The Intersection of Biology and Materials Science

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Abstract

This article is based on the plenary address given by George M. Whitesides of Harvard University on March 30, 2005, at the Materials Research Society Spring Meeting in San Francisco. Materials science and biomedicine are arguably two of the most exciting fields in science today. Research at the border between them will inevitably be a major focus, and the applications of materials science to problems in biomedicine—that is, biomaterials science—will bud into an important new branch of materials science. Accelerating the growth of this area requires an understanding of two very different fields, and being both thoughtful and entrepreneurial in considering "Why?" "How?" and "Where?" to put them together. In this fusion, biomedicine will, we believe, set the agenda; materials science will follow, and materials scientists must learn biology to be effective.

Keywords: *biological, biomedical, nanoscale.*

Introduction

Materials science and engineering is on a plateau. As a field, it has been one of the most successful in modern applied science. Since its appearance as a separate discipline following World War II, it has created an enormous store of technology.[1] The early phases of growth that formed it have, however, slowed, and its practitioners (a mixture of individuals with backgrounds largely in the physical sciences and engineering—metallurgy and ceramics, physics, chemistry, and various branches of engineering) now have the opportunity and the stimulus to look for something new. One opportunity is biomaterials.

A Short History of Materials Science and Engineering

Materials science and engineering (MS&E) has grown in four overlapping epochs, each associated with a set of technologies.

1. The Cold War. Materials science is a child of the Cold War. It was created—largely by the U.S. Defense Advanced Research Projects Agency (DARPA) and by the large corporate defense contractors—as a part of the effort of the U.S. to secure the technology needed to ensure its military capability. In this first phase of growth, MS&E was focused on structures and developed many important materials for high-performance mechanical systems and military technologies, such as alloys for airframes and engines, ceramics for armor, carbon–carbon composites for aircraft and missiles, actinide metals for weapons, and electromagnetic composites for stealth. This period has (at least for the moment) largely ended; the current needs of the military—technologies for urban and jungle warfare, for universal surveillance, for net-centric warfare (centered on information/sensor/communications networks), and for related subjects—are no longer based in large mechanical systems.

2. The birth of information technology. Stimulated both by issues in national security and by the wealth of commercial opportunities created by information technology (IT), materials science developed an important sub-specialty of materials and systems for IT: electronics-grade silicon, gallium arsenide, optical fiber, magnetic recording media, integrated circuits, liquid crystals and displays, ceramic packaging, lasers, and the accompanying processing technologies. The development and refinement of the materials science underlying IT continues at a high level today, with nanotechnology, cost-reduction, and consumer electronics among the foci of research. Still, the end of Moore's law is in sight, and the technologies of interconnectivity and information management are at least as important in IT as the technologies of microprocessors, memory, and displays.

3. The commercialization of materials technologies in consumer products. The usefulness of materials science also permeated commercial technology, and the extensions of MS&E to soft matter—polymers, gels, liquid crystals, organic light-emitting diodes (OLEDs)—were stimulated by the myriad applications in which cost was crucially important. The modern automobile, cellular telephone, television, and civilian airplane are products of this development.

4. Globalization. A current stage of development in MS&E is that accompanying globalization. In this new period of expansion and competition, cost has become even more important, and the issues of processes and logistics—management of purchasing and manufacturing, availability and cost of labor, and access to markets—have mixed into materials science a new set of considerations and metrics. The technology of globalization is as interesting and as complicated as that in any of the earlier epochs but may contain more economics, regulation, supply chain management and sourcing, and information management than it does pure science and engineering.

What is the Next Big Thing for Materials Science?

A 50-year history of productive reinvention suggests that as the field of materials science has reinvented itself into new areas in the past, it will continue to do so in the future. What will MS&E turn to next? There are many important and interesting fields.

Biomedicine/biomaterials/biomimetics represents an obvious opportunity, and is the subject of this article.

IT/photonics continues to grow; we seem, as a society, to have an endless appetite for information: processing it, storing it, shipping it, searching it, and managing it. New technologies will certainly require new systems, but MS&E will be a part—although only a part—of the growth of these technologies.

Intelligent machines—able to perform many tasks that have historically required humans—seem an inevitable response both to military concerns (the lethality of the modern battlefield) and to commercial concerns (the importance of reducing labor costs in many areas of manufacturing focused on consumer markets).

Technology for globalization: As economies adapt to globalization—the distribution of all aspects of technology across the globe, to whatever regions provide the greatest competitive advantage—new technologies are developing that provide acceptable performance at ever lower cost. MS&E is a part—again, only a part—of the development of the technologies that underpin globalization.

Technology for developing economies: As the enormous populations of Asia (and later, of South America and of Africa) enter the global market, they will demand appropriate technologies but at lower prices than those that Europe, North America, and Japan will tolerate. The basic commodities that support a developed society—food, energy, housing, transportation, water, communications, and healthcare—all need to be provided in forms that are economically acceptable. These economic developments will require specific and perhaps new uses of materials.

Commodity infrastructure: Energy, water, and food are more and more important, and providing these commodities to large populations will require new capabilities of MS&E.

Sustainable materials: The development of materials derived from renewable raw materials and for low environmental impact is becoming an ever more important part of global stewardship.

Invention of new materials and nanotechnology: In the developed world, the familiar classes of materials have been extensively exploited, and there is a broad sense among materials scientists that, to some extent, "the cupboard is bare"; there are now few unexploited materials—if a known material can be put to good use, it already has been. There is, as a consequence, a renewed interest in an activity that MS&E has always been good at: invention. Nanotechnology is one product of this interest in new classes of materials.

Biology and Medicine

Biology is—now and probably for the foreseeable future—the area of fundamental science in which the growth of knowledge is the most rapid. It is also the area of science that is the most visible to the public. The need for improved medicine for the treatment of disease—or, defined broadly, for the amelioration, correction, and prevention of dysfunction in health—is an area of human need that seems unlikely ever to disappear. The combination of biology and medicine—generally referred to as "biomedicine" to emphasize the complementarity of the two areas—thus represents a most exciting blend of science and technology and an obvious area of potential opportunity for development as a part of MS&E.

Biomedicine has a number of other interesting characteristics that make it attractive as an area for research, and especially so in the U.S.

The U.S. is the clear global leader in cell and molecular biology. The United States lead in biomedicine rests on a foundation of ample, long-term federal support for both fundamental and applied research in biology and medicine, with active participation by both research universities and hospitals. A successful healthcare industry provides the vehicle for the commercialization of new technologies. Knowledge available in one country is, of course, available globally, but the proximity of departments of MS&E in the U.S. to world-leading departments of biology, and to research-oriented hospitals, could be an enormous advantage in the development of biomaterials science.

The healthcare industry is large but actively looking for new products and technologies. The U.S. healthcare industry has been exceptionally successful and is always used as an example to illustrate the ability of U.S. industry to take an important area of science and convert it into commercial technology that makes a real difference in the lives of citizens. But the future of conventional healthcare is less rosy than the past. Among the problems facing the pharmaceutical and clinical analytical industries—the parts of the healthcare industry that are most closely tied to biomaterials—are these four: (1) the number of new drugs approaching entry into the commercial market is dwindling; (2) issues concerning regulation and liability are becoming increasingly burdensome; (3) targets for new drugs and the diseases against which drugs are actively being developed are becoming more difficult and obscure; (4) the complexities of globalization—especially in national purchasing and in intellectual property—are making it difficult to maintain profitability. The complex situation of the global healthcare sector may, in the long term, improve or degrade the capability of the pharmaceutical companies, but for now, healthcare remains the essential outlet for biomaterials. And it is searching for new, relevant technologies and markets.

The market size in healthcare can only get bigger. We all get older; we all will eventually die. The end state is certain; only the path to that state is amenable to management. We look to healthcare to put off the inevitable as long as possible.

Federal support for biomedicine is generous, consistent, and focused on fundamental research. Much of the strength in the U.S. in medicine comes from a very active community working in molecular and cellular biology in universities and in medical schools. This community of researchers has been supported by the National Institutes of Health generously and stably for decades. The levels of investment in biomedical research in Europe and Asia are also increasing rapidly, although this work tends to be more focused on applications than that in the U.S.

Technology transfer for medically relevant technologies is relatively easy. The interactions between the research universities and hospitals, the venture capital community, the Food and Drug Administration (FDA), doctors, and insurance companies are basically good: the processes that develop applied, commercial technology from fundamental science probably work better in biomedicine than in any other area of science.

There are growing uses for applied biology outside of healthcare. The opportunities for new science (and new materials) in biology are much broader than healthcare: they are beginning to have a major influence on crop production and on veterinary medicine, and have the potential to be important in areas such as energy production (through considerations of biomass), environmental stewardship, and sustainability.

Classes of Opportunities for MS&E in Biomedicine

Biomedicine offers a number of opportunities for materials researchers. Classifying these opportunities can start with the needs of healthcare and biomedicine and ask how MS&E can contribute to their solution, or it can start with the competencies that materials science has already developed and search for applications in biomedicine. The former is probably the more stimulating approach, since it will suggest new opportunities. Also, there are few opportunities for carbon–carbon rocket throat nozzles in medicine.

What Does Biomedicine Need?

The healthcare system is a major part of the economy of every developed country, and it is impractical to construct anything like a comprehensive list of needs that materials science might help to satisfy: representative examples will have to serve, and comprehensive discussions of existing applications suggest the breadth of need.[2–10] It is important to recognize that the great majority of the structures in organisms are living (in contrast to hair and nails, for example). Even what appear to be “simple” structures—such as bones and teeth—are in fact dynamic and are continually remodeled by cellular processes.[11–14] Biomaterials, then, can either serve as imperfect but functional replacements for a limited set of biological structures and functions, or provide functions that do not exist in living organisms. Functional replacements include artificial joints and bones (e.g., for hip replacement), dental implants, replacement lenses, artificial blood vessels, electrodes for cardiac pacemakers and cochlear implants, and resorbable sutures; functional supplements include drug delivery systems; stents; a wide variety of tubing (cannulas, catheters, infusion lines); superparamagnetic, surfactant-stabilized magnetite particles for contrast enhancement in magnetic resonance imaging; meshes for hernia repair; contact lenses; and silicone implants (Figure 1). Wherever a part of an organism fails, there may be an opportunity for biomaterials to help replace the function it provides. Even the failure of complex organs—for example, the pancreas[15] and its ability to deliver insulin, glucagons, and other hormones—can be compensated by some combination of drugs and materials-based delivery systems.

Are there broad characteristics shared by these applications? There are at least two: to be useful, they must be (1) biocompatible and (2) able to clear the regulatory hurdles of the FDA. Both are matters that subsume a range of technologies.

What Does Biological Research Need?

Aside from repair of dysfunction and disease, modern biology is so rich intellectually and so active in discovery that there is a separate range of opportunities for MS&E that would be purely focused on contributing tools to research in biomedicine. Much of the advance of modern biology has, in fact, been made possible by an infrastructure provided by materials science and chemistry. Polymeric gels are essential for DNA sequencing, characterizing and purifying proteins, and a range of other applications. Capillary electrophoresis—the technique now most widely used in high-throughput sequencing of DNA—uses highly engineered silica capillaries for separations and solid-state lasers and photodiodes for detectors. Membranes are used throughout molecular biology. Self-assembled monolayers have become important in attached cell culture.[16–19] Microfluidic devices based on soft lithography are used in the crystallization of proteins for crystallography (Figure 2),[20–22] and for a range of other applications in biology. Developing materials to fill applications in research biology can be much less complicated than developing them for clinical medicine, and thus is an attractive area of research for initial work in biomaterials science.

What Does Materials Science Offer?

Materials research offers, of course, the ability to select materials from a wide range of candidates (or to develop new ones) for appropriateness to a particular application, to form this material into desired shapes, and to tailor its surface chemistry—if required—to improve biocompatibility. The very breadth of this capability is both a strength and a weakness: lack of focus on the specific characteristics that are required for specific applications in medicine or research can lead to endless reinvention of the wheel, or to devices that do not, in fact, have an application.

Materials from biology. Biology also offers materials *to* materials science. Biological materials often have complex, hierarchical structures that cannot (or cannot easily) be duplicated in synthetic materials and may offer the additional advantages of sustainable production, biodegradability, and environmental friendliness. Efforts to exploit advanced biology as a source of materials have been interesting[8,23–25] but so far relatively unproductive. The conventional biologically derived materials—wood, animal, plant, and insect fibers, skin, fur, various polymers—had been developed extensively before materials science was invented. More recently identified biological materials—poly(lactic acid), chitin, engineered proteins—have not, in general, competed well with petrochemically derived commodities on the basis of cost and mechanical or electrical/magnetic/optical properties. Issues of cost, application to local production in developing economies, independence of petroleum-derived feedstocks,

Figure 1. Materials in biomedicine include those used to make functional replacements, such as contact lenses (left), dental screws to replace teeth (center; courtesy of Pacific Precision, Calif.), and silicone gels (right; courtesy of Mentor Corp., Calif.) for implants.

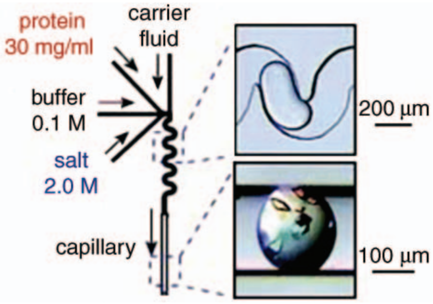

Figure 2. Proteins can be crystallized in a microfluidic channel (adapted from Reference 20). An aqueous plug in a water-immiscible solution (top) serves as a microreactor in the channel. Flowing solutions into winding channels mixes the protein and precipitant, and nucleates the growth of crystals (bottom). These microfluidic systems are fabricated in poly(dimethylsiloxane) (PDMS) using soft lithography.[2–6]

and unusual properties make it worthwhile to rethink bio-derived materials from a fresh perspective.

Materials for biology. We can speculate, however, that as materials science turns to the development of materials specifically *for* biological applications, materials *from* biology or using biological components may become much more important. While recombinant proteins may not rival polyamides for low-cost applications as fibers, they may be uniquely suitable as adhesives for tissues. The interest in polylactides, poly(beta-hydroxybutyrates), and oligopeptide-decorated gels all provide examples.[26–30]

Biomimetic systems. Biology is replete with extraordinarily elegant solutions to problems in materials science. The shells of mollusks and the dentin of teeth both teach lessons in building tough structures from relatively weak materials (calcium carbonate and calcium phosphate). Enzymes are catalysts of extraordinary sophistication made from linear strings of amino acids, spontaneously folded (that is, self-assembled) into complex, functional, three-dimensional structures. Bone is a multifunctional material that supports mechanical loads, houses the tissue (marrow) that makes blood cells, and remodels as its host grows and ages. Biology has explored many, many strategies for sensing, self-healing, propulsion, and building functional structures. The brain is an extraordinarily flexible, adaptive, fluid-cooled, glucose- and oxygen-fueled microprocessor, operating on principles entirely different from those used in semiconductor devices. Biological systems offer an almost endless and unfamiliar (to most engineers) range of stimulating designs for functional materials and systems to materials science. Learning how to mimic these systems—especially dynamic and adaptive systems—offers opportunities to make fundamentally new types of materials systems.

Hybrid living/non-living systems. The two reigning areas of technology today—information technology and biotechnology—focus on information and life, respectively. When two fields are as active as these, there will inevitably be important interactions at the border between them. One of the opportunities for the future is building devices and systems that fuse the function of living and non-living systems: the paradigmatic problem is: "How do I plug my computer into my brain?" Regardless of the desirability of finding an answer to this question, the broader issue of connecting the biological to the abiological will inevitably be one of the important parts of future science, and MS&E can contribute crucially to all aspects of this problem.

Biological Function: The Hierarchy from Molecules to Organisms and the Importance of Biological Assays in Biomedical Research

What *are* organisms? It is important for materials science to understand the complex hierarchy—from molecules to multicellular ecologies—that characterizes living systems. The most elementary unit of biology is the cell: it is the simplest structure that is *alive* (Figure 3). The structure, organization, and operation of the cell is more complicated than we can presently describe in any detail, but when considered from the point of view of a scientific reductionist, it is a collection of molecules which form a complex network of catalysts, sensors, structural elements, information processors, transducers, and other functional systems, and which communicate among themselves using molecular signals and molecular recognition in a remarkable range of ways. Different cell types organize into tissues, and tissues organize into organs. Collections of organs form an organism. All of this complexity counts; it all contributes to the function of the organism. From the vantage of materials science, the natural wish to simplify—to capture the essential structural elements and neglect the messy molecular biology—will lead, at best, only to partial solutions.

> Even what appear to be "simple" structures—such as bones and teeth—are in fact dynamic and are continually remodeled by cellular processes.

Biological structures are also almost all multifunctional. Although it is already possible to replace some part of the structural characteristics of bone by titanium, it is not possible to replicate the multiple functions and capabilities of bone.

MS&E has always focused on *functional* assays. Structure is important to the extent that it contributes to function, but not otherwise. Function is as important in biomaterials science as in more familiar areas of materials science, but the biochemical and biological assays required to measure function in biology are almost entirely unfamiliar to materials scientists. We understand completely that making a honeycomb structure as a heat exchanger is useless unless that structure conducts heat. There is a tendency—because of the unfamiliarity of biological assays—to make a honeycomb structure in a plausible polymer simply because it can be made, and to hope that it might be useful as a scaffold for growing cells. Without having the knowledge or the familiarity with cell and tissue culture to determine the ability of the polymer to function as a scaffold for tissue growth, this kind of work can generate results that are not very relevant to biomedicine. Biomaterials science must be guided by biologically relevant assays, and those assays, in addition to being unfamiliar, are in many cases technically very difficult—often more difficult than the materials science itself. That inconvenient fact notwithstanding, an essential part of the development of biomaterials science is to develop a very high level of expertise in relevant bioassays. This expertise can develop in many ways, but the most plausible, and the one that would take place most rapidly, would be that occurring in active, interactive collaborations between materials scientists and biologists—collaborations in which, in general, the biologists must lead.

Current biomaterials technology: using materials science in biomedicine. The current uses of synthetic materials in biomedicine have been reviewed extensively.[31–37] We refer to these reviews but again emphasize the point that current materials used in biomedicine have only a small fraction of the sophistication of the naturally occurring materials that they replace. Synthetic materials and structures are, in general, poor or partial replacements for naturally occurring ones. They are more satisfactory when they serve a function that does not exist in nature (for example, delivery of a drug by erosion of a polymeric matrix *in vivo*; alteration of the relaxation time of protons in water to improve contrast in magnetic resonance imaging).

Problems with high and low biological content. In choosing problems, it is useful for the materials scientist to consider the biological content of the problem and to choose those with a level of biology that matches what the science can provide and what the problem requires. We illustrate this point with three examples:

1. Controlled release is a problem with a relatively low level of biological content.[38–43] The materials system used is designed primarily to serve a physical function—to release its contents according to a programmed schedule—and to be sufficiently biocompatible to function for a period of time that is often relatively short.

2. "Fracture putty" (a name we have made up for a product that does not yet exist) would be an example of a material with intermediate biological complexity. The need is in treating broken bones. In current medical practice, a complex fracture of a bone would be immobilized, often with screws or pins that are complicated to align and fix and are potential sources of infection. These fixtures often require further orthopedic attention when the fracture has healed. A material that would allow the orthopedic surgeon to align and immobilize the bones and fragments quickly and conveniently, to form a structure that would allow the patient to use the broken bone immediately, to stimulate healing and resist infection, and to be replaced by normal bone over some period of time would be most useful. "Fracture putty" poses many technical problems—but probably not insuperable ones—for the materials science community.

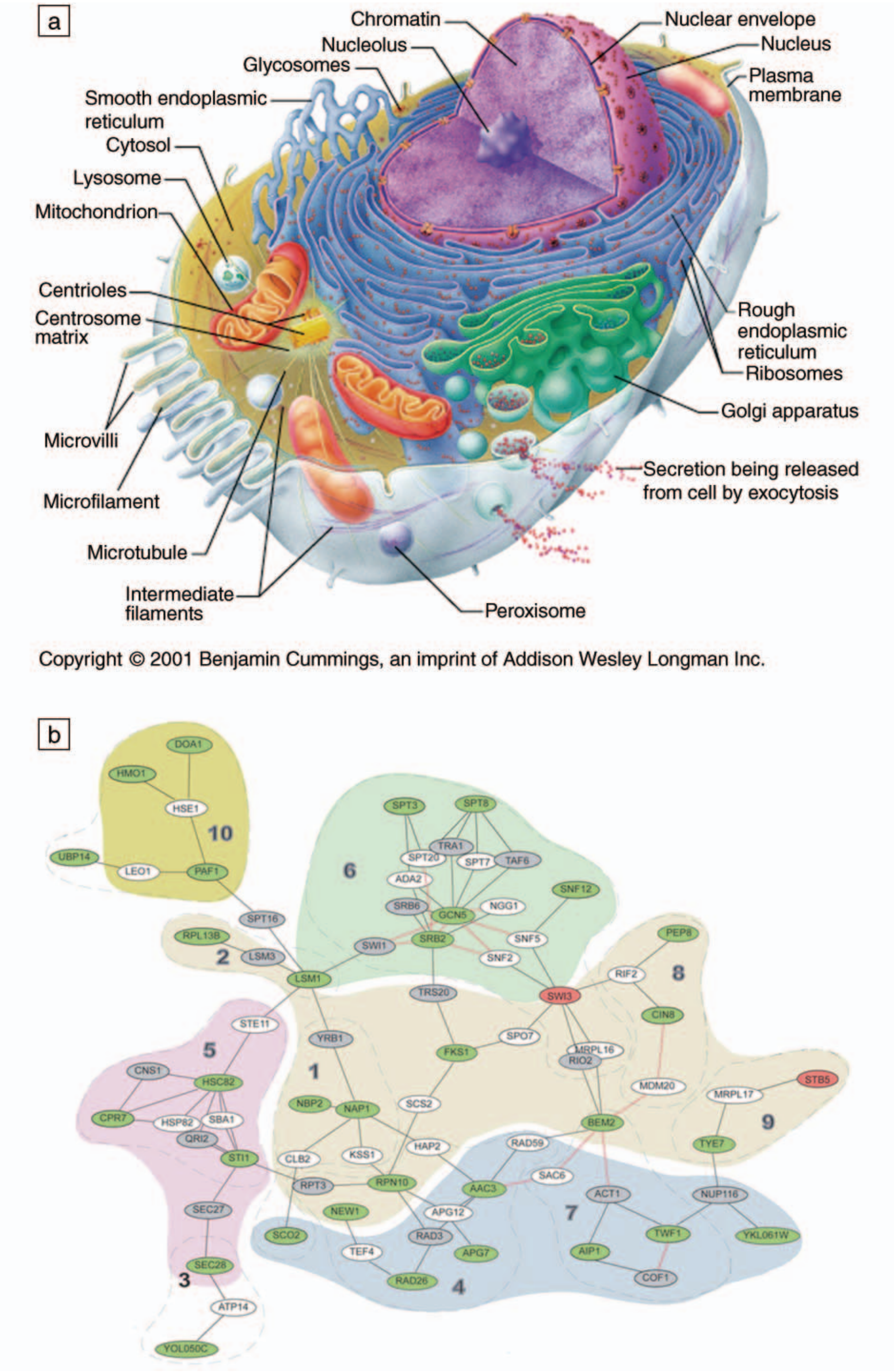

Figure 3. (a) The cell is a complex structure with many compartments and organelles possessing individual and interdependent functions. A large portion of the cell's metabolic activity serves to produce proteins, which are functionally linked to many other proteins in a cell. (b) Protein networks are used to diagram the complicated interconnected nature of protein interactions (copyright © 2004 Public Library of Science).

3. Replacement organs represent problems of high biological content. Although patients can survive for various periods of time with specific functions of some organs (heart, lungs, kidneys) replaced by synthetic devices, these devices are used only when there is no alternative. Complete, long-term replacement of even very simple structures (for example, the heart, which is primarily a mechanical pump, or a urinary sphincter) is a dauntingly difficult task,[15,43–48] and one to which MS&E can sometimes contribute, but in which most of the key technical problems lie in the biology.

The best opportunities for materials science in clinical medicine would seem to us to be in problems of low and intermediate biological content.

Selected Opportunities for MS&E Research in Biomedically Related Areas

What are examples of opportunities for materials science to contribute technically to biomedicine? The complete set is very large; the following subset includes some of our favorites. The choices in this list are entirely idiosyncratic and personal: they represent only a few of the opportunities that the field offers. This list focuses on problems with broad application but in which there is a substantial need for new science; it is not a list of pre-commercial engineering problems.

Biocompatible systems. High on our list is the science of biocompatibility. Understanding this subject at a level that would make it possible to design materials for biocompatibility would make it possible to improve healthcare in areas ranging from prostheses to the management of diabetes (through improved implanted sensors and indwelling pumps). The fundamental biological science underlying the biocompatibility of synthetic materials and structures is, however, not understood, and is unlikely to be explored in any depth by biologists working alone. How does an organism recognize a material as synthetic and unnatural? What are the mechanisms it uses to seal it off and reject it? How do synthetic materials activate and damage cells and tissues inappropriately? How can a synthetic material be made to mimic a naturally occurring one? These are all questions to whose solutions competent, creative teams of materials scientists, biologists, and clinicians will be able to contribute.

Functional but temporary scaffolds and patches. Much of medicine is now concerned with repair: broken bones, torn ligaments, damaged tissues. Materials that provide temporary function ("fracture putty" is an example; various kinds of adhesives to join tissues are another) while stimulating and guiding the healing of the wound would be useful throughout medicine. To develop such materials, of course, one would have to combine the structural and adhesive characteristics required for temporary repair with a deep understanding of biocompatibility and wound healing.[32,39,49–53]

Gels. We can synthesize a range of gels.[39,54] Gels are also used throughout complex organisms: in joints, in the eye, in thrombi, on the surface of cells and organs. Combining a deep understanding of the complex physical characteristics of gels with sophisticated, designed biological function is just beginning.

Nanoparticles in biomedicine. Nanoscience is now generating a range of new types of nanoparticles with a range of compositions and structures; the sophistication in function that these structures offer will only increase with time. They have two immediate applications in biomedicine. First, since nanoparticles are small relative to the cell, they are potentially invaluable tools for investigating the cell.[55–61] Second, because their size can be controlled, from that of large molecules to that of small cells, their ability to escape the vasculature *in vivo* can also be controlled. Third, their biological activities are important in understanding the broader question of the toxicity (or lack thereof) of nanoparticles generally.[60,62–64] This issue is an important one for the development of nanoparticles in the future. Fourth, because they are small, they can circulate systemically in the bloodstream and thus serve in roles such as magnetic resonance enhancement,[65] iron delivery (for the production of red blood cells), and drug delivery (to improve the availability of serum-insoluble drugs).[66,67]

> Biomedicine will define the problems, provide the resources, and set the agenda. Materials science will follow, not lead.

The cellular workbench. Because understanding the cell is one key to understanding life, any tool that provides more and better information about the cell will be useful to cell biologists. Many tools used to study the cell will, of course, be biological, but the physical sciences—especially materials science—offer an orthogonal range. Small magnetic particles to stimulate the cell and to report on its response,[68] sub-wavelength optical structures to provide deep sub-cellular resolution of biological structure,[61] small electrodes able to interrogate the cell electrically—these represent examples.

Systems combining electrical and biological function. The border between information technology and biology will eventually be an important one. Neural prostheses may benefit from effective electrical stimulation. Bone healing can be accelerated with electrical stimulation[69–71] by mechanisms that are not currently understood. Electrochemical release of drugs, and of cells in patterned culture, are now actively explored.[16] Biology does not normally use electron currents: it uses currents of ions and molecules. IT does not use ions and molecules; it uses electrons and photons. Bridging this gap will open many opportunities.

Biosensors. "If you can't measure it, you can't control it" is an adage of systems engineering. Sensors for biological function come in almost countless different varieties, but they share the commonality that they measure biological function. Some (in the future, probably many) biosensors will be implanted in the body; for implanted devices, biocompatibility is obviously a key characteristic.

Biomimetic structures. One of the areas where biology has many ideas to offer materials science is in so-called biomimetic systems: that is, in the design of materials, structures, and systems that mimic (without necessarily using biological components) sophisticated functions of biological structures. Examples of biological structures that are now stimulating non-biological research include actuators such as muscle and hydrostats (an example of hydraulic engineering in living systems), the wide range of eyes developed by different life forms, and neuromorphic systems for sensing, computation, and control.

Self-healing materials systems. One of the most remarkable characteristics of living systems is their ability to heal themselves using only endogenous resources. Understanding the strategies they use for this purpose, and implementing these strategies in synthetic systems, would provide many new opportunities.

Low-cost systems. A problem of a different sort is cost. In a world where competition is global, cost is often the most important parameter of a system. Cost is also crucial in sharing the benefits of medical technology with developing countries, in reducing the costs of healthcare in the developed world, and in ensuring broad access to effective healthcare across societies. Providing the functions of biomedicine—from diagnostics to functional replacement and repair—at acceptable cost requires that many aspects of our current biomedical systems be redesigned to lower their cost. MS&E must contribute to this re-engineering.

Competition: Is the Solution to a Problem in Biomaterials or in Biology?

An important issue to consider in choosing problems in biomaterials is the competition for materials-based solutions versus purely biological approaches. There is no reason to try to solve a problem using synthetic materials if there is a high probability that the final solution will be a biological one. The probability of a successful synthetic solution will go down as the biological content of the problem goes up. Consider, for example: What to do when an organ or complex structure fails? This problem can, in principle, be addressed in at least four ways:

1. Artificial prostheses. The failed part can be replaced with a synthetic part. This solution is the one now used (with differing degrees of success), for example, in replacement of joints and lenses.

2. Transplantation. For more complex structures (for example, kidneys or lungs), transplantation is the current solution. Transplantation is a stopgap, and a very expensive one, but it is all that is available for failures in complex organs.

3. "Grown" replacements. The promise of tissue engineering is to grow organs, or parts of organs, for use in replacement.[2,47] Tissue engineering is very early in its development, but cultured skin is now sometimes used in grafts for burn patients (Figure 4). It will probably be possible to grow increasingly complicated, biologically relevant structures in the future.

4. Regenerative medicine. A further (perhaps ultimate) class of solution is to direct the body to regenerate tissues or organs that have failed or are failing. Instead of leaving a heart with a scar after a heart attack, the body would be directed to have

Figure 4. Materials science has successfully created some purely synthetic replacements for complex biological systems: examples include hip joints (left, courtesy of Diamond at Work), skin (center, courtesy of Integra Lifesciences), and an artificial heart (right, courtesy of Abiomed).

the damaged heart regenerate into a fully functional form—or even better, to cause the arteries damaged by atherosclerosis and inflammation to heal themselves before the heart attack occurs.

In some instances (for example, lenses for the eye or the replacement of a tooth), a synthetic material may always be preferred because it will be less expensive and more quickly available. In others, more complex biological strategies may not be able to compete with synthetic strategies in the foreseeable future. Still, ultimately, biology has the potential to offer a superior solution to the problem of replacing function *in vivo*, and the capabilities of biomedicine are growing at an astonishing rate. Biomedicine will have capabilities in 25 years that we cannot imagine now. Biomaterials science has a broad future, but the complexity of biological problems and the extraordinary growth in capability of biomedicine will limit it to problems with only modest biological complexity, or to those for which there are no biological solutions. Unless, of course, biomaterials science makes progress in understanding the fundamental science of biocompatibility, functional integration of living and nonliving structures, and interfacing synthetic systems with the nervous system as rapidly as fundamental biology has made progress in genomics, cell biology, and metabolism!

Problems of a Different Kind

In addition to the problems in human medicine and in biomedical research on which this discussion has focused, there are a wide range of problems in the broader world of applied biology to which materials science might contribute: these include veterinary medicine, plant biology, environmental science, biological production of commodities (energy, food, water), and others. In our opinion, two of these deserve special mention, both because they are important to national security (in a broad definition of the term) and because solutions to them are severely constrained in cost (and cost reduction is an area in which MS&E may have an intrinsic advantage over complex biology, and where it can certainly contribute).

Healthcare in developing countries. Sharing the benefits of U.S.-style healthcare with less wealthy countries is both an ethical issue and an issue in national security: so long as those in developed countries are conspicuously healthier and live substantially longer than others, they will be a focus of discontent. Some of the benefits of the U.S. healthcare system are simply too complex to be shared, but others—clean water, affordable and inexpensive diagnostic systems, simple prostheses such as eyeglasses and hearing aids—provide problems to which materials science could contribute.

Biodefense. Two of the most serious threats of terrorism to our society are nuclear weapons and biological weapons. Biological weapons represent a "dual" problem, since many aspects of bioweapons are similar to aspects of natural but emerging disease. Materials science can contribute to defenses against both, but many of the systems needed for biodefense—detectors, analytical systems, filters, protective gear, self-decontaminating surfaces, water purification systems—have particularly strong materials components. Since these types of systems will also probably eventually be very widely distributed, there is some commonality between them and systems used in healthcare in developing countries.

How to Proceed?

Biomedicine provides a broad, new, exciting set of problems for MS&E. What is required to capitalize on these opportunities? Biomaterials science will develop, we believe, as a new, independent field, more distinct from the existing areas of materials science than are, for example, structural materials and electronic materials. To develop this new field, there must be people eager to create it, opportunities for them to learn the new land they are colonizing, and resources for them to work with. Developing the people and resources can occur by happenstance but will progress more rapidly if those trying to develop the field think about as many of its parts as they can. We suggest four imperatives, if the objective is to grow the field of biomaterials science and engineering rapidly and effectively.

Make the case for biomaterials science. Given the range of opportunities, it might seem unnecessary to make a case for the value of biomaterials science: the opportunities should speak for themselves. Not so. The medical profession, in general, does not think of materials science as an important contributor to healthcare, and research biologists are simply too occupied with exploring the biology to worry about the origin of the tools and materials that they use. The field of biomaterials needs a clearly articulated vision; one that is comprehensible and compelling—not to materials scientists—but to cardiologists and epidemiologists and genomicists: the *users* have to be convinced, since they understand the problems to which biomaterials must be applied, and they control the financial resources on which biomaterials must be built. Dollars for ocular adhesives must compete with dollars for oncology.

Learn the field. Because problems in biomedicine are defined by doctors and biologists, and because the biomedical community controls the resources used to support research in biomedicine, individual materials scientists must learn biology. There are, of course, courses in biomaterials science, but they tend to be strong on materials and weak on biology. There is too much to biology for even biologists to have a broad view of the whole field; certainly materials scientists cannot easily do so. But somehow they must be able to learn enough *real* biology to manipulate cells, assay enzymes, and sequence DNA. Perhaps most importantly, they must learn how to collaborate with doctors and biologists. Running a "mouse house"—a facility to house mice to be used in testing biomaterials in intact organisms—is expensive, is highly regulated, and requires specialized management. Designing, interpreting, and conducting experiments in animals are even more difficult.

Develop a pathway for transferring technology. One of the key reasons for the success of biotechnology was the availability of a mechanism—startup companies financed by venture capital and access to markets through established pharmaceutical companies—to transfer university technology into commercial development. This transfer is an important one: it attracts amounts of capital for development of the technology far larger than what the federal government can fund, it provides exciting careers for students, and it generates products that the voting public can understand. Biomaterials science is close enough to biomedicine that the availability of capital should not, in principal, be a problem, but developing a system for technology transfer that works is not simple, and that which will evolve for biomaterials will be different from that which has evolved for biopharmaceuticals.

Engage the Materials Research Society. And what of MRS? How can it contribute? MRS is a respected professional organization that speaks for the materials research community. It spans university, industry, and government laboratories. It has the potential to catalyze the activities that will be required for biomaterials science to grow to its full potential. The vigor of materials science and engineering, as a discipline, may well depend, in part, on the willingness of MRS to get involved, and on its effectiveness in doing so.

Summing Up

Let us summarize our opinions about biomaterials science in four points:

1. Materials science should follow and serve, not lead. The hard part of biomaterials is the biology; the important applications of biomaterials are in medicine and biomedical research. Biomedicine will define the problems, provide the resources, and set the agenda. Materials science will follow, not lead. Following does not make the problems less interesting or important, but it does require materials science to learn biology, not the other way around.

2. The fundamental biology is not in place for much of biomaterials science. Biomaterials is, in most part, not an engineering problem—it is still a problem in fundamental science. We do not know what biocompatibility really is and hence cannot design it into products. We do not know how cells become tissues—much less organs—and hence cannot design scaffolds that effectively promote organ growth. We do not know how to transduce binary information from computers into action potentials in neurons, and hence we cannot engineer prostheses that talk to nerves. The major emphasis has to be on the fundamental science, not on the engineering application of science that is already known. This emphasis on fundamental science must, however, be balanced by immediate, visible, and effective contributions to problems in medicine and public health.

3. Biomedical problems are systems problems: materials are only one piece of the puzzle. In the end, biomaterials will function in medicine, and sometimes in humans. They will be only a part of the solution, and they must learn how to fit into the manipulation of very complex systems, rather than being single-point solutions to well-delimited problems.

4. In the land of the blind, the one-eyed man is king. Despite all the difficulties of learning a new field, making a place for a new discipline, and taking a secondary rather than primary role, the opportunities for MS&E in biology and medicine are breathtakingly interesting. Biomaterials science is a field that is still in its infancy. Those who take the plunge will have, we believe, endless fun. Those who know something about both materials and medicine will be able to explore a new field with many exciting problems and with very little competition. It will not be possible to know the answers at the beginning, but knowing enough to get started will suffice.

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