fossil fuel sources—such as oil shale, tar sands, methane hydrates that are found at the high pressure of the deep sea, and coal, oil, and gas that current extraction technology leaves behind—will also be required.

Chemists and chemical engineers have developed processes for the gasification of coal, converting it by chemical transformation into *syngas*, a cleaner, more convenient energy source. They have also devised ways to convert coal into a liquid that can be used in place of gasoline in combustion engines. However, whether coal is used as a solid or converted to a liquid or gas, when it is burned the result is still carbon dioxide, a greenhouse gas.

Some chemical processes use energy directly to drive the transformation. For example, the conversion of iron ore, iron oxide, to iron metal requires chemical energy to remove the oxygen atoms. In early times the iron ore was heated with charcoal; in more recent times it is heated with refined coal (coke), but in both cases the result is conversion of coal or wood into carbon monoxide, which is toxic but can be burned to carbon dioxide to generate needed heat. There is now interest in devising processes that do not use carbon in this way, but use electrical energy to avoid the production of carbon oxides.

There is also interest in finding feasible and harmless ways to capture and permanently sequester carbon dioxide underground or in the oceans, thereby preventing its accumulation in the atmosphere.[2] Carbon dioxide concentration in the

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[2] *Carbon Management: Implications for R&D in the Chemical Sciences,* National Research Council, National Academy Press, Washington, D.C., 2001.

atmosphere has increased by about one-third since the beginning of the industrial revolution. Unless combustion of fossil fuels is halted, or unless carbon dioxide from fossil fuel burning is completely and permanently sequestered, carbon dioxide concentrations in the atmosphere will inevitably continue to rise with potentially significant consequences for global warming.

Alternatives to Fossil Fuels

Solar Energy

Almost all of our energy has come from the sun. This is obvious when we burn wood, in which solar energy has been in a sense stored in a tree by photosynthesis. When whale oil was a significant fuel it was only a little more indirect—the whales ate plant material that was also produced by sunlight, and then converted that food energy into the energy in their oil. Petroleum, natural gas, and coal are also just stored forms of solar energy, from plants and animals that lived and were buried long ago, while hydroelectric and wind power are derived from more contemporary solar-driven oceanic evaporation and atmospheric pressure gradients.

In photosynthesis, plants convert carbon dioxide into oxygen of the air and carbonaceous materials of the plant; burning the plants simply sends the carbon back to carbon dioxide again. Thus the cycle—carbon dioxide plus light to form plant material and oxygen, then burning the plant material to consume the oxygen and regenerate carbon dioxide and liberate energy—is one way to capture the energy of the sun. The critical need is to avoid overloading the cycle, producing carbon dioxide faster than it can be recycled into plant material—a significant concern for current levels of fossil fuel combustion.

Although energy systems are currently dominated by fossil fuels, alternatives need to be developed. There is no obvious single solution, but a variety of approaches could make useful contributions. One plan would be to grow special grasses or other plants that are particularly efficient at converting sunlight into biomass (plant matter), then convert the biomass to electricity either by burning or by some version of a fuel cell. Genetic engineering may permit us to design new green plants that are particularly efficient at converting sunlight into useful fuels. Water and arable land would be needed for this scheme, but it is argued that we do not yet need all the arable land for the production of food and fiber. Another alternative would be to encourage the growth of phytoplankton in the ocean by intentional fertilization with limiting micronutrients such as iron. The process would serve as a mechanism for sequestering some carbon dioxide from the atmosphere; the resulting organic material would not be harvested as fuel but some instead would sink into the ocean depths before completing the cycle back into carbon dioxide. As with other proposals for carbon sequestration, there is no scientific consensus on its efficacy and safety.

Scientists, including chemists and chemical engineers, have also been pursuing the direct capture of solar energy, either for heating or for directly generating electricity.[3] One plan would cover significant amounts of arid desert and other surfaces such as rooftops with photovoltaic cells that directly convert solar energy into electricity. At the present time, photovoltaics can convert as much as 30% of the incident sunlight to electricity. The technical challenge, however, is to devise materials and manufacturing processes for photocells that are cheap, long lasting, and efficient in the conversion of light to electricity; ways are also needed to collect, store, and distribute the energy when and where it is needed. These problems have not yet been completely solved. A related advance is the invention of electrically conductive polymers, which are not metals. Alan J. Heeger, Alan G. MacDiarmid, and Hideki Shirakawa received a Nobel Prize in 2000 for opening up this important new area of science.

In an alternative way to take advantage of the sun's energy, photocells are under development using sunlight to drive chemical transformations, perhaps even producing chemicals that in turn could be used to generate electricity. For example, the photochemical generation of hydrogen, by splitting water, could be combined with a hydrogen fuel cell in this way. This area strongly depends on basic research in photochemistry.

Nuclear Energy

An alternative to solar energy is provided by nuclear energy—currently the source of 7% of the world's total energy and 20% of U.S. electrical energy. Chemists and chemical engineers have devised the processes for producing the nuclear fuels from crude uranium ores. In many countries nuclear power plants are major sources of electricity (as much as 75% in France), but one of the problems is nuclear waste. A typical nuclear energy plant produces 20 metric tons of radioactive waste each year. Chemists and chemical engineers are working to devise methods to separate the radioactive material from the inert material in which it is produced. If this is successful the volume of radioactive substances to be handled will be much less, and some of the purified radioactive materials may be available for other uses (including medical diagnostics and treatment). As another approach, converting the waste products to tough ceramics could make them stable for very long periods of time. The development of safe methods for dealing with radioactive waste—together with public acceptance of them—pose a challenge to which chemists and chemical engineers can respond.[4]

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[3] For further discussion of this topic, see ref. 1 and ref. 2.

[4] See for example: *Electrometallurgical Techniques for DOE Spent Fuel Treatment: Final Report,* National Research Council, National Academy Press, Washington, D.C., 2000; *Alternatives for High-Level Waste Salt Processing at the Savannah River Site,* National Research Council, National Academy Press, Washington, D.C., 2000.

Nuclear energy offers many advantages if the waste problem can be solved. The fuel is inexpensive, the energy can be generated near where it is to be used, and there are no greenhouse or acid rain effects. Of course, a special problem with nuclear energy is the hazard if the plant is run carelessly, and it is possible that the operation of a nuclear power plant could be diverted to develop material for nuclear weapons or the radioactive by-products could be used in terrorist attacks. However, it is important to solve these problems so that the currently negative public perception of nuclear energy undergoes a change, and permits nuclear energy to make its full possible contribution to the world, particularly after we have stopped burning fossil fuels.

Whether nuclear power generation increases as a contributor to our energy supply or merely continues on its present course, the aging population of nuclear chemists and engineers poses a significant concern. There has been a steady reduction in the number of university programs in nuclear chemistry, radiochemistry, and nuclear engineering—and in the number of graduates they produce.[5] Unless a new pool of expertise is developed, it will become increasingly difficult to safely operate existing reactors, manage the radioactive waste that will be produced (along with that which already exists), and clean up radioactive contamination from earlier activities.

Water and Wind

Approximately 10% of U.S. electrical energy is produced by hydroelectric dams.[6] Although there are few economic and environmentally acceptable dam sites remaining, in some places it is possible to use wind power, or perhaps even the ocean tides, to generate electricity. Here the opportunity for chemists and chemical engineers is the invention and production of modern materials that can make such approaches possible.

Energy Efficiency, Conversion, Storage, and Distribution

In recent years, much attention has been devoted to improving the efficiency with which energy is produced and used by society in general and also in chemical manufacturing. Higher fuel efficiency in automobiles, better insulation materials and construction practices for homes, and energy efficient lighting and ap-

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[5] *Nuclear Education and Training: Cause for Concern?* The Nuclear Energy Agency, Organisation for Economic Co-operation and Development (OECD), Paris, 2000 [*http://www.nea.fr/html/ndd/reports/2000/nea2428-education.pdf*]; *Training Requirements for Chemists in Nuclear Medicine, Nuclear Industry, and Related Areas,* Report of a Workshop, National Research Council, National Academy Press, Washington, D.C., 1988.

[6] *Renewable Power Pathways: A Review of The U.S. Department of Energy's Renewable Energy Programs,* National Research Council, National Academy Press, Washington, D.C., 2000, p. 116.

pliances are familiar examples. Internal combustion-electric hybrid vehicles are another area in which multidisciplinary science and engineering research is striving to produce extremely efficient, if perhaps not yet economically practical, transportation systems. For electrical power generation, complex systems such as coal-gasification combined-cycle and natural gas combined-cycle are being installed to reduce the amount of carbon dioxide produced per unit of electricity generated. A combined-cycle generator increases efficiency by capturing heat from the gas-turbine exhaust stream and produces additional power with a steam turbine. As a consequence of electricity deregulation, various heat and power cogeneration and distributed power generation schemes with micro turbines or fuel cells are also being explored. Again, contributions by chemists and chemical engineers will be critical, especially in the development of high-temperature and other advanced materials.

Electrochemical Cells

Instead of burning fuels such as petroleum or coal or natural gas to produce steam for electrical turbines, electrochemistry can be used to generate electricity directly from chemical reactions—thus avoiding the waste of energy and the pollution that comes from combustion. This approach is particularly attractive for use in portable energy sources and vehicles. A common example of such an electrochemical cell is an old-style flashlight battery that cannot be recharged. In such a battery, a metal such as zinc gives up electrons as it is oxidized to a zinc ion, while another material such as manganese dioxide is reduced by those electrons to form manganese ions. The battery is constructed with separators or membranes in such a way that the electrons from the zinc must travel outside the battery through an external circuit before returning to the battery to reduce the manganese dioxide. In this way electricity is used directly. The zinc metal and the manganese dioxide were both originally made in a factory by oxidation-reduction reactions of zinc salts and from manganese salts, so the battery represents a convenient way to store and deliver electricity.

Batteries have been developed from many pairs of chemicals capable of being oxidized and reduced. Some systems are rechargeable; after the chemicals in the battery have been exhausted, the reactions can be reversed by the application of an external source of electricity. The lead-acid automobile battery is a familiar example. In many applications, such as cell phones and laptop computers, the weight of a portable electricity supply is critical. This has led to the development of batteries based on lightweight lithium chemistry, for which challenges still remain.

Electrochemists have also learned how to make electrochemical cells in which one of the reactants is continuously supplied from outside the cell rather than contained within. One example is the zinc-air cell in which particles of zinc metal contained in the cell react with the oxygen of the air brought in from outside the cell to make zinc oxide, again with the generation of electricity. One can imagine a scenario in which such a cell could replace the petroleum-fueled engine of an automobile. The vehicle would be driven by an electric motor with the electricity supplied from a zinc-air cell. When all the zinc had been oxidized, a "service station" would remove the part of the cell with the zinc oxide and replace it with a fresh supply of zinc metal. The station would return the zinc oxide to a factory where electricity would be used to convert it back to zinc metal.

Fuel Cells

Electrochemical cells in which *both* reactants are continuously supplied from outside the cell, particularly those in which the reactants are oxygen and an otherwise combustible fuel, are generally referred to as fuel cells. Chemists and chemical engineers have devised a large number of fuel cells that differ in the reactants used, as well as in the separators, electrolytes, catalysts, operating temperatures, and other construction details. One example uses hydrogen and air. The cell reaction converts hydrogen fuel and the oxygen from the air to water, just as if the hydrogen were being burned. But this process generates electricity directly with a greater energy efficiency than that obtained from a process such as burning the hydrogen in a combustion turbine generator. A hydrogen fuel cell also operates in a cycle. The reaction of hydrogen and oxygen in the fuel cell to produce water is one part of the cycle. Elsewhere, a source of electricity could be used to electrolyze water and generate hydrogen and oxygen. The net result is to move energy from an electrical generating plant to a remote fuel cell.

A fuel cell avoids the production of nitrogen oxide pollutants that are generally formed in combustion processes. Nitrogen oxides formed during generation of the energy needed for production of hydrogen (or other fuel) can be removed by scrubbing the exhaust gases in the generating plant. Hydrogen fuel cells were first used in the space program (with pure oxygen rather than air), but they are being developed for a variety of terrestrial applications that range from portable electronics, to vehicles, to back-up emergency power systems.

There are still many unsolved problems for hydrogen fuel cells. One is the rate of reaction of the oxygen at the electrodes, which is not yet as rapid as desired. Related to this is the high cost of current membrane and catalyst systems. Another unsolved problem is how to transport and store hydrogen safely for use with the fuel cell. For space applications, hydrogen has been stored as a cryogenic liquid. For terrestrial applications, one approach is to store the hydrogen as a very high-pressure gas in very strong lightweight cylinders made of advanced composite materials. Chemists and engineers are working on other approaches, such as adsorbing the hydrogen on carbon or spongy nickel, or as metal hydrides that can be stored safely at low pressure. But this and related problems have not yet been solved. When they are, we could have what has been called the "hydrogen economy."

In another version of a fuel cell, a carbon compound such as methanol (from natural gas or from the reaction of coal with water) reacts directly in an electrochemical cell with the oxygen in air to form water and carbon dioxide. This approach has fewer problems with storage of the fuel, and it has higher efficiency than power production from combustion of the same fuel—but it still produces carbon dioxide with its contribution to global warming. The performance of current fuel-cell catalysts may be degraded by carbon monoxide, an intermediate in the reaction with carbon-based fuels. In yet another variant, a hydrocarbon is caused to react with water in a separate device called a reformer to produce hydrogen along with a mixture of carbon monoxide and carbon dioxide; after separation, the hydrogen can be fed to a conventional hydrogen fuel cell. This approach avoids carbon monoxide degradation of the fuel cell performance, but it still produces carbon dioxide.

Although there is still much to do to make fuel cells widely practical, experimental automobiles have recently been exhibited that are powered by fuel cells. Thus there is every reason to expect fuel cells to play a major role in electricity production in the future.

Storage Batteries

In the above scenarios the energy to produce the reactants for a battery or fuel cell was supplied in a factory, but another possibility is a storage battery that can be easily and quickly recharged either at a service station or at home. The familiar lead/acid car battery is an example, but it is not good enough to replace combustion of gasoline as the main power source in typical transportation vehicles. The batteries are too heavy and take too long to recharge.

What is needed is a high-capacity storage battery that is lightweight, inexpensive, long lasting, and rechargeable. The batteries now used in golf carts and in some recent electric automobiles do not meet all these criteria, but there is active research by chemists and chemical engineers to develop such batteries. When they exist, drivers will be able to stop at a service station and recharge their batteries in 10 to 15 minutes, then drive on for another 300 miles before a recharge is needed. In another scenario, the drivers might simply trade in their depleted batteries for others that have been recharged by a service station. When the problems are solved, we will be able to reduce our dependence on petroleum-fueled automotive engines.

We also use small rechargeable batteries to power cell phones and portable computers. They are reasonably light and have the capacity to go for some hours before requiring recharging, but improvements are still needed. As chemists and chemical engineers develop better battery technology we can expect to be freed from the need to recharge the batteries in our computers or cell phones quite so often.

Energy Distribution

Portable energy is important for vehicles and small electronic objects such as cell phones, but we also need to distribute energy from the generating plant to the place where it is to be used. Whether it is generated using photocells in the desert, by growing biomass in agricultural areas, or by operating nuclear power plants, it must go from there to the manufacturing plants and homes where it is needed. Currently this is done with power lines made of ordinary conducting materials such as copper or aluminum, but the electrical resistance of those metals results in considerable loss of energy. Thus there is great interest among chemical scientists in developing practical superconducting materials for power distribution.

Superconductors pass electricity with no resistive loss, but so far they operate only at extremely low temperatures, and are impractical for power distribution. However, as the basic science of materials progresses it is hoped that eventually superconductors will become practical for operation closer to normal temperatures while carrying a large current flow. This is a particularly difficult challenge, but if it can be met, the rewards will be enormous. There is already progress—superconducting power cables that can operate when cooled by liquid nitrogen are being made for short-distance power distribution in some urban areas.

The approach described above involves the idea that there is a central power plant from which electricity is distributed, but there is another choice. It might be possible to distribute the power generation itself, having small generators locally sited where the power is used. Already many large buildings have their own power generators (as do some private homes), although these are primarily for emergency use. This distributed approach offers the advantage that power is generated locally and only when needed, so energy losses from transmission would not cause problems. For this approach, fuel cells may have an important role if they become practical and can operate using locally available fuels.

CHALLENGES AND OPPORTUNITIES FOR THE FUTURE

A variety of opportunities and challenges have been described in the preceding section along with an indication of where current progress is inadequate. We must eventually learn how to operate in a world that is not energized by burning fossil fuels, and the opportunities and challenges are clear. In the meantime, while we are still burning coal and hydrocarbons, we need to learn how to deal with the carbon dioxide that is produced. This must be done to address the problem of global climate change and to eliminate the environmentally harmful side products of combustion. We need to devise better ways to use solar energy, for example by creating practical cells for conversion of sunlight to electricity. We need to replace combustion by fuel cell technology, and we need to solve the problem of how to transport and store hydrogen. We need to invent rechargeable batteries that are practical for vehicles that have electric motors instead of gasoline engines. Advances in both basic and applied chemistry and chemical engineering are needed to achieve these goals.

WHY ALL THIS IS IMPORTANT

The challenges and opportunities in the field of energy are critical for a world in which inexpensive, readily available fossil fuels will eventually be exhausted. Unless we learn how to generate and store energy, not just burn up the fuels formed in earlier times, we will be unable to continue to advance the human condition or even maintain it at its current level. The problems are of central importance, but they can be solved—and the chemical sciences are a necessary part of the solution.

11

National and Personal Security[1]

Some Challenges for Chemists and Chemical Engineers

- Invent strong, lightweight, and multipurpose materials for military use in vehicles, armaments, and protective clothing.
- Devise ways to detect mines, both on land and in the sea.
- Develop robust and reliable sensors for detection of chemical agents, biological agents, radioactive materials, and explosives.
- Develop portable miniaturized analytical devices for personal protection or remote deployment.
- Develop effective ways for mitigation of chemical, radiological, and biological terrorist attacks, and devise ways to decontaminate the sites of such attacks.
- Invent effective antivirals and antibiotics for response to attacks with biological agents.
- Invent ways to detect dangerous materials in our food or water, and to detoxify them.

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[1] As part of the overall project on Challenges for the Chemical Sciences in the 21st Century, a workshop on National Security and Homeland Defense has led to a separate report: *Challenges for the Chemical Sciences in the 21st Century: National Security & Homeland Defense,* National Research Council, National Academies Press, Washington, D.C., 2002. The reader is urged to consult that report for further information.

Science and technology have always played a major role in national security, particularly to arm and protect our military forces. The September 11, 2001, attack on our country has directed tremendous attention to science and technology and ways that it might be mobilized for national security and homeland defense. The very real threat of future acts of catastrophic terrorism has become a significant force for shaping research directions in chemistry and chemical engineering. The most critical needs for national security are inherently chemical capabilities, such as the means to analyze and detect threats by providing intelligence and warning, and the ability to respond to an attack by mitigating damage and decontaminating a site. Achieving these goals will require concerted basic and applied research in chemistry and chemical engineering.

The personal security of our citizens also benefits directly from science and technology. Our police forces are equipped with light, strong bulletproof vests made of modern synthetic materials, and fire rescue personnel wear protective clothing made from temperature-resistant polymers. The smoke detectors and carbon monoxide detectors in our homes are based on chemical processes that detect dangerous substances. Personal security is enhanced in the broadest sense by water purification and by the chemical testing procedures that assure us of clean water and food.

GOALS

Chemical science and technology must contribute to the enhancement of national and personal security by providing fundamental understanding and new developments—to defend against military, terrorist, or criminal attack and to give warning of accidental or natural disasters. Chemists and chemical engineers will need to make new discoveries in basic science and apply them to the creation of useful materials and devices. These activities will need to address the threats to both military personnel and the civilian population. The range of threats in turn will include military or terrorist attacks on a massive scale, other assaults against just a few individuals, natural disasters, industrial accidents, transportation-related mishaps, and accidents in the home. The goals, to which chemical scientists can contribute, begin with early detection and prevention of an attack or event—but if prevention is not possible, they extend to mitigation of the effects and subsequent remediation of damage.

PROGRESS TO DATE

Military

Ever since World War II spurred the development of technological advances such as radar, synthetic antimalarials, and synthetic rubber, our nation's strengths in science and technology have enabled us to prevail in the battlefield and marketplace. The United States currently has a military equipped with materials, communication devices, and supplies that result from fundamental research in materials synthesis and processing, electronics development, and biomedical advances.

Nuclear weapons, frightening and dangerous as they may be, are nevertheless a significant component of our overall national defense. A major national effort at this point is to make sure that they are not used in a war, or allowed to spread into less responsible hands. Chemistry played a large role in the development of nuclear weapons, enabling the chemical and isotopic separations procedures by which weapons-grade fissile materials could be isolated from highly complex mixtures. It was a remarkable achievement, solving a very difficult problem. Now analytical chemistry is heavily involved in detecting evidence for nuclear test explosions, to try to prevent the proliferation of nuclear weapons.

The production of weapons-grade uranium or plutonium is both technically challenging and expensive. Consequently, the source of this threat has been limited primarily to industrialized countries. In contrast, both industrialized and less developed countries might turn to the production of chemical weapons or biological weapons using dangerous viruses or bacteria. These are forbidden by international agreement,[2] but agreements do not necessarily provide a strong defense. Consequently, the U.S. military has put considerable effort into developing protective clothing and procedures to protect troops against chemical and biological weapons. The protective materials, and detoxifying procedures and substances, are the products of modern chemistry and chemical engineering.

A major contribution from chemistry and chemical engineering has been the development of materials with important military applications. Chemists and chemical engineers, working with experts from areas such as electronics, materials science, and physics, have contributed to such developments as new explosives and propellants, reactive armor (a complex material with an explosive layer that can reduce the penetration of an incoming projectile), and stealth materials that reduce the detectability of aircraft by radar.

Personal Security

Our personal civilian security is greatly enhanced by many contributions from chemistry and chemical engineering, often through integrated R&D efforts with teams of scientists from many disciplines. Law enforcement employs forensic tools that rely heavily on chemical analysis, and emergency response teams use a variety of protective clothing and equipment that rely on modern materials chemistry and engineering. As mentioned above, individual security extends to chemical detection methods in the home.

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[2] The Biological and Toxin Weapons Convention, *http://projects.sipri.se/cbw/docs/bw-btwc-mainpage.html*; the Chemical Weapons Convention, *http://www.opcw.nl/*.

CHALLENGES AND OPPORTUNITIES FOR THE FUTURE

Military

New research is needed to equip our military for new types of combat in diverse environments, and against well-equipped opponents. Increasingly, combat may occur in difficult areas, such as jungles or cities. These new situations require that soldiers be independent agents who are able to carry their weapons, communications, and supplies. Chemical scientists need to develop lightweight strong materials that could replace the heavy metal armor in fighting vehicles; new ultratough composites are a likely choice. Other lightweight materials will be needed for surveillance vehicles and to equip rapid response forces. Military vehicles will need better batteries and fuel cells to provide portable energy sources (Chapter 10).

The materials for uniforms and equipment will need to provide protection from chemical and biological agents (and perhaps detect them as well), be lightweight, and provide climate control to maintain performance in extreme environments. New medicines—antivirals, antibiotics, and antifungals—will be needed to maintain the health of troops deployed in such locations. In urban areas, advanced materials are needed for robots that can enter buildings before soldiers.

Combat medicine poses special problems. Chemical science and technology can aid in the rapid detection and treatment of injuries from chemical and biological weapons and other new weapons such as lasers. We need to develop blood substitutes with a long shelf life, and improved biocompatible materials for dealing with wounds. For the Navy, there are special needs such as analytical systems that can sample the seawater to detect and identify other vessels. We need good ways to detect mines, both at sea and on land. Land mines present a continued threat to civilians after hostilities have ended, and chemical techniques are needed to detect these explosive devices.

Of course our national security also depends on deterring problems before they arise. We need to develop new analytical chemistry techniques that are capable of detecting the production of materials in violation of the chemical and biological weapons treaties. Related detection technologies are needed to detect chemical agents and warn personnel accordingly. The new instrumentation will need to be versatile, robust, and portable—with miniaturization using approaches such as microfluidics as a likely goal.

Biological

Biological warfare agents present a greatly increased threat because the original viruses or bacteria can multiply and infect additional people. Considerable concern has been expressed over the possibility that a terrorist group might obtain a sample of the smallpox virus. Until recently, it was believed that smallpox had been eradicated, with the exception of samples at two specialized facilities (in the United States and Russia). Other biological agents also create concern. For example, *bacillus anthracis* (anthrax) has long been viewed as a potential weapon because it can be converted to hardy spores for delivery as a dry powder. The events of 2001 showed anthrax to be a dangerous organism, but it is not transmitted from one human to another. Consequently, the death toll from anthrax-containing letters was relatively low, although the societal and psychological impact was huge.

How can chemists and chemical engineers respond? To guard against biological attacks, it will be necessary to develop rapid and reliable methods of detection. As the events of 2001 demonstrated, it is not acceptable to culture a sample and wait days to learn if a particular biological agent is present; it must be identified prior to the onset of symptoms. And if the agent is found, we will need new therapies (antivirals, antibiotics) and reliable methods for decontaminating the site of attack. Protection of personnel will also require new vaccines and new approaches for delivering drugs and vaccines. The development of new drugs and vaccines will need to be carried out in full recognition that genetically modified pathogens could be used in an enemy attack. All of this will require concerted research by chemists and chemical engineers in collaboration with other scientists; these studies necessarily will be interdisciplinary.

Chemical

Chemical warfare agents are extremely toxic and very fast acting. Chemical scientists must develop better understanding of their mechanisms of action, and use this information to devise possible remedies. At present, the logical response to the chemical threat is prevention of exposure. Consequently, sensors and other fast analytical techniques must be developed. Rapid and reliable methods of decontamination are needed in the event that a chemical agent is detected. One concept, the "lab on a chip," involves producing complete analytical systems in a compact electronic form; such small devices could then be deployed by airdrop and allow remote inspection. Such miniaturized analytical systems also could be carried by individual soldiers—providing them with individualized real-time detection capability for chemical and biological agents.

The chemical industry is an important part of the U.S. economy. The manufacturing sites, and the chemicals they make, store, and transport, represent targets for terrorist attack—either by causing a release of toxic chemicals or by diversion of chemicals for other purposes. The industry needs to be sure that it has broad up-to-date information from analyses and risk assessments of chemical plant safety, of site security, and of chemical transport security. These analyses need to be coupled with detection capabilities for response, verification and tracking. Even with good plans in place, appropriate procedures are also essential for dealing with any attacks. Chemists and chemical engineers will be challenged to develop new products and processes that make the chemical industry inherently more secure. Once again, mitigation and decontamination procedures require the attention of chemists and engineers.

Nuclear and Radiological

Countries and groups that lack access to nuclear weapons may still have opportunities to obtain radioactive materials such as spent nuclear fuel. A bomb in which a conventional explosive charge causes dispersal of radioactive material is known as a "dirty bomb." Such a device could result in psychological effects exceeding the physical damage it caused. Once again, new techniques are needed for detection (of both the explosive and radioactive material), and decontamination procedures would be essential if such a device were used.

Research by chemists and chemical engineers will be needed for the development of new analytical techniques to detect nuclear proliferation threats and treaty violations. This will require establishing the characteristic signatures of both production and testing of weapons. Detection of these signatures will depend on chemical spectroscopy techniques, and advances in remote sensing.

Within the context of the U.S. weapons programs, the ban on testing nuclear weapons requires that other methods be developed to ensure the safety and reliability of existing weapons. As part of the stockpile stewardship program, it will be necessary to understand—through laboratory experiments and via computer simulation and modeling—the long-term changes that could affect the performance of the weapons in the stockpile. These include chemical effects such as corrosion as well as the results of self-irradiation on both nuclear and nonnuclear components of the weapons. What are the aging processes and their consequences on various components—including high explosives, electronics, and mechanical—and how will this affect performance? Successful modeling will require fundamental understanding of materials over all length scales and of their chemical behavior under extremes of temperature and pressure.

Explosives

Bombings have long been a central threat from terrorism, and several major bombing attacks have been carried out in the United States over the last decade. Two earlier reports from the National Research Council outlined a number of opportunities for technical contributions by chemical scientists.[3] The recommen-

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[3] *Containing the Threat of Illegal Bombings: An Integrated National Strategy for Marking, Tagging, Rendering Inert, and Licensing Explosives and Their Precursors,* National Research Council, National Academy Press, Washington, D.C., 1998; *Black and Smokeless Powders: Technologies for Finding Bombs and the Bomb Makers,* National Research Council, National Academy Press, Washington, D.C., 1998.

dations in those reports emphasized further research to develop new and improved detection techniques, but new voluntary and regulatory approaches to controlling explosives and their precursor chemicals were suggested if the level of threat increases.

Root Causes

One of many underlying problems leading to conflict is the difference in standard of living between industrialized and developing countries.[4] Much of this difference could be mitigated by technology to improve energy, information infrastructure, medicine and public health infrastructure, food, water, shelter, clothing, and other absolute necessities for poorer nations. A task for chemistry and chemical engineering is to improve the means to feed and shelter the world, to extend to less-wealthy nations some fraction of the benefits we enjoy.

Personal Security

In most respects, the terrorist threats to civilian populations are parallel to the military threats from chemical and biological agents, radiological materials, and explosives. Detection—with all its challenges to the chemical sciences—remains the key. But the response must be quite different if an attack takes place on a civilian target. In such a case, we would not be looking at a specific concentration of troops under management of senior military officers—whose goal must be a sufficient survival level that will enable the battle to be continued and won. In a civilian situation, reduction of casualties must take first priority.

Important opportunities in the area of response are found in the early stages of emergency response. Emergency personnel need improved materials—including clothing, gas masks, and gloves—for personal protection. These will need to be lightweight and long-lasting, with significant improvements over the current generation of protection suits that are too heavy, too hot, and too cumbersome.

The time scale for chemical and biological attacks is quite different. Explosives and chemical warfare agents such as nerve gases kill in seconds or minutes, but even the existence of a biological attack might not be recognized for days or weeks. The first responders in a chemical or explosive attack will be alerted by damage and casualties, and they will need to enter the disaster zone. They will need the appropriate protective gear along with the detection equipment to tell them what threat or agent(s) they are facing. Moreover, they will need equipment and chemicals that will allow them to decontaminate the site by destroying or removing whatever harmful agents may be present. Finally, their analytical equip-

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[4] *Discouraging Terrorism: Some Implications of 9/11,* National Research Council, National Academy Press, Washington, D.C., 2002, p. 29.

ment will need the sensitivity and accuracy to tell them when decontamination has progressed adequately so that the disaster zone can again be declared safe. All of the new equipment and instrumentation will require the work of chemists and chemical engineers.

Biological attacks will likely be recognized not from a summons to the site of attack but by the steady accumulation of unusual data collected by medical personnel at hospital emergency rooms. Only when the collated data are properly interpreted will the biological attack be recognized as such. But then it will be necessary to engage our medical and public health systems quickly. To be ready for such an event, chemists and chemical engineers will need to carry out extensive work in collaboration with others in the biomedical field. It will be necessary to develop new and better vaccines, antivirals, and antibiotics. Better, faster ways of making and delivering these materials will have to be developed so that they are available in time to save lives. If a biological attack should take place, improved detection methods for biological agents will be needed immediately. A rapid, accurate, and reliable method is needed for detecting and identifying infected individuals before clinical symptoms appear. Many biological warfare agents produce conditions that are curable only if treated prior to the appearance of clinical symptoms. Waiting for the symptoms of a lethal disease to appear will not be an acceptable alternative. Chemists and chemical engineers will need to develop sensors, instruments, and analytical procedures to identify pathogens rapidly and reliably—thereby enabling medical personnel to respond accordingly.

Protection of our food and water supplies against terrorist attack presents a major challenge, because the supply chain is so extensive and open. But it is a challenge that chemists and chemical engineers should accept. Moreover, the threats to food and water are not limited to terrorism—a variety of natural disasters could wreak havoc as well.

WHY ALL THIS IS IMPORTANT

A compelling sense of urgency was felt throughout the United States after the terrorist attacks of September 2001. For chemists and chemical engineers, this has emerged as motivation to align their research directions in ways that can help deter terrorism and protect our country from attack. Chemistry and chemical engineering have major roles to play in furthering our defensive capabilities against both military opponents and terrorists.

All of the areas of research discussed in this chapter will require interdisciplinary collaborations among chemists, engineers, biologists, physicists, and materials scientists. This critical area of national need should be the catalyst for breaking down disciplinary barriers and promoting interaction among scientific and engineering communities.

Among the many areas of research that can contribute to our national security, several stand out from the rest as central to the chemical sciences—materials, medicines, and sensors. Advanced materials will play a crucial role in military and civilian protection, and advanced research in structured and functional materials on a nanoscopic scale will be an important focus for chemists and chemical engineers. The very real threat of virulent biological agents will drive chemists, biochemists, and chemical engineers to seek new prophylactic treatments, therapies, and protective vaccines. The need to protect millions of civilians in our own communities against acts of catastrophic terrorism must be a central priority for those working with analytical sensors and detectors, and for those working with genomics and analysis of pathogenesis. There cannot be many more important goals.

12

How to Achieve These Goals

U.S. prosperity depends on high technology, and much of that depends on chemical expertise. For most of the past decade, the chemical industry has been one of the few U.S. manufacturing industries to have a positive balance of trade. Indeed, the chemical process industries, which perform chemical transformations in the course of manufacturing their products, are as much as one-third of the entire U.S. manufacturing sector in terms of value added. The scope of the chemical sciences endeavor is vast, contributing far beyond the traditional aspects of chemistry and chemical engineering. As a consequence, opportunities for fundamental and creative science—and major contributions to technology and society—will remain in the hands of chemical scientists for a long time. New fundamental chemical insights will increase our scientific understanding, and the practical importance of future discoveries will have enormous potential. These new discoveries—medicines to cure and prevent diseases, solutions to meet our energy needs, paradigm shifts in electronic materials, increased industrial sustainability, and protection from terrorist attacks—all require the efforts of chemists and chemical engineers. The health and well-being of the chemical enterprise will directly affect the health and well-being of our nation and its economy.[1]

If these achievements are to occur, however, it will not be by the work of chemists and chemical engineers acting alone. Many parts of society and experts in other areas of science and technology will be partners with chemists and chemi-

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[1] *Chemical & Engineering News,* 78 (41), 60-61, 2000; *Chemical & Engineering News,* 79 (46), 38-39, 2001; *Chemistry Today and Tomorrow: The Central, Useful, and Creative Science,* Ronald Breslow, American Chemical Society, Washington, D.C., 1997.

cal engineers if the chemical sciences are to achieve solutions to all these challenges. The following section suggests opportunities for the path forward.

CHEMISTS AND CHEMICAL ENGINEERS

The Practice of Chemistry and Chemical Engineering

Future research for chemical scientists will increasingly involve working in multidisciplinary teams. This means not just analytical chemists with inorganic chemists or chemists with chemical engineers, but chemical scientists working with physicists and electrical engineers to develop electronic materials and devices, chemical scientists working with biologists and physicians in the development of medicines and the understanding of life processes, chemical engineers working with physicians to develop artificial materials and organs for the body, and chemical scientists working with business leaders and resource managers to develop sustainable and profitable processes for our world.

The need for multidisciplinary teams to understand the fundamental science of the future as well as to address the technical challenges ahead will require a shift in the way we train graduate students, award tenure, and fund research. It is desirable that graduate students be involved in projects that include other disciplines, and their classwork should involve a broader array of subjects than just their primary specialty. Tenure has traditionally been built upon individual research. Perhaps a demonstrated ability to collaborate with those in other disciplines should be considered a strong asset for tenure. To truly foster collaborative research, funding agencies need to provide awards that are larger than the present awards that are expected to fund only one principal investigator.

Besides doing multidisciplinary research, chemical scientists in the coming years will need to team with those from other sectors. Government and academe need to work together in order to most effectively solve the problems facing the nation in homeland defense and security. Industry and academia need to work together to enhance the transfer of technology to the marketplace and to keep academe in touch with the needs of industry. Government and industry need to team to better address the problems they face together.[2]

The Training of Chemists and Chemical Engineers

As in any reexamination of the field, chemists and chemical engineers should ask serious questions about current practices. Does the divisional structure in academic chemistry departments discourage multi-investigator research, or encourage artificial distinctions? Are the traditional divisions still the best structure

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[2] *Research Teams and Partnerships: Trends in the Chemical Sciences,* National Research Council, National Academy Press, Washington, D.C., 1999.

for educating students or do these divisions encourage narrowness? Is it reasonable that the traditional education of chemists involves no contact with the field of chemical engineering? Since most chemical engineers are no longer doing research in areas related to the undergraduate classes that they teach, what does that imply about the need for changing the chemical engineering curriculum? These are all areas that will be debated and acted on in the near future.[3]

Regarding undergraduate education, most students are exposed to chemistry courses because they are considering careers in the health sciences. These introductory courses are an opportunity and responsibility to convey the excitement of the chemical sciences. There are three basic types of students who might take chemistry in an undergraduate setting: One is the chemistry major, one is a science major, and one is a nonscience student. Only about 10 percent or fewer students in the first-year chemistry class will go on to become professional chemists or chemical engineers.[4] Clearly introductory courses must include certain material to build the foundation for advanced work, but this does not mean that the wonder and excitement of chemistry cannot be emphasized. Basic science curricula needs to be developed for non-science undergraduate students. Chemists and chemical engineers should take the lead in collaborating with their scientific colleagues to develop a comprehensive science and technology course to enhance the understanding by non-scientists of the scientific method and the wonder and value of science. It is necessary for scientists and engineers to define the minimum amount of science an educated person with a bachelor's degree in any field should have.

In both chemistry and chemical engineering, greater opportunity and encouragement needs to be given for undergraduates to have a research experience. This needs to be offered through the universities, through programs such as Research Experiences for Undergraduates, through cooperative education programs and summer opportunities at government laboratories.

Chemical scientists must communicate more effectively with other sectors of society, technical and nontechnical alike, beyond the chemical science community. They must put their discoveries and their goals into words that make sense to nonchemists. It cannot be assumed that everyone will recognize that "aromatic" might not refer to odor or that a "reaction" might be something other than the response to a surprise. Chemists and chemical engineers must describe to the media what is important in chemistry. We should recognize the journalist's need for news that the public can understand and the opportunity that this represents to transmit important contributions of the chemical sciences. Perhaps most important, chemical scientists must communicate more effectively with their elected representatives and other government officials. The unified field of chemistry

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[3] *Graduate Education in the Chemical Sciences: Issues for the 21st Century,* National Research Council, National Academy Press, Washington, D.C., 2000.

[4] *Chemical & Engineering News,* 79 (31), 5, 2001

TABLE 12-1 Full-time Graduate Students in Chemistry and Chemical Engineering.[a]

Field	1993	2000
Chemistry	17,204	15,707
Chemical Engineering	6,079	5,865

[a] Data from *Federal Investment in R&D*, E. Eiseman, K. Koizumi, and D. Fossum, RAND Science and Technology Policy Institute, Arlington, VA, 2002 (Table 17), p. 99.

and chemical engineering has an exciting story to tell, with intellectual excitement and practical applications that are critical to modern civilization. The story must be told to those whose decisions affect the resources needed to solve the challenges that are outlined in this report. These goals in the realm of communication constitute a serious challenge to chemical scientists and engineers—to accept an enhanced commitment to professional responsibility and involvement that would provide enormous benefit to their field.

Chemists and chemical engineers can broaden their perceptions and interactions; one goal of this joint report is to facilitate movement in this direction. Name changes in both chemistry and chemical engineering departments have reflected this progression in recent years. Chemical scientists can work to mutual benefit with experts from many other areas—electrical engineers, pharmacologists, materials scientists, and solid-state physicists to name just a few.

The pool of chemists and engineers must be expanded by attracting more women and minorities[5] to the fields that chemical scientists find so rewarding and exciting, as we discuss further in the next section. We must examine our current practices and beliefs to see how to fully tap the talents of all members of our society. U.S. chemistry and chemical engineering benefit from the immigration of individuals with the needed skills who have been trained both here and in other countries. However, the challenges are so great, and the demand for talent so large, that it is important to attract more of the brightest American students into these fields. Despite the needs of our technological society for chemists and chemical engineers (see below), graduate school enrollments in the United States have declined a bit over the last decade (Table 12-1).

Chemists and chemical engineers will need to be active ambassadors for their fields by recruiting new students and describing the satisfaction and rewards of a life on the frontier—in this case the molecular frontier. This will require visits to schools to talk about the careers and opportunities. It is critical that such

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[5] For background information on these chemical workforce issues see: *Women in the Chemical Workforce,* National Research Council, National Academy Press, Washington, D.C., 2000; *Minorities in the Chemical Workforce: Diversity Models that Work,* National Research Council, The National Academies Press, Washington, D.C., 2003.

visits include students in the entire range from kindergarten through high school. Students need to learn early that there are exciting things to do in creative science, including in particular the chemical sciences, and that they could play a role in inventing solutions to the challenges that humanity faces. Many students have never met a chemist or chemical engineer, and it may be essential to see that they do.

Finally, chemists and chemical engineers must accept the important challenges that they alone can meet. Some of the challenges are described in this report, but the chemical sciences community must continuously expand the list—and always stand ready to accept new ideas and meet new goals. Some of the most exciting advances in science have come from basic scientific exploration, so we must continue to encourage those who simply want to expand the frontiers of fundamental understanding.

EDUCATORS

As mentioned above, it is important to convey the excitement of the chemical sciences to students. Science is about discovery, but chemistry and chemical engineering also extend to invention. Showing students how data can be used to make a scientific deduction gives more of a flavor of the science than does simply learning a set of facts about the science. For example, students can gain real contact with primary scientific data and its interpretation if they are asked to look at an NMR spectrum of a compound and deduce its structure. Asking them to invent an experiment that will answer a chemical question can also be stimulating. Asking them how they could synthesize a given compound makes them use their knowledge in a creative way. Some of this can be done in standard lecture and laboratory courses, but it is also important to encourage creativity by promoting science fairs in which high school students can compete by entering their own research projects.

Educators should take advantage of the availability of professional chemists and chemical engineers, who can speak to the students either in class or in some special forum. Contact with practicing scientists can help students put a human face on a possible future career. It is especially important that women and minority scientists also play a role in such outreach to students, to show that indeed the profession welcomes all with the talent to contribute. Some of this effort should be directed toward the early parts of K-12 education. The future of the chemical sciences may depend on the ability of educators to convince young students that "it's cool to be excited by chemistry."

THE MEDIA

Chemistry is to a large extent invisible in newspapers, news magazines, television, and radio. If the message from chemists and chemical engineers is so exciting, why is it not a focus of media attention? Part of the reason is the tendency of chemical scientists to present their work in such a complex and technical way that it does not translate readily to a general format. Some argue that chemical results are too complicated to present to the public—but that does not seem to inhibit those working in physics, biology, and astronomy, where news coverage of new discoveries seems much more common. Consequently, the challenge is clear. Chemists and chemical engineers must become more proficient in their communication skills—particularly in their interactions with the journalists who will write the final stories. The goals and achievements of chemistry and chemical engineering—in basic science and in meeting human needs—provide ample justification for efforts to work with the media.

As described in this report, the role of chemistry and chemical engineering in modern society is both important and central. It is therefore essential that this message be made clear to the public, to decision makers, and to opinion leaders. As an example, when a new medicine or electronics breakthrough is announced, credit is usually given to those who carried out the last steps—the physicians who tested the drug that was invented by chemists, or the electronics experts who assembled the chemical science and engineering advances into the final version of a chip. As a result, the chemical scientists with responsibility for the original invention may not receive any credit whatsoever, and the public may not recognize that chemists and chemical engineers made essential contributions. Chemical scientists and their professional organizations will need to work with media experts if such patterns are to be changed.

THE GENERAL PUBLIC

If chemical scientists are to be successful in their efforts to improve the educational experience of their students, they will need help from the public. One step is to assure that there is a general understanding of the ways that chemistry is central to understanding life itself, and to providing the medicines, products, modern materials, and processes that support human needs. But the necessary second step is to enlist the public's support—to have them approve of students' desires to enter the chemical sciences and contribute to its goals and challenges. If parents encourage their sons and daughters to take up such careers, and if the public encourages financial support for research and education in chemistry and chemical engineering, then progress can be expected.

In a recent poll of the general public conducted by the American Chemical Society,[6] chemistry as a career option was ranked third in a list of eight scientific professions, and chemists scored high as visionary, innovative, and results-oriented. Also, 59% said that chemicals made their lives better. These results sug-

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[6] *Chemical & Engineering News,* 78, 41, 60-61, 2000.

TABLE 12-2 Doctoral Scientists and Engineers Employed in the United States in 1999.[a]

Field	Subfield	Number Employed	
Physical Sciences			110,300
	Chemistry	55,810	
Engineering			95,890
	Chemical Engineering	12,520	
Total		68,330	206,190

[a] Data from *Federal Investment in R&D*, E. Eiseman, K. Koizumi, and D. Fossum, RAND Science and Technology Policy Institute, Arlington, VA, 2002 (Table 23), p. 107.

gest that the public would indeed endorse the goals suggested here for enhancing the infrastructure for education and research in the chemical sciences.

GOVERNMENT AND PRIVATE FOUNDATIONS

Research and education go hand in hand in chemistry and chemical engineering. While it is possible to teach students about the chemistry of the past by lectures alone, participation in research gives them a chance to learn what science really is, and to engage their creative and critical imaginations. In this way, the support of research directly contributes to the education of chemical scientists. It can also provide those students who want to go into other fields—law, business, government—with a real understanding of the basic and applied work in chemistry and chemical engineering.

The unemployment rate for chemists has remained low during the past few years,[7] reaching only the normal rate (2%) for people who are moving from one job to another. Of course, this low unemployment rate can and does rise to some extent in periods when the economy is weak, but chemistry and chemical engineering have a huge advantage over many other disciplines. There is a very large industry that uses chemistry to produce its products, so the opportunities for those who are chemically trained include industrial jobs—not just the academic jobs that some other disciplines have as their only option. Indeed, about two-thirds of the members of the American Chemical Society work in chemically related industries. The Bureau of Labor Statistics reports that in 2000, employment in the United States included more than 92,000 chemists and materials scientists, 73,000 chemical technicians, and 33,000 chemical engineers.[8] Table 12-2 shows that

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[7] *Chemical & Engineering News,* 79, 46, 38-39, 2001.

[8] U.S. Department of Labor, Bureau of Labor Statistics: Occupational Outlook Handbook, 2002-03 Edition, *http://www.bls.gov/oco/home.htm.*

chemists comprised just over fifty percent of the doctoral level physical scientists in the U.S. workforce in 1999, while chemists and chemical engineers together made up approximately one-third of all the doctoral-level physical scientists and engineers.

The basic research in our fields is now done largely in universities. It can have incredibly important practical results, but those results cannot normally be predicted in advance. Who would have thought that the basic study of induced energy emission from excited states of atoms and molecules that led to the laser would wind up giving us a better way to record music, or read supermarket prices? Would a music company have funded that research? Who would have thought that our increased understanding of the chemistry of life would have led to the creation of biotechnology as an entirely new industry? The industry that benefited from the basic research could not have funded it, since it did not yet exist.

U.S. companies swiftly use the new leads from basic research in U.S. universities, in part because they have good contacts, and in part because they hire students or even faculty who have played a role in creating that basic knowledge. However, support of the research itself is mainly the function of the federal government, and to a lesser extent of private foundations. A recent study carried out by the Council for Chemical Research finds that on average, every $1 invested in chemical R&D today produces $2 in corporate operating income over six years—an average annual return of 17% after taxes.[9] The study also reports a strong linkage of industrial patents to publicly funded academic research.

Federal agencies have been the major supporters of research and education in the chemical sciences. For example, the National Institutes of Health (NIH) provide very important support to health-related science in universities, including health-related chemistry and chemical engineering. This support has been directed to basic science as well as to more applied studies. Thus NIH has supported the basic work to understand the chemistry of proteins and of nucleic acids, fundamental building blocks of living systems. To assure continued support by the NIH, it is important that the health relevance of chemistry and chemical engineering be clearly and explicitly recognized. After all, chemistry underlies the understanding of the basic processes of life, as was described in Chapter 7. Also, the pharmaceutical industry, agriculture, and sanitation are the three principal contributors to human health, and all three are heavily based on chemistry. Chemists and chemical engineers constitute a large fraction of the scientists doing research in pharmaceutical companies, inventing the medicines and the processes for manufacturing them. Their education and training in U.S. universities is possible only with adequate support by the NIH, support with both research grants and training grants.

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[9] *Measuring Up: Research & Development Counts in the Chemical Industry,* Council for Chemical Research, Washington, D.C., 2000; *http://www.ccrhq.org/news/studyindex.html.*

TABLE 12-3 Federal Funding for Research in Science and Engineering (Millions of 2000 Dollars)[a]

Field	1970	1975	1980	1985	1990	1995	2000
Total, all S&E	18,104	18,606	22,141	23,467	26,860	31,005	38,471
Physical sciences, total	3,496	3,032	3,819	4,431	4,731	4,665	4,788
Chemistry	841	790	868	946	946	942	1,226
Engineering, total	5,687	4,749	5,403	5,262	5,250	6,224	6,346
Chemical Engineering	404	232	184	370	301	268	197

[a] Data from *Federal Investment in R&D*, E. Eiseman, K. Koizumi, and D. Fossum, RAND Science and Technology Policy Institute, Arlington, VA, 2002 (Table 13), p. 89.

The National Science Foundation (NSF) provides support to all the basic sciences and engineering in universities. NSF support of chemistry is very important, both the support directed to fundamental research initiated by individual investigators and the research done in research centers such as those aimed at developing new materials or at understanding and improving the environment. The support is critical, but more is needed for the chemistry division of NSF to achieve its objectives.[10] Considering the importance of basic and applied chemistry and chemical engineering to the economic future of the United States, it seems that an increase in the ability of NSF to support fundamental and applied chemical science is warranted.

The Department of Energy (DOE), the Department of Defense (DOD), the Environmental Protection Agency (EPA), all help support fundamental and applied chemistry and chemical engineering. Their support is fully justified, as previous sections of this report make clear. The Department of Agriculture (DOA) also has a program of external support for chemistry and chemical engineering in universities, in line with the role that chemistry and chemical engineering play in agriculture.

Table 12-3 summarizes federal funding for research in the physical sciences and engineering over the last several decades. The numbers are reported in constant dollars to facilitate comparisons across different years while minimizing the effects of inflation. While there has been an overall steady increase in federal support since 1970, the support for chemistry has lagged considerably behind the overall trend, and the support for chemical engineering has actually decreased. Strong support for chemistry and chemical engineering in the future will be essential for scientific and technical progress—both to facilitate new discoveries and to provide the technical workforce that will be needed to sustain the U.S. economy.

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[10] *Chemical & Engineering News,* 80, 42, 37-39, 2002.

There is another way that federal government officials could provide support for the conclusions of this report—endorse the importance of the challenges and goals that it describes. The federal government has a clear stake in supporting enhanced education and training of chemical scientists and in encouraging recruitment of more U.S. students to these fields. The major role of the chemical industry emphasizes how the economic future of the United States depends on continued scientific excellence in chemistry and chemical engineering.

Many private foundations have agendas that are somewhat narrowly focused—for example, on a disease such as cancer. They often recognize the role that chemical scientists play in understanding the basic biology of the disease and in inventing medicines for treatment or procedures for delivering such medicines. Although their funding cannot replace federal support, the special programs they create are valuable as support for research and education. Other foundations provide extremely valuable support for young chemical scientists at the early stages of their careers—when their records of accomplishment may not yet be adequate to let them compete successfully for federal funding.

INDUSTRY

The chemical industry is involved with all parts of the chemical sciences. U.S. companies hire university graduates, carry out R&D programs, engage in joint efforts with universities and national laboratories, and generate ideas that stimulate further research in the academic arena. Consequently, it is of central importance to the chemical industry that the health of chemistry and chemical engineering be maintained. There are many ways that U.S. companies can help. One is to continue the demonstrated progress in environmentally benign manufacturing as exemplified by the Responsible Care program. Past practices that led to well-publicized problems are now recognized, changes have been implemented, and improvements continue to be made. The more chemistry-based industry can improve its public reputation, the better the consequences for chemists and chemical engineers.

When a new medicine is announced, it is important that companies publicly recognize the chemistry that went into its creation and the chemical engineering that went into the manufacturing process. When other valuable new products are introduced, companies should not be afraid to describe the contribution of chemical scientists. The negative public reactions from past problems with chemical manufacturing have led some companies to nearly hide the fact that they do chemistry. But if chemical companies can discuss behavior of which they are proud, they may be willing to assert that they indeed do chemistry, and do it well. Pretending otherwise demeans the entire profession and the incredible contributions that it makes.

There is a serious problem with public perception that the chemical industry needs to correct. In a survey of 1,012 U.S. adults commissioned by the American

Chemical Society (see above) only 43% had a favorable opinion of the chemical industry. It was ranked lowest among a list of 10 industries, and only 1 in 10 respondents felt very well informed about the role of chemicals in improving human health. The situation is not appreciably better elsewhere. In Canada only 40% of adults in a 1999 survey had a favorable view of the chemical industry, and only 18% felt that the industry was excellent or good at being honest. A survey of 9,000 Western European citizens by the European Chemical Industry Council showed that only 45% had a favorable view of the chemical industry. There is still a lot of work to do to change these opinions and perceptions.

Chemistry departments and chemical engineering departments in universities need more help from industry. After all, companies need both the research advances and the trained people that universities produce. At one time these companies provided significant support, for example in the form of fellowships for Ph.D. students. As research support shifted to the federal government in the second half of the 20th century, many of these industrial programs disappeared. They are now needed again, especially in the form of graduate fellowships, as some of the federal fellowship programs have been terminated.

As industrial R&D moves forward in an increasingly interdisciplinary fashion, it will be important for the chemical industry to recognize this trend in its hiring procedures. If interdisciplinary and multidisciplinary work is to be encouraged, industry will need to seek and hire people who have worked at the intersections of chemistry and chemical engineering with biology, physics, and other sciences.

GRAND CHALLENGES

This report has summarized the contributions that chemical science and engineering have already made to human welfare and to economic strength. It has focused to some extent on these contributions to the United States, but in truth all of humanity benefits from advances in medicines, in a better environment, in energy production and distribution, in materials production, information science, and national security. On the one hand, this report draws attention to the rich intellectual challenge of understanding our world through the chemical sciences. On the other hand, it points out the very close connection between basic research and useful applications in the chemical sciences. Basic science creates opportunities for exciting practical advances, but work to solve practical problems often stimulates enquiry into new areas of basic science. Thus, the connections among all aspects of chemistry and chemical engineering are strong and important.

There is still much to be done. In every chapter of this report some of the remaining challenges for the field are described, together with the importance of meeting those challenges. In addition, some especially exciting challenges start each chapter. Chemistry and chemical engineering are very diverse fields, which do not focus on only one or two central problems. This is in part their strength, since it means that they can make contributions to wide areas of human understanding and human welfare. At the same time, it is a problem because great advances can be made in one area without necessarily revolutionizing the entire field. Some of the challenges are specific, but others are quite broad, with potential impact well beyond the chemical sciences. These are listed here as some overriding themes, described as *grand challenges*—they are broad opportunities that if met could have huge benefits to society. While they are goals not yet reached, we propose that they can be realistically addressed with the new and developing strengths in theories and procedures in the chemical sciences. As we continue to push forward the frontiers of science, we will increasingly do so by working with our colleagues in other disciplines. In this way, the chemical sciences will be able to contribute in remarkable ways to an improved future for our country, for humanity, and for our planet.

We caution the reader that these grand challenges should not be taken as the only areas for worthwhile research. The history of science shows again and again that large revolutions in thought can arise from discoveries that were made by individuals or teams who were not constrained by someone else's list. Chemistry and chemical engineering enter the 21st century with exciting science ahead and major contributions to make. The committee hopes this report will stimulate young people to join them in meeting these challenges, and that society will support continued efforts of chemists and chemical engineers in their work on and beyond the molecular frontier.

Some Grand Challenges for Chemists and Chemical Engineers

- **Learn how to synthesize and manufacture any new substance that can have scientific or practical interest, using compact synthetic schemes and processes with high selectivity for the desired product, and with low energy consumption and benign environmental effects in the process.** This goal will require continuing progress in the development of new methods for synthesis and manufacturing. Human welfare will continue to benefit from new substances, including medicines and specialized materials.
- **Develop new materials and measurement devices that will protect citizens against terrorism, accident, crime, and disease, in part by detecting and identifying dangerous substances and organisms using methods with high sensitivity and selectivity.** Rapid and reliable detection of dangerous disease organisms, highly toxic chemicals, and concealed explosives (including those in land

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mines), is the first important step in responding to threats. The next important step for chemists and chemical engineers will be to devise methods to deal with such threats, including those involved in terrorist or military attacks.

- **Understand and control how molecules react—over all time scales and the full range of molecular size.** This fundamental understanding will let us design new reactions and manufacturing processes and will provide fundamental insights into the science of chemistry. Major advances that will contribute to this goal over the next decades include: the predictive computational modeling of molecular motions using large-scale parallel processing arrays; the ability to investigate and manipulate individual molecules, not just collections of molecules; and the generation of ultrafast electron pulses and optical pulses down to x-ray wavelengths, to observe molecular structures during chemical reactions. This is but one area in which increased understanding will lead to a greater ability to improve the practical applications of the chemical sciences.
- **Learn how to design and produce new substances, materials, and molecular devices with properties that can be predicted, tailored, and tuned before production.** This ability would greatly streamline the search for new useful substances, avoiding considerable trial and error. Recent and projected advances in chemical theory and computation should make this possible.
- **Understand the chemistry of living systems in detail.** Understand how various different proteins and nucleic acids and small biological molecules assemble into chemically defined functional complexes, and indeed understand all the complex chemical interactions among the various components of living cells. Explaining the processes of life in chemical terms is one of the great challenges continuing into the future, and the chemistry behind thought and memory is an especially exciting challenge. This is an area in which great progress has been made, as biology increasingly becomes a chemical science (and chemistry increasingly becomes a life science).
- **Develop medicines and therapies that can cure currently untreatable diseases.** In spite of the great progress that has been made in the invention of new medicines by chemists, and new materials and delivery vehicles by engineers, the challenges in these directions are vast. New medicines to deal with cancer, viral diseases, and many other maladies will enormously improve human welfare.
- **Develop self-assembly as a useful approach to the synthesis and manufacturing of complex systems and materials.** Mixtures of

properly designed chemical components can organize themselves into complex assemblies with structures from the nanoscale to the macroscale, in a fashion similar to biological assembly. Taking this methodology from the laboratory experimentation to the practical manufacturing arena could revolutionize chemical processing.

- **Understand the complex chemistry of the earth, including land, sea, atmosphere, and biosphere, so we can maintain its livability.** This is a fundamental challenge to the natural science of our field, and it is key to helping design policies that will prevent environmental degradation. In addition, chemical scientists will use this understanding to create new methods to deal with pollution and other threats to our earth.
- **Develop unlimited and inexpensive energy (with new ways of energy generation, storage, and transportation) to pave the way to a truly sustainable future.** Our current ways of generating and using energy consume limited resources and produce environmental problems. There are very exciting prospects for fuel cells to permit an economy based on hydrogen (generated in various ways) rather than fossil fuels, ways to harness the energy of sunlight for our use, and superconductors that will permit efficient energy distribution.
- **Design and develop self-optimizing chemical systems.** Building on the approach that allows optimization of biological systems through evolution, this would let a system produce the optimal new substance, and produce it as a single product rather than as a mixture from which the desired component must be isolated and identified. Self-optimizing systems would allow visionary chemical scientists to use this approach to make new medicines, catalysts, and other important chemical products—in part by combining new approaches to informatics with rapid experimental screening methods.
- **Revolutionize the design of chemical processes to make them safe, compact, flexible, energy efficient, environmentally benign, and conducive to the rapid commercialization of new products.** This points to the major goal of modern chemical engineering, in which many new factors are important for an optimal manufacturing process. Great progress has been made in developing Green Chemistry, but more is needed as we continue to meet human needs with the production of important chemical products using processes that are completely harmless to the earth and its inhabitants.
- **Communicate effectively to the general public the contributions that chemistry and chemical engineering make to society.** Chem-

continues

ists and chemical engineers need to learn how to communicate effectively to the general public — both through the media and directly — to explain what chemists and chemical engineers do and to convey the goals and achievements of the chemical sciences in pursuit of a better world.

- **Attract the best and the brightest young students into the chemical sciences, to help meet these challenges.** They can contribute to critical human needs while following exciting careers, working on and beyond the molecular frontier.

Appendixes

A

Biographical Sketches of Steering Committee Members

Ronald Breslow (*Co-Chair*) is University Professor of Chemistry, Columbia University, and a founder of a new pharmaceutical company. He received his B.A. (1952), M.A. (1954), and Ph.D. (1955) from Harvard University. His research area is organic chemistry with specialization in biochemical model systems, biomimetic synthetic methods, reaction mechanisms, and aromaticity and antiaromaticity. He served as president of the American Chemical Society in 1996 and has authored a book for the general public, *Chemistry Today and Tomorrow: The Central, Useful, and Creative Science*. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society. He received the U.S. National Medal of Science in 1991.

Matthew V. Tirrell (*Co-Chair*) is Dean of the College of Engineering at the University of California at Santa Barbara. He was previously Professor and Head of the Department of Chemical Engineering and Materials Science at the University of Minnesota, where he served as Director of its Biomedical Engineering Institute. He received a B.S. from Northwestern University and a Ph.D. from University of Massachusetts. His interests are in transport and interfacial properties of polymers, with particular emphasis on molecular-scale mechanical measurements, bioadhesion, and new materials development. He is a member of the National Academy of Engineering.

Jacqueline K. Barton is Arthur and Marian Hanisch Memorial Professor of Chemistry at the California Institute of Technology. She received her A.B. from Barnard College in 1974 and her Ph.D. from Columbia University in 1979. She did subsequent postdoctoral work at both AT&T Bell Laboratories and Yale University. Her research areas are biophysical chemistry and inorganic chemistry. She has focused on studies of recognition and reaction of nucleic acids by transition metal complexes, and particularly DNA-mediated charge transport chemistry. She is a member of the Board of Directors of the Dow Chemical Company and a member of the National Academy of Sciences.

Mark A. Barteau is Robert L. Pigford Professor and Chair of the Department of Chemical Engineering at the University of Delaware. He received his B.S. degree from Washington University in 1976 and his M.S. (1977) and Ph.D. (1981) from Stanford University. His research area is chemical engineering with specialized interests in application of surface techniques to reactions on nonmetals, hydrocarbon and oxygenate chemistry on metals and metal oxides, scanning probe microscopies, and catalysis by metal oxides.

Carolyn R. Bertozzi is Professor of Chemistry and Molecular and Cell Biology at the University of California, Berkeley, a Junior Investigator of the Howard Hughes Medical Institute, and Faculty Associate of the Materials Sciences and Physical Biosciences divisions of the Lawrence Berkeley National Laboratory. She received her A.B. from Harvard University in 1988 and her Ph.D. from the University of California, Berkeley, in 1993. Her research focuses on organic chemistry and the combination of molecular and cell biology to investigate the biological functions of glycoconjugates and to develop new therapeutic strategies.

Robert A. Brown is Warren K. Lewis Professor of Chemical Engineering and Provost at the Massachusetts Institute of Technology. He received his B.S. (1973) and M.S. (1975) from the University of Texas, Austin, and his Ph.D. from the University of Minnesota in 1979. His research area is chemical engineering with specialization in fluid mechanics and transport phenomena, crystal growth from the melt, microdefect formation in semiconductors and viscoelastic fluids, bifurcation theory applied to transitions in flow problems, and finite element methods for nonlinear transport problems. He is a member of the National Academy of Engineering, the National Academy of Sciences, and the American Academy of Arts and Sciences.

Alice P. Gast (*BCST liaison*) is Vice President for Research and Associate Provost at the Massachusetts Institute of Technology, where she coordinates policy regarding research and graduate education and oversees the Institute's large interschool laboratories. In addition to her administrative positions, she is the Robert T. Haslam Professor of Chemical Engineering. Prior to her appointment at MIT, Dr. Gast was Associate Chair and Professor of the Department of Chemical Engineering at Stanford University, having joined the Stanford faculty in 1985. She received her B.Sc. in chemical engineering (1980) from the University of Southern California and her M.A. (1981) and Ph.D. (1984) from Princeton. Her research expertise is in the area of complex fluids and colloids, with a focus on frontiers of the chemical physics of colloidal and polymer solutions, polymer adsorption, and, most recently, proteins, using experimental scattering methods and statistical mechanics. She is a member of the National Academy of Engineering.

Ignacio E. Grossmann is Rudolph H. and Florence Dean Professor and head of the chemical engineering department at Carnegie Mellon University. He received his B.Sc. (1974) from Universidad Iberoamericana, Mexico, and his M.Sc. (1975) and Ph.D. (1977) degrees from Imperial College, London. He joined Carnegie Mellon in 1979 and has focused his research on the synthesis of integrated flow sheets, batch processes, and mixed-integer optimization. The goals of his work are to develop novel mathematical programming models and techniques in process systems engineering. He was elected to the Mexican Academy of Engineering in 1999, and he is a member of the National Academy of Engineering.

James M. Meyer retired in 2001 as Vice President of DuPont Central Research and Development. He joined DuPont in 1969 and held a variety of research and management positions related to elastomers and polymers. He moved to Central Research and Development in 1992 as director of materials science and engineering, and he assumed his current position in 1996. Dr. Meyer received his B.S. degree in chemistry from Indiana University and his Ph.D. degree in inorganic chemistry from Northwestern University.

Royce W. Murray is Kenan Professor of Chemistry at the University of North Carolina at Chapel Hill. He received his B.S. from Birmingham Southern College in 1957 and his Ph.D. from Northwestern University in 1960. His research areas are analytical chemistry and materials science with specialized interests in electrochemical techniques and reactions, chemically derivatized surfaces in electrochemistry and analytical chemistry, electrocatalysis, polymer films and membranes, solid state electrochemistry and transport phenomena, and molecular electronics. He is a member of the National Academy of Sciences.

Paul J. Reider is Vice President of Chemistry Research at Amgen, Inc. Before moving to Amgen in 2002, he was Vice President of Process Research at Merck Research Laboratories. His research has focused on synthetic organic and natural product chemistry for the development of pharmaceuticals, and he has worked extensively on drugs for AIDS, asthma, arthritis, and bacterial infections. He received his A.B. from Washington Square College in 1972 and his Ph.D. from the University of Vermont in organic chemistry in 1978. As a National Research Awardee (NIH) he did his postdoctoral work at Colorado State University.

William R. Roush is Warner Lambert/Parke Davis Professor of Chemistry at the University of Michigan. He received his B.S. from the University of California, Los Angeles, in 1974 and his Ph.D. from Harvard University in 1977. His research area is organic chemistry, with specialized interests in organic synthesis and natural products chemistry, stereochemistry of organic reactions, development of new methods and regents, asymmetric synthesis, and oligosaccharide synthesis.

Michael L. Shuler is Director and Professor of the School of Chemical Engineering and Director of Bioengineering at Cornell University. He received his B.S. from the University of Notre Dame in 1969 and his Ph.D. from the University of Minnesota in 1973. His research area is chemical engineering with specialized interests in mathematical models of cellular growth, plant cell suspension cultures, utilization of genetically modified cells, insect cell cultures, novel bioreactors, environmental biotechnology, and pharmacokinetic models and cell culture analog systems. He is a member of the National Academy of Engineering.

Jeffrey J. Siirola is a Research Fellow in the Chemical Process Research Laboratory at Eastman Chemical Company in Kingsport, TN. He received his B.S. degree in chemical engineering from the University of Utah in 1967 and his Ph.D. in chemical engineering from the University of Wisconsin-Madison in 1970. His research centers on chemical processing, including chemical process synthesis, computer-aided conceptual process engineering, engineering design theory and methodology, chemical technology, assessment, resource conservation and recovery, artificial intelligence, nonnumeric (symbolic) computer programming, and chemical engineering education. He is a member of the National Academy of Engineering.

George M. Whitesides is Mallinckrodt Professor of Chemistry at Harvard University. He received his A.B. from Harvard College in 1960 and his Ph.D. from the California Institute of Technology in 1964. His research areas are Materials Science and Organic Chemistry, with specific focus in surface chemistry, materials science, self-assembly, capillary electrophoresis, organic solid state, molecular virology, directed ligand discovery, and protein chemistry. He is a member of the National Academy of Sciences, and he received the U.S. National Medal of Science in 1998.

Peter G. Wolynes is Professor of Chemistry and Biochemistry at the University of California, San Diego. He was previously Professor of Chemistry at the University of Illinois at Urbana-Champaign. He received his A.B. from Indiana University in 1971 and his Ph.D. from Harvard University in 1976. His research area is physical chemistry with specialized interests in chemical physics of condensed matter, quantum dynamics and reaction kinetics in liquids, dynamics of complex fluids, phase transitions and the glassy state, and biophysical applications of statistical mechanics, especially protein folding. He is a member of the National Academy of Sciences.

Richard N. Zare is Marguerite Blake Wilbur Professor in Natural Science in the Department of Chemistry at Stanford University. He received his B.A. in 1961 and his Ph.D. in 1964 from Harvard University. His research areas are physical and analytical chemistry with specialized interests in application of lasers to chemical problems, molecular structure, molecular reaction dynamics, and chemical analysis. Zare has been a member of various NRC committees and served as co-chair of the Commission on Physical Sciences, Mathematics, and Applications and chair of the National Science Board. He is a member of the National Academy of Sciences, and he received the U.S. National Medal of Science in 1983.

B

Statement of Task

The overview report will identify recent advances and current challenges in fundamental understanding of the basic science, and it will explore the impact beyond the chemical sciences that these advances have had in the past. It will also explore the possibilities for such impact in the future, recognizing that such developments are frequently serendipitous. Issues to be addressed include:

- Discovery: Identify major discoveries or advances in the chemical sciences during the last several decades, and evaluate their impact—including the length of time for impact beyond basic chemical sciences to be realized.
- Interfaces: Identify the major discoveries and challenges at the interfaces between chemistry/chemical engineering and such areas as biology, environmental science, materials science, medicine, and physics.
- Challenges: Identify the grand challenges that exist in the chemical sciences today. Explore how advances at the interfaces create new challenges in the core disciplines.
- Infrastructure: Identify infrastructure that will be required to allow the potential of future advances in the chemical sciences to be realized. Identify opportunities that exist to integrate research and teaching, broaden the participation of underrepresented groups, improve the infrastructure for research and education, and demonstrate the value of these activities to society.

C

Contributors

When the Challenges for the Chemical Sciences in the 21st Century project was initiated in 2000, the Committee solicited input from the chemical sciences community. A specific request for input was sent via e-mail to a large number of scientists and engineers, and a general request for information appeared in *Chemical & Engineering News*.[1] In addition to the responses to these requests, input from the broader community was obtained as the committee wrote this report, when individual members of the committee consulted with their colleagues to obtain specific and detailed technical input. The committee is pleased to acknowledge the assistance of all these contributors:

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[1] "Your Ideas, Please!" Madeleine Jacobs, Editor-in-chief, *Chemical & Engineering News,* 78(14), April 3, 2000.

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