Grand Challenges in Interfacing Engineering With Life Sciences and Medicine

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***Abstract*—This paper summarizes the discussions held during the First IEEE Life Sciences Grand Challenges Conference, held on October 4–5, 2012, at the National Academy of Sciences, Washington, DC, and the grand challenges identified by the conference participants. Despite tremendous efforts to develop the knowledge and ability that are essential in addressing biomedical and health problems using engineering methodologies, the optimization of this approach toward engineering the life sciences and healthcare remains a grand challenge. The conference was aimed at high-level discussions by participants representing various sectors, including academia, government, and industry. Grand challenges were identified by the conference participants in five areas including engineering the brain and nervous system; engineering the cardiovascular system; engineering of cancer diagnostics, therapeutics, and prevention; translation of discoveries to clinical applications; and education and training. A number of these challenges are identified and summarized in this paper.**

***Index Terms*—Bioengineering, biomedical engineering, engineering, grand challenges, healthcare, life science, medicine.**

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I. Introduction

The 20th century was regarded as the century of extraordinary progress in the physical sciences and engineering. The beginning of the 21st century, which is noted as the bio-era, presents an outstanding opportunity to engineer biological systems using advances in the physical sciences and engineering. Despite significant efforts to develop the knowledge and ability that are essential for addressing biomedical and health problems using engineering methodologies, the optimization of this approach toward engineering the life sciences and healthcare remains a grand challenge.

As the pace of research and development continues to accelerate, how to address the most significant challenges that face the scientific community and how to best invest public resources to achieve the largest impact on society are of paramount importance. Public discussions and debates become essential in identifying and removing those difficulties that could otherwise become roadblocks to progress and innovation.

This paper summarizes the discussions at the First IEEE Life Sciences Grand Challenges Conference, held on October 4–5, 2012, at the National Academy of Sciences, Washington, DC. The conference was co-sponsored by the National Science Foundation (NSF) and the Institute for Engineering in Medicine (IEM) of the University of Minnesota and was endorsed by the International Academy of Medical and Biological Engineering. Experts from academia, industry, and the government were invited to make presentations about what they saw as the grand challenges in engineering the life sciences and medicine for the future. In addition to three keynote lectures, five grand challenges were identified and covered by the invited speakers, as well as discussed by all meeting participants: 1) brain disorders and the nervous system; 2) heart diseases and the cardiovascular system; 3) cancer; 4) translation: from bench to bedside; and 5) education and training. Despite the wide breadth of topics covered at this conference, it was remarkable that many of the grand challenges highlighted by the speakers seemed to resonate in other areas, too.

The keynote lecture by Nobel Laureate Dr. Phillip Sharp articulated the view that the "*third revolution*" in the life sciences would be brought about only through interdisciplinary collaboration with engineering, physical, and computational sciences. He outlined remarkable opportunities for revolutions in engineering, including sensitive and quantitative measuring/imaging; dynamic control technologies; understanding how drugs can work together, or not; and advanced manufacturing principles and rapid prototyping in genetic engineering, process development, and device fabrication to address problems of slow and expensive design–build–test cycles that plague all bioindustries. Advances in information technology are required for the real-time acquisition, storage and processing of large, often massively parallel datasets, as much is to be gained from a more complete understanding of normal and disease conditions through quantitative models, which, in turn, could lead to better-informed and engaged patients. Getting the required interdisciplinary collaboration to successfully take off is indeed a grand challenge itself, but the potential benefits are enormous. Indeed, the analogy was drawn that just as electrons in physics ultimately ushered in today's information technology, the discovery of genes in biology is transforming the life sciences, whereby methods from the engineering, physical, and computational sciences will dramatically advance our ability to understand and control biological phenomena.

The keynote lecture by Dr. Charles Vest, the president of the U.S. National Academy of Engineering and president emeritus of the Massachusetts Institute of Technology, focused on the role of technological innovation in serving the globe. He started by pointing out how the current U.S. academic model of doing research driven by the needs of industry, which was put in place after the Second World War based on the recommendations of the Vannevar Bush panel, has been tremendously successful. However, with today's information superhighway, the focus should be on forging global collaborations and ensuring the most widespread dissemination of knowledge by taking advantage of the available technological resources. Dr. Vest stressed that even while making these changes, we have to ensure that "basic" and "use-inspired basic" research remains strong because these stand the test of time. Particular instances from the past that he mentioned are the work of Thomas Edison, Louis Pasteur, and Niels Bohr.

The keynote lecture by Dr. Roderic Pettigrew, the director of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the National Institutes of Health (NIH), highlighted the considerable progress NIBIB has made in advancing medicine and healthcare using engineering approaches and the need for expertise across several disciplines in order to address the current and emerging challenges in healthcare and biomedical innovation. It was pointed out that engineering, which has had a traditional role in translating basic sciences research into practical applications, is likely to play a crucial role in the translation of biomedical research into precisely targeted and individualized therapies. Dr. Pettigrew referred to this as "precision medicine," which represents a unique feature and future direction of engineering the life sciences and medicine.

The grand challenge in education and training was a common theme that was articulated by several of the invited speakers and discussed warmly in the breakout sessions. Carrying out cutting-edge interdisciplinary research at the interface of the life sciences and engineering will require a workforce that is adequately trained in both the biological and quantitative sciences. Having deep understanding in one of the areas while possessing superficial understanding in the other will no longer suffice. The demands of educating this new workforce are just beginning to be addressed, and there are a limited number of training programs supported by the NIH and NSF geared toward this objective. Such interdisciplinary training needs to become much more widespread before it can have a meaningful impact.

Another grand challenge articulated and debated at the conference was the large number of regulatory hurdles that one faces in carrying out translational research. For instance, it was pointed out that the approval process for medical devices in the U.S. is so time-consuming and tedious that it often discourages innovators from trying to bring their products to the market. This, of course, has to be carefully weighed against the responsibility of the regulatory agencies to ensure the safety of the public. Thus, the main regulatory science challenge concerns the development of approval procedures that are much faster yet do not compromise public safety.

Several grand challenges in research that interfaces engineering and life sciences were identified from the plenary panel discussions and breakout sessions. New opportunities for engineering research to further treatment and management of brain disorders, cardiovascular diseases, and cancer were discussed. A number of challenges were identified in these areas that need to be addressed in order to significantly advance the state of the art.

The following is a summary of discussions by invited speakers and meeting participants on each of the five grand challenges debated during the conference.

II. The Grand Challenges

A. *Grand Challenges in Engineering the Brain and Nervous Systems*

In the field of neurotechnology, we have made tremendous progress gathering foundational knowledge of the brain and the nervous system, and in recent years, we have begun translating this knowledge to build technology to diagnose and treat some neurological and mental diseases [1]. Still, many questions and challenges remain. Out of more than 400 neurological disorders currently identified by the National Institute of Neurological Disorders and Stroke, we are currently only focused on a relatively small number of diseases and disorders of the nervous system (e.g., paralysis, Parkinson's, epilepsy, pain, stroke, and maladies of hearing and sight). Despite advances in fabrication, current neurotechnology solutions predominantly rely on miniature (microscale or larger) devices with components based upon or adapted from legacy systems. Additionally, despite vastly increased computational capacity, very little modeling of interactions between the brain and implanted systems is used to guide device development. Technology-guided neurosurgery is a young and growing field, but there are even greater opportunities.

Two major obstacles continue to face the field of neurotechnology: our limited understanding of normal and diseased nervous system function and our limited technological approaches to measuring and manipulating neural circuits. We still have limited understanding of how the brain works, especially brain plasticity and development, and little is known of dynamic brain networks and their integration with cellular processes. Though current technology enables observation of intracellular neural activity in the intact brain for a few hours, we lack the technology to measure these processes over longer timescales and in many neurons simultaneously. We also lack the ability to precisely monitor and modulate the nervous system using noninvasive approaches. Additionally, we do not have the computational tools to fully understand the current and future neural data required to explain brain disorders and diseases. While we can record the extracellular activity of small neural populations, one of the bigger challenges in developing the technological systems to address brain disorders is identifying how much information we actually need for the application of interest. Understanding the functions of the nervous system and using that understanding to address clinical problems require an ability to interface with the nervous system that is beyond our current capabilities. The challenge of enhancing this ability is multifaceted. Systems engineering and materials research are needed to address issues such as heating of batteries during recharging, microscale interconnects between leads, and localized acquisition of data. Also, significant research is needed to enhance our ability to interact with the nervous system noninvasively, including a multi-degree-of-freedom noninvasive brain–machine interface. A substantial obstacle is how we can scale up neural interfaces for long-term performance. Current technology requires chronic electrodes to survive in the brain for decades. If we continue to pursue this solution, we need to understand why electrodes fail. Finally, we need to promote better crosstalk and communication between neurobiologists, neuroscientists, neurologists, neurosurgeons, and neuroengineers.

The grand challenge for the next decade is to precisely decode, restore, and improve nervous system function. Reliable methods must be developed to prevent, diagnose, treat, and cure neurological and mental diseases. Solutions for each and every neurological problem should be optimized. These solutions should provide a consistent, fault-tolerant, and secure solution for neural-controlled movement and sensory systems. Miniature devices should be integrated systems (developed using tools beyond traditional design methodologies). The modeling framework that will have a meaningful impact on the development of these integrated systems will target multiple spatial scales (from cellular levels to tissue and organ levels) as well as varying temporal scales. High-resolution spatiotemporal imaging techniques should be developed that can precisely decode neural systems' functions, guiding rational restoring and improving the neural functions. Universal design methodologies and systems engineering tools and methods should address issues dealing with power consumption, wireless power transmission, packaging, materials, and biology. Brain–computer interfaces need to have scaled-up input/output, with the ultimate goal of producing thought-provoked action at a distance and establishing noninvasive capability to interface the brain with the computers. Neuroengineers should think beyond electrical solutions, adopting less-invasive and noninvasive solutions and/or those with novel sensing and stimulation modalities (e.g., light, magnetic, and pharmacological). The field should integrate neurotechnology devices with regeneration of neural tissue to maximize therapeutic value. In the next decade, we should pursue the development of long-term (decade lifetime), high-throughput, high-bandwidth, high-reliability, scalable neural interfaces for information extraction and delivery. As individual technologies are developed, they must be refined to the state in which they can be widely shared and reused throughout the community to accelerate translation. We are at a juncture in research and development history where the field is primed to redesign the current technology from the ground up with a more holistic approach that encompasses all scales of the nervous system, driven by computational models. Our goal is to produce next-generation devices that adapt to changes in the nervous system and/or environment throughout the lifetime, ultimately reducing the widespread burden of neurological and mental diseases on the society as a whole. Lastly, research on next-generation devices will benefit from efforts that will specifically target strategies for a seamless transition between fundamental research and systems engineering, regulatory science and clinical trials, and, finally, product.

B. Grand Challenges in Engineering Cardiovascular Systems

Chronic diseases such as heart disease and stroke are the major cause of death in almost all countries, and as such cardiovascular disease presents challenging problems in diagnosis, treatment, repair, or replacement. Engineering has played a central role in our understanding of cardiac electrodynamics and elastomechanics, and in the development of diagnostic instruments, prosthetic valves, pacemakers, implantable cardioverters/defibrillators (ICDs), and automated external defibrillators (AEDs), and it should continue to do so.

Of all the diagnostic methods for cardiovascular disease, the greatest challenges lie in the area of noninvasive monitoring of diseases such as hypertension or arrhythmias, prediction of adverse events, and the need for a comprehensive computational and systems approach to describe the cardiovascular system for applications in diagnosis and virtual prototyping. There are also serious obstacles to the treatment of cardiovascular disease, such as the need to accelerate drug development, and increase the reliability and longevity of ICDs and reduce their power requirements (ideally to the point of enabling conscious atrial defibrillation). There is also great potential for advanced neural feedback and other control strategies to regulate the heart, particularly immediately after a heart attack. The engineering of cardiac tissue, propelled by the development of strategies for creating patient-specific induced pluripotent stem cells, presents remarkable challenges, yet paradigm-shifting opportunities, in tissue regeneration and repair. The computational, multiscale modeling of electrical, mechanical, metabolic, and immunological cardiovascular phenomena presents significant challenges in model generation, specification, and validation of simulated cardiovascular systems that can be used in the discovery and development of drug and medical devices [2]. Finally, instrumented, integrated, multiorgan microphysiological systems have as their greatest impediment the development of functional, working hearts at the scale of one-thousandth to one-millionth of the adult human heart [3].

While the unresolved issues in cardiovascular systems are at first glance either medical or biological in nature, many areas of engineering can play critical roles in addressing them, defining the systems nature of many of the problems, providing new diagnostic technologies, and devising advanced instruments and devices. With regard to diagnosis, the continuing increase in spatiotemporal resolution of MRI, CT, positron emission tomography (PET) imaging, and electrocardiographic imaging is the result of engineering advances, and there is no reason to think that this trend has reached its apex. The growing quantity and quality of physiological data from both imaging and advanced analytical chemistry assays can now support the specification of detailed, quantitative models of cardiac function that may enable clinical diagnosis with improved sensitivity and specificity. A great clinical diagnostic challenge may be to better understand the state of atherosclerotic plaque and quantify the associated health risk. Another great clinical challenge is to elucidate mechanisms of arrhythmias and heart failure. Hence, there is a need to continue to advance the core technologies required to characterize, predict, monitor, and reduce/treat atherosclerotic plaque, hypertension and heart failure, and develop beacon imagers that announce cardiovascular disease without the need to "search for the needle in a haystack."

The greatest potential for engineering contributions to treatment of cardiovascular disease may lie in the development of new engineering approaches to accelerate drug development, increase the reliability and longevity of ICDs and reduce their power requirements, and implement advanced neural feedback and control for cardiac regulation, particularly immediately after a heart attack. There is a need to improve biotic/abiotic interfaces, microelectronics, batteries, and sensing/control algorithms required for implantable devices; develop low-voltage control algorithms to pace out of atrial fibrillation; address issues with reliable microchip manufacture and how these affect regulatory decisions on approval and recall of devices; and learn how to harvest mechanical energy from the heart to power devices. It should be possible to accelerate drug development by creating automated biological explorers, i.e., robot scientists that apply machine learning to address biological complexity and enable accelerated, optimal experimental design for tests of drug efficacy and toxicity.

The frontier of repair of cardiac damage and disease lies with tissue engineering or regenerative medicine. Progress in a number of associated areas should yield immediate scientific and clinical benefits. There is a remarkable need to specify both intrinsic and extrinsic factors of the bioenvironment and their time course for the creation of cardiac tissues that grow, vascularize, functionally integrate both electrically and mechanically with the patient's cardiovascular system, and remodel appropriately in response to age and exercise. There is an opportunity to develop novel cell-based therapies for cardiac regeneration postmyocardial infarction, and tissue-engineered pacemakers that are self-renewing.

With regard to simulation, continuing efforts will improve and extend fully integrated, realistic computational models of the cardiovascular system that include electrical, mechanical, metabolic, and inflammatory phenomena to drive treatment planning and personalized medicine, and determine what must be known to prevent and reverse cardiovascular disease. There remains a significant challenge to obtain the data required to specify and validate computational models. While some of these data may be obtained through improved diagnostic approaches discussed earlier, there is a major gap between what can be obtained from humans and what is needed to fully specify metabolic, mechanical, electrical, and immune signaling models. Hence, there is a recently emerging trend to create miniature experimental models of working hearts engineered using human cells [3]. These will be coupled with other microphysiological organ systems to create *in vitro* abstractions of multiple interacting organs that will enable acquisition of high-throughput and high-content functional data that would be impossible in intact animals or humans. These systems present an unprecedented breadth of challenges across all areas of engineering.

With regard to prevention, an effective solution to control chronic diseases such as those of the cardiovascular system is to commence monitoring and modifying risk factors and other possible causes leading to the development of the diseases before noticeable symptoms of illness have developed [4]. In essence, future healthcare systems should encourage the Participation of all nations for the Prevention of illnesses and the early Prediction of diseases such that Preemptive treatment is delivered to realize Pervasive and Personalized healthcare, i.e., the paradigm of the six-Ps medicine [5]. Health informatics plays an important role in implementing the six-Ps medicine and improving human health. Health informatics here refers to the application of information technologies, including the processing, integration/interpretation, storage, transmission, acquisition, and retrieval of health information, to understand the mechanism of and prevent the development of diseases. Effective management of the vast amount of health information generated by the dramatic progress in the six-Ps medicine requires new strategies and innovation across multiple disciplines. Advancing health informatics has been identified as one of 14 grand challenges in engineering in the 21st century by the U.S. National Academy of Engineering [6]. In cardiovascular health informatics, these include developing highly sensitive and fast methods for detecting biomarkers, and real-time, multimodal, and high-resolution imaging for the early and noninvasive diagnosis of cardiovascular diseases such as vulnerable plaque; creating unobtrusive methods and devices for the continuous monitoring of vulnerable patients; designing wearable medical devices and body sensor networks (BSNs); and integrating multiscale and multimodal information for the early detection, early prediction, early diagnosis, and early treatment of acute heart diseases.

C. Grand Challenges in the Engineering Diagnostics, Therapeutics, and Preventions of Cancer

Cancer is arguably one of the most complex diseases. There are many immediate and daunting challenges in clinical care. The first is early detection of cancer, when it is more amenable to treatment. Novel micro/nano-based technologies can facilitate detection of cancer biomarkers at lower concentrations. Technology aimed at visualizing cellular structures and molecular signatures of tissues in a live body can also facilitate early detection and diagnosis of cancer. The second challenge is to differentially target treatment specifically toward cancer cells while sparing the normal cell population. A third challenge is to tailor cancer therapy to each individual patient. Other challenges include the determination of the new treatment regime when the cancer care model is evolving from terminal illness to a chronic condition that people may be able to live with for years after diagnosis. Properly piecing together data from multiple sources, along with prior information, to construct models possessing excellent predictive value is an ultimate key challenge in cancer studies. To address these clinical challenges, there exist multiple engineering challenges and opportunities in design and development of technology and tools, as well as algorithms and models.

1) Experimental Measurement of Multiscale Molecular, Cellular, Tissue, and Population Spatial-Temporal Patterns: A major difficulty in understanding cancer is the lack of experimental data necessary to fully characterize the complex systems underlying cancer development and to provide early diagnosis for effective treatment and targeted therapy. Existing engineering theories and tools were largely developed for man-made systems, where data gathering for identification of system behavior under different perturbations rarely poses any problem. However, well-developed approaches such as control theory are currently impractical and cannot be effectively applied, due to the lack of sufficient experimental data. Bioengineers are uniquely positioned to make major contributions by developing devices (including nanodevices) to generate a large amount of experimental data. We have made tremendous progress in developing devices to continuously measure physiological signals at the macroscopic level. However, we have had less success in measuring cellular, subcellular, and molecular signals. One challenge is to develop nanodevices to measure temporal–spatial biological signals at multiscale, thereby enabling the monitoring of the dynamics of protein network signals and cellular signals for most, if not all, cancer cells throughout their entire life span, in a population of cells associated with a tissue.

In cancer diagnosis, as more subtypes of cancer are being identified, with each subtype leading to different prognosis and treatment outcomes, microfluidic or quantum dots (QDs) technologies are being used to design molecular-level multiplexing assays to assess multiple disease biomarkers simultaneously for more accurate diagnosis. However, the main obstacle for this technology is the lack of a "gold standard" to measure the true cancer status. For example, it is difficult to adjust the QDs' intrinsic signal intensity so that they can contribute equally in tumor biopsy multiplexing during *in vitro* diagnosis and allow deconvolution of the multiplexed optical signals to recover each QD-tagged tissue biomarker expression for cancer diagnosis. In cancer therapy, a main direction in nanodevice development is to design active and smart drugs for targeted delivery. Efforts are now concentrated on the design of biocompatible and controllable nanorobots with systemic delivery mechanisms. With expected progress in understanding how nanoparticle drugs stay within the body and how they would cross the vessel barriers, nanotherapeutics present opportunities for bioengineers to make major contributions.

2) Biomarker Discoveries: At a more practical level, it is challenging to identify reliable molecular-level biomarkers for cancer diagnosis, treatment, and prognosis. This includes monitoring each individual patient's response to cancer chemo- and radiation therapies, with quantitative and precise assessment of health state at the molecular level. Currently, there have been limited genomics, proteomics, and epigenomics biomarkers developed. As there are enormous numbers of DNA, RNA, and protein molecules, with properties and functions unknown, it is challenging to uncover and validate effective biomarkers reliably from high-throughput data. Once identified and rigorously validated, the biomarker must pass the qualification process for regulatory acceptance—a final hurdle in translation.

3) Development of Mechanistic Models of Key Processes of Cancer at Multiscale Levels: With progress in data collection, a challenge is to integrate information from genomics, proteomics, epigenetics, networks, cells, tissues, organs, and populations to develop mechanistic models of physical processes responsible for cancer development. For example, it is unclear how cell types in the microvascular environment contribute to angiogenesis. It is also not clear how best to characterize cancer heterogeneity, in itself versus in its microenvironment, and *in vitro* versus *in vivo*. With rapid progress in techniques such as chromosomal conformation captures and computational algorithms, bioengineers may be able to develop physical models describing the folding and tangling of chromosomes, which will allow us to go beyond using methylation, CpGs, and histone modifications as simply biomarkers for disease correlation. This would allow us to gain physical insight into how these modifications decorate, modify, or alter chromosomal architecture and how they allow opening, closing, and compacting of genes, leading to different gene expressions and cellular states. Success will further lead to the development of engineered tools to manipulate chromosomal architecture for specific genetic and epigenetic programs important for altered and enhanced cellular properties.

4) Effective Empirical Models and Tools of Human Health for Cancer Prevention by Combining Both Mechanistic and Correlational Empirical Relationships: An important direction for bioengineers is to incorporate information from multiple dimensions, including molecular and physiological measurement, cognitive measurement, environmental factors, and dietary information, all with time series information to build empirical models of cancer. Bioengineers can contribute uniquely by directly interfacing instrumentation, measurement devices, data recording and generation, imaging information, experimental design, and computational modeling of cell migration, metabolism, growth, differentiation, and death. We will be able to integrate, develop, and validate empirical models. We will also be able to achieve very fast cycles of model development and modifications that can be personalized to individual patients' health conditions. It is envisioned that this approach will enable us to reduce cancer risk in the general population by 10–15%.

5) A Grand Theory, Model, and Toolset for Quantifying and Manipulating the Personal Fitness Landscape of Health in Cancer Health Informatics: Similar to the evolutionary landscape of Waddington, a landscape picture of the physiological states of cells is emerging. With sufficient understanding of key biological processes, we may be able to construct a probability landscape of network models, where the largest basin of the greatest attractor is that of the healthy state, and other smaller basins of higher altitude correspond to different disease states. Complex diseases such as cancer, represented by these elevated metastates, may be reached from multiple paths, corresponding to the heterogeneous nature of cancer cells with different environmental and genetic alterations. Ultimately, bioengineers may be able to quantitatively define personalized baseline health states through measurements, simulations, and models. Success will depend on the development of data measurement as well as on development of spatial-temporal dynamic multiscale models, integrating chemical master equations and Gillespie stochastic network algorithms, stochastic differential equation models, and ordinary differential equation models, all embedded into individual cells for a full spatiotemporal description of heterogeneous cell populations.

6) Personalized Medicine and Cancer Health Informatics: With advances in the grand theory and our modeling technology, it is envisioned that we will be able to develop tools to construct a personalized health landscape that will provide an individualized roadmap toward improved health. It will allow delineation of different causes of disease for different individuals and will also lead to prescriptions of different treatment strategies. For cancer care, recording a personal health record (PHR) outside the clinical setting will be important, not only because it can assist in-clinic diagnosis, treatment, and prognosis of cancer, but also because it can provide the foundation to turn cancer from terminal illness to a chronic condition. This critical need has created a fast-growing trajectory for cancer health informatics, with its focus on data analytics, including data processing, knowledge modeling, and decision making. With more mobile health sensors, wearable sensors, and ambient sensors available in person, in home, and in public, with more computational engineers trained to interrogate "Big-Data," and with more in-depth collaborations among engineers, care providers, industries, and patients, this research will see its fruition.

D. Grand Challenges in Translating Discoveries to Clinical Applications

Despite tremendous efforts and progress in discovering mechanisms of diseases and developing methods and tools to enable biomedical research, significant translational barriers exist between basic discoveries and clinical applications.

One such obstacle is effective communication and collaboration among engineers, clinicians, and biologists. On the engineering side, it is crucial that bioengineers understand biological and physiological systems [7], of course, but they also need to bring their knowledge of device design and fabrication, measurement, modeling, optimization, and computation to bear not only on problems already well specified, but also on the identification of the key issues that hamper bench-to-bedside translation. It is also necessary to build effective alliances, partnerships, or consortia to put together teams with sufficient clinical, biological, and engineering expertise. The breadth of biomedical engineering is ever increasing, expanding from its historical origins in the quantitative measurement and modeling of organ-level physiological systems, and now also encompassing the realm of tissue engineering, nanotechnology, neuroengineering, synthetic biology, and molecular engineering. This places greater demands on communication and collaboration.

Innovation is another critical element for addressing the unmet needs in medical research and healthcare and a prerequisite for successful translation. One essential aspect is to be able to develop a clear view of what is new or innovative, what is needed from each partner in order to realize success, and what is each partner's perspective on why the problem at hand is worth solving. Innovation is a skill that can be enhanced through appropriate education, training, and tools, for example, in senior-design project courses, and possibly by broadening the engineering curriculum to encompass aspects of market analysis and engineering management. Innovation is the seed for translation, and it can benefit from careful nurturing and cross-disciplinary fertilization.

Moving our discussion from the personnel realm to the physical one, one current trend is to facilitate translation via rapid virtual prototyping. In the engineering world of hardware and software development, the use of computer-aided design (CAD) and computer-aided machining (CAM) has enabled the continued exponential growth in device complexity. Each generation provides more capability, which is then applied to build the next generation. These tools are now being employed in applied computation, virtual prototyping, and interactive graphics, visualization, and feedback to the designer. Virtual prototyping enables rapid cycles of testing and exploring new ideas for medical device design. With the ever-increasing speed and decreasing cost of these tools, the ability to apply them to personalized medicine is emerging. While animal experiments and clinical testing remain essential, rapid virtual prototyping may speed up the translation from bench to bedside. It may be used to address personal variation in anatomy and variation in materials, and can be customized to suit the individual situation. Clinical decisions can be made based on individual assessment and design rather than generic rules and simplistic measurements. Experimental and clinical validation of these methods is critical to maintain confidence.

Just as virtual prototyping is proving ever more valuable, the application of computer modeling of physiological phenomena can accelerate the translation of basic results to the clinical setting, with applications as diverse as validation of new defibrillation electrode configurations and the development of predictive models of drug response. Biomedical engineers are well equipped to utilize their breadth of mathematical modeling skills to span the full distance between basic science and clinical application. There will be remarkable opportunities for the development and utilization of individualized, computational physiological models, such as those currently under development to predict the development of heart and brain diseases and cancer, but translated to the individual patient.

Other recent information technology revolutions will undoubtedly affect the speed of translation, most notably the ease with which low-cost smartphone apps can be created, for example, for point-of-care and low-resource diagnosis and the guiding of treatment, cloud computing to solve massively parallel simulation problems, and even crowd-sourced solutions to computational or engineering challenges.

The rapid changes in these interconnected fields present an unprecedented capability for improvements in care. Valuable information is gained through continued advances in the scale of information technology, extending access to a wide variety of data sources, and many kinds of individual personal sensors that monitor and record with precision. In addition, the capacity to analyze and apply this information is being extended by computing that enables automation of information processing in a way that combines the talents of people working together with computer software tools. Viewed through the eyes of opportunity, this sequence of seeing where information systems can be applied, solving previously difficult problems with new methods, and learning what works and what doesn't yet work is the classic cycle of innovative improvements.

However, it is important to recognize the distinction between a "device" as developed in a laboratory and a "product" that can be sold for use in the clinic. As pointed out by Davidow [8] in his classic 1986 treatise on marketing high technology, superior technological devices do not necessarily prevail in the marketplace. It is the integration of devices with human-friendly support structures that provides a pathway for new customers to follow when adopting new technology that paves the way to widespread utilization of novel techniques, and hence, their successful translation. This same commercial industrial lesson is relevant to the task of translating biomedical discoveries into widely adopted clinical applications. The key requirement is to provide a comprehensive support package, consisting of human-level commercial support, training, and education programs in addition to the underlying competent technological implementation of the basic discovery. In the context of training and support of clinical applications, the first level of support must be aimed at the regulatory process, and later more widespread levels of support will be required to achieve success in the clinical applications marketplace.

The ultimate challenge in translation from basic research to the clinic involves medical device and drug regulation. Earlier, we discussed regulatory hurdles, and accelerated translation could benefit from opportunities to improve the effectiveness of regulatory science—the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products. Increased public and private partnership and collaboration are much needed and may play a critical role in improving the regulatory process and patient safety and in reducing the cost of healthcare. The recent establishment of the Medical Device Innovation Consortium (MDIC) by the LifeScience Alley represents an important movement in this direction [9]. The MDIC, in collaboration with FDA, aims to promote medical device regulatory science with a focus on speeding the development, assessment, and review of new medical devices. In overcoming the translational barriers, technological innovation alone is not enough. We must work with all stakeholders and policy makers to ensure that technological breakthroughs will benefit the general population.

E. Grand Challenges in Education and Training in Engineering Life Sciences and Medicine

Over the past few decades, the biomedical and engineering sciences have become increasingly interdependent, resulting in true integrative approaches to both scientific discovery and application of technology [10]. This trend of convergence is accelerating. In the biological sciences, the genome has been sequenced and many of the molecules it encodes characterized. The next basic frontier in the biological sciences relates to defining the rules that govern the behavior of complex biomolecular systems. Success in this effort requires understanding at a systems level. Engineering pedagogy is unique in that it includes basic systems theory and the concepts of control that are central to engineering science. Similarly, advances in engineering science have benefited from designing principles learned from the investigation of biological systems.

1) Interdisciplinary Education and Research: Converging technologies are defined as the synthesis of knowledge from traditional academic science disciplines in order to engineer innovative technology for the benefit of society. This "involves the coming together of different fields of study—particularly, engineering and the life, computational, and physical sciences—through collaboration among research groups and the integration of approaches that were originally viewed as distinct and potentially contradictory," according to the third revolution document, MIT [11]. The challenge has been the successful integration of relevant disciplines in a graduate educational framework.

Following the Committee on Science, Engineering, and Public Policy (COSEPUP) report [12], the National Science Foundation launched the Integrative Graduate Education and Research Traineeship (IGERT) in 1998 with the explicit goal of training Ph.D. students to learn how to transcend disciplinary boundaries to solve highly interdisciplinary problems and to develop communication and other professional skills to be successful across a range of careers beyond academia. An important goal of IGERT was to bring about an institutional cultural change that breaks down disciplinary barriers and institutionalizes the impact of IGERT after the funding is over, thereby facilitating interdisciplinary research endeavors at that institution. The term "interdisciplinary" was used in 1995 in the COSEPUP report, and it captures the spirit of the concept of convergence today. IGERT is a rare but important program that exclusively focuses on training Ph.D. students in an interdisciplinary environment and continues to make an impact on traditional disciplinary academic institutional culture. In 2011, building on the IGERT platform, the program introduced the additional training requirement of preparing Ph.D. graduates to be equipped through hands-on experience to determine how their research discoveries may be translated into innovations for society.

Being one the pioneers in facilitating interdisciplinary research and training, early IGERT awards show a loose trend of more awards advancing the state of the art through cutting-edge interdisciplinary science. These were followed by a mix of awards for engineering research and applications, and encouraged by the requirement for training in innovation skills. Recent awards show a mix of cutting-edge science, applications, and translational research and training. As mentioned earlier, converging technologies foster innovation and solve society's complex problems at the interface of multiple disciplines. Through the fostering of interdisciplinary research and training at the Ph.D. level, IGERT and other interdisciplinary researchers have been notably successful in receiving awards that recognize innovation and translational outcomes even before the innovation skills training requirement was introduced.

The concept of interdisciplinary training has also been enthusiastically embraced by other federal agencies and private foundations, resulting in the NIH Roadmap Interdisciplinary Research Training Initiatives and, more recently, the Roadmap Interdisciplinary Research Consortia program. The Howard Hughes Medical Institute (HHMI)–NIBIB Interfaces Initiative for Graduate Research Education, a public–private partnership intended to develop and support interdisciplinary training programs that facilitate academic institutional change and integrate the biological and physical sciences, was begun in 2005. Many of these programs have used innovative boot camps to introduce trainees to the concepts of each other's disciplines and team challenges to encourage trainees to work together on difficult, open-ended problems [13]. More recently, HHMI and NIBIB have used small Training Innovation Program Supplements to allow Interfaces and other interdisciplinary programs to disseminate their best education strategies and interdisciplinary practices and to help other institutions to develop similar programs.

2) Recent Investments in Innovation: NIH has established a number of training programs to address training in interdisciplinary fields. In addition to its standard institutional training, individual fellowships and career development programs, NIH has launched many new programs at both the undergraduate, graduate, and early-career levels. At the undergraduate level, NIBIB has initiated a new program to support biomedical engineering team-based design and, more recently, launched Design by Biomedical Undergraduate Teams (DEBUT), a prize competition to award innovative engineering solutions to important clinical problems [14]. As many educational institutions have begun to develop and share, through videoconferencing, web-based Massive Open On-line Courses (MOOCs) and seminars, federal funding agencies have begun to explore how they can support such online interactive learning and web-based collaboration tools. Many NIH- and NSF-funded multi-institutional training programs, which mentor students and postdoctoral fellows across partnering institutions, have also begun to develop. NIH is also thinking about how to provide increased support for interdisciplinary science and early investigators working in such interdisciplinary spaces. At the postgraduate level, a number of innovative Common Fund programs, including the new Director's Early Independence Awards as well as the earlier Pioneer and New Innovator Awards, have been developed to shorten the transition to research independence and to support innovative, pioneering approaches to major research challenges.

3) Biomedical Research Workforce Issues: The most important grand challenge in education is to effectively prepare the next generation of engineers and scientists to address the grand challenges of the future. There is an increasing recognition that the long training time and low early-career salaries for many biological disciplines may be making a research career less attractive to the best and brightest students. Furthermore, the upsurge in U.S.-trained Ph.D. graduates, the increased influx of foreign-trained Ph.D.s and the aging of the academic workforce have made launching a traditional academic career increasingly difficult and led to a large upsurge in Ph.D. graduates seeking other employment. Despite these known problems, most NIH training programs are largely focused on preparing students for academic careers [15]. In addition, only 20%–30% of graduate students are supported by NIH or NSF training programs with the remainder being supported by research assistantships and graduate fellowships. NIH is now exploring how to ensure that all graduate students, whether supported by training or research grants, receive equivalent training and how to best train students for academic and nonacademic research and research-related careers. It will be important to consider where Ph.D. graduates are currently finding jobs and what the future workforce needs for these graduates are as we consider the future of graduate biomedical engineering education.

4) Training of Future Physicians: The frontiers in medical science also include understanding diseases as well as the response to environmental conditions. Succeeding will involve interpretation of molecular physiology and pathophysiology across levels of organization (i.e., cell, organ, system, organismal, and societal levels) and, finally, translation into therapeutic intervention strategies.

How do we prepare physicians to understand, use, and develop these tools? Over the past few years in the United States, several expert committees have been convened to address this question [16]. They have each recommended that the basic training of MDs be changed. Both premed and medical education must evolve to adapt to tomorrow's medicine. Several expert review panels have called for physician training to include more quantitative science. Various models of premed education that incorporate tools characteristic of engineering pedagogy have been tested.

Future physicians will engage in the practice of personalized medicine where clinical trials on different populations will not adequately inform decisions. Rather, they will utilize modeling and simulation to predict the clinical responses to candidate therapeutic interventions for their patients. The efficient strategy to accomplish this transformation in preparing future physicians includes closer collaboration between medical and engineering schools. A view of the whole patient as a system and not a collection of organs, the rising role of genetics, and the integration of behavioral with biological science, to name a few, would be needed. There is a need for some degree of convergence between the goals of medical education and educating biomedical engineers. Future medical education needs to: 1) build on a stronger scientific foundation and 2) equip MD graduates with a toolkit for lifelong learning, including applying quantitative skills and reasoning and modern tools for clinical decision making [16].

5) Increase the Number of Domestic Students Interested in STEM Education: There has been a steady trend of declining commitment to science and technology careers among America's youth. While less than 20% of underrepresented minorities (URMs) who start college majoring in a science, technology, engineering, and mathematics (STEM) discipline graduate with a STEM degree, that number is still only 32% for white students and 42% for Asian students. Other studies quoted claimed that the higher the scores of the student, the more prestigious the university, and the higher the AP scores, the more likely that the students who started in STEM will leave that major during their first year. So, not only is retention low for STEM disciplines, but especially among high-achieving students. This problem is somewhat unique to the U.S., where only 6% of 24-year-old students have a first degree in a STEM discipline, and only 2% of URMs. How we change public attitudes about STEM careers while not compromising academic rigor represents a challenge. Not only we are recruiting and retaining a low percentage of STEM majors, but there are many more among the public at large that started in such a major and quit, further hurting perceptions of careers in science and engineering. The educational programs are particularly low with regard to domestic and international diversity. Domestically, it will be important to change attitudes toward STEM. Primary, secondary, and university faculty need to be more nurturing toward STEM subjects. This is particularly important with regard to programs for students of color.

6) Convergence of Life Sciences, Physical Sciences, and Engineering in Undergraduate Coursework: Interdisciplinary topics should be taught considering all disciplines involved. Life science, physical science, and engineering need to be integrated into biomedical engineering or bioengineering courses, not just presented as separate courses. There are great opportunities for team teaching between life and physical sciences in biomedical engineering, but more should be done in this area. Students tend to focus on the physical or biological aspects of biomedical engineering without seeing the convergence of the two general areas.

7) Emphasize New Areas in Education: There needs to be more emphasis on teaching convergence of life sciences and engineering sciences, especially those that are important for industry such as regulatory science, ethics, design, and business issues. These topics can be integrated into current courses as well as new courses. The constraint of the maximum number of credits for undergraduate courses presents a challenge as to how to fit everything in. Perhaps the possibility of a five-year biomedical engineering curriculum needs to be reconsidered.

8) Technology in Education: Of the many technological advances that have been applied to biomedical engineering education in recent years, some are just "gimmicks," while others have been carefully studied and found to be helpful. Some of these include reverse classes where lectures are given in small modules on the web and students come to the classroom for problem solving and discussion. The web can also be used to advantage for demonstrations, especially of clinical issues that large groups could not easily observe. Instant messaging and audio- and videoconferencing with a course instructor can be useful to answer questions, but this can be time-consuming for the instructor. Perhaps electronic office hours are the way to go. There is also the opportunity to use social media for interaction between instructor and students and students themselves for beyond the classroom instruction. Some universities now have entire courses on the web and give a certificate for completing them. In this case, special problems with regard to homework grading, examinations, and interaction with the instructor have emerged due to very large enrollments, but creative solutions have also evolved. The effort to prepare such courses, however, is astronomical, and there are few rewards to faculty, especially junior faculty members to make this effort. On the other hand, an important advantage of this technology is that it allows access to courses to individuals who would otherwise not find them accessible due to limitations of location, disability, or cost.

9) Experiential Learning: Clinical immersion and internships/coops have been used by some biomedical engineering undergraduate and graduate programs, and found to be effective educational tools. There are, however, challenges that need to be overcome with these experiential methods. Although they can be very effective and popular with students, the availability of these experiences can be limited due to limited number of opportunities, location, time commitment, and costs. There was discussion of the need for more potential funding sources to support such activities as there are currently very limited sources for this type of funding.

In summary, the future of biomedical engineering education faces a wide range of challenges. Emerging disciplines and a systemic viewpoint require new models of education, and this challenge is further complicated by ongoing challenges of recruiting future researchers into the STEM disciplines.

III. Conclusion

This summary and analysis of the First IEEE Life Sciences Grand Challenges Conference, held on October 4–5, 2012, in Washington, DC, briefly discuss the major challenges that face the scientific community. While many challenges exist in scientific explorations interfacing engineering with the life sciences, the participants of this conference identified those in engineering the brain and nervous systems, cardiovascular systems, and cancer diagnostics, therapeutics, and prevention as among the most pressing that biomedical and health research is facing. The impact of meeting these challenges is determined in part by the success of translating basic science results to the clinic for treatment and the home and workplace for prevention. Of equal importance are the grand challenges of the education and training of future generations. These grand challenges may merit a call to action for investigators to develop the capabilities of our society for research, education, and translation in this exciting and critically important interdisciplinary endeavor, as well as for funding agencies to continue or expand their support of these highly important fields.

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