Abstract

With the burst of Information Technology (IT) bubble at the beginning of this century, people are looking for the next wave of technology in which to invest. While we believe that biomedical applications and systems are this next stage, unfortunately, the engineering and bioscience communities are unprepared for the many challenges. In order to connect the engineering and the biomedical science communities, we established the LifeScience Systems and Applications (LiSSA) Technical Committee within IEEE Circuits and Systems Society in 2005—an initiative supported by the National Institutes of Health (NIH) through a conference grant to enable dialogue between the engineering and biomedical science communities. Henceforth, we have organized several annual workshops with different themes on the NIH campus. After each workshop, a white paper is published in IEEE circuits and systems magazine to present the major challenges in various chosen theme areas. Recently, we chose "Biomarker Development and Applications" as our workshop theme. For the first time, we invited eight IEEE societies and various NIH institutes to send their representatives for face-to-face dialogue. This article presents the major challenges in biomarker development and applications based on the general consensus of the conference. The aim of the article is to serve as a wake-up call for more engineers to participate in crucial life-science application and systems research.

A Wake-Up Call for the Engineering and Biomedical Science Communities

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1. Introduction

Today, only a very small portion of engineers are actively engaged in biomedical research. Of these, only a rare few are funded by the National Institutes of Health (NIH). This dearth owes perhaps to fundamental differences between engineering and biomedical research: the engineering disciplines are highly mathematical and technical, whereas biomedical research is less mathematical and more problem driven. Each field is faced with unique challenges. The biomedical

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community lacks critical techniques and suitable tools to deal with enormous heterogeneous, multi-scale data coming out of high throughput devices that threaten to overwhelm them. Meanwhile, the engineering community continues to refine their considerable modeling and analysis techniques on various 'toy' problems, and worrying about a lack of real-world, life-science applications. If the two fields were to interconnect, their respective strengths would go a long way to remedying many current problems. The question that arises is how to begin engaging the broader engineering communities worldwide in solving complex disease problems and increase the productivity of scientific discoveries.

In the most recent update to its roadmap (http://nihroadmap.nih.gov/), the NIH has identified five initiatives: (i) Building Blocks, Biological Pathways, and Networks: In this set of NIH Roadmap initiatives, researchers will focus on the development of new technologies to accelerate discovery and facilitate comprehensive study of biological pathways and networks. (ii) Molecular Libraries and Imaging: NIH anticipates that these projects will also facilitate the development of new drugs by providing early stage chemical compounds that will enable researchers in the public and private sectors to validate new drug targets, which could then move into the drug-development pipeline. (iii) Structural Biology**:** A critical goal of the Structural Biology Roadmap will be the development of a broad inventory of protein structures for research as well as sophisticated new computer-based methods to analyze these data. (iv) Bioinformatics and Computational Biology: By embarking on the Bioinformatics and Computational Biology initiatives, the NIH Roadmap is paving a future "information superhighway" dedicated to advancing medical research. (v) Nanomedicine: Nanotechnology involves the creation and use of materials and devices at the level of molecules and atoms. Nanomedicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve. All five areas require a greater focus on quantitative techniques, multi-disciplinary teams and a systems approach for life science research. As biology becomes a more quantitative and information-driven science, numerous challenges arise in the development of informatics approaches to address biological questions and make an impact on health research and clinical medicine. These challenges will call on biologists, engineers, mathematicians, chemists, physicists and computer scientists to work together to develop a better understanding of integrative biology.

The theme for our recent workshop on "Biomarker Development and Application," was a direct result of the NIH roadmap. This workshop, the third in the series, was held in the Lister Hill Auditorium on the NIH campus, and saw the attendance of over 150 engineers and biomedical scientists representing the science and engineering community, industries, and government agencies worldwide. The previous two workshops were jointly sponsored by the National Library of Medicine (NLM) and the Institute of Electrical and Electronic Engineers (IEEE) Circuits and Systems (CAS) Society. The success of the first two workshops led to the third LiSSA meeting sponsored by both IEEE and NIH, and the formation of a joint planning committee for future workshop programs. This committee includes program directors and scientific staff from the NIH institutes involved in the Biomedical Information Science and Technology (BISTI) initiative, as well as the officers and technical committee chairs from seven diverse societies within IEEE. The objective is to have eager electrical and computer engineers apply their expertise and technologies to biomarker development.

2. Major Challenges for Biomarker Development and Applications

As an initiation to biomarkers, the workshop began with two tutorial-style overview seminars. The first of these was given by Dr. Leigh Anderson of the Plasma Proteome Institute, entitled "Barriers on the Road to New Protein Biomarkers: Confronting the Biomarker Verification Bottleneck". In his talk, Dr. Anderson addressed the challenges of finding new protein biomarkers, giving an example of difficulties from both systems biology and clinical research perspectives. The second presentation, entitled "Imaging & Translational Research," was given by Dr. John J. Kotyk of Washington University in St. Louis, and addressed the combinations of translational research and imaging techniques that are currently used in drug discovery and biomarker development.

Following the tutorial overviews were four invited technical talks. The first was in the area of devices, assays, and other novel technologies for biomarker development, and was presented by Dr. Richard D. Smith from

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Pacific Northwest National Lab at Richland, Washington. The title was "New Technologies for Biomarker Development and Application." The second presentation, entitled "Biomedical Imaging for Biomarker Development," was given by Dr. King Li from the Methodist Hospital, Houston, Texas. The third seminar was given by Dr. Michael Hehenberger from IBM Healthcare & Life Sciences about "Bioinformatics for Biomarker Development." The fourth talk given by Dr. Ian A. Blair of University of Pennsylvania, Philadelphia, PA was in the area of biomarker applications in public and environmental health. The title was "Exposure and Biological Response—Biomarkers of Cigarette Smoke". Breakout sessions followed these presentations, where recommendations on large-scale challenges and their short-term and long-term resolution strategies were sought from the leading scientists, engineers and government agents participating in the meeting. Conclusions from these sessions are summarized in the following:

2.1 Devices, Assays, and Other Novel Technologies for Biomarker Development

In this breakout session three questions were asked, and was jointly chaired by Dr. Salvatore Sechi from NIDDK/NIH and the invited session speaker, Dr. Richard D. Smith.

(Sec. 2.1, Question 1) **What are the challenges in the area? What are the most critical applications or techniques needed?**

The consensus of the group was the development of inexpensive assays (e.g. micro-fluidics) for possible point of care usage—inexpensive pre-screening tests that can later be re-assessed by more robust tests. One real-world example of this type of test is the usage of mass spectrometry (MS), which has proven to be very inexpensive when used in centralized facilities (e.g. new born screening). Micro-fluidic devices in conjunction with MS technologies show great promise in eliminating cross contamination of tests, given their disposable nature; however, simultaneously measuring many molecules with the type of Good Laboratory Practice (GLP) and standards usually required in a clinical setting remains a challenge. Another obstacle in micro-fluidics is clear understanding of surface effects in interactions with different assays, such as blood cells. The validation of biomarkers and biomarker tools represent a major goal in the development of biomarker technology. Current lab-on-chip technology is neither practical, nor well validated, and the search continues for a good application to showcase the utility of micro-fluidics in a clinical setting.

Because tackling these challenges will require large expenses, different paradigms to justify them need to be considered. Novel biomarker technology has many potential applications in *in-vivo* diagnostics, though the challenge of finding and funding such applications must be addressed.

(Sec. 2.1, Question 2) **What are the short-term (two-year) and mid-term (five-year) goals?**

The major short-term goal is more interaction between the clinical or biomedical, and engineering communities. The NIBIB/NSF workshop on "Improving Health Care Accessibility Through Point-of-Care Technologies" is a good example. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and other institutes have also been fostering this interaction, but much work is still needed, including the meetings on clinical proteomics in diabetes. NIH can perform a valuable role in fostering these interactions. The mid-term goal is the design of approaches that could facilitate inter-lab validation of new methodologies, the application of microfluidics to a clinical problem in a small human population pilot study, and better coupling of micro-fluidic and MS technologies.

(Sec. 2.1, Question 3) **How can the engineering and biomedical communities be brought together to solve the aforementioned challenges?**

Applications of micro-fluidics and the development of better integrated devices will require increased interaction between engineers and biomedical researchers. As a first stage in achieving these goals, more meetings in targeted areas must be developed.

2.2 Biomedical Imaging for Biomarker Development

This break-out session was jointly chaired by Dr. Fred Prior from Washington University in St. Louis and the invited session speaker, M.D. King Li; the following two questions were addressed:

(Sec. 2.2, Question 1) **What do you think are the challenges in the area?**

Because medical imaging systems are optimized for clinical visualization, the major challenges for this area are quantitative measurement and standardization. To achieve these goals, changes in the fundamental paradigms of radiology must occur. Currently, image processing and analysis techniques are not standardized or properly validated, making quantitative imaging and biomarker development difficult. Without quantitative measurements, biomarkers are just abstract concepts and difficult to standardize, since quantitative measurements are needed to pinpoint errors. At present, investigators must carefully analyze their own measurement processes and ensure reproducibility, but there is no standard by which cross investigators'

results can be compared. Furthermore, current radiology reimbursement is unrelated to quantitative measures, and based on Dr. Li's observations, only 10% of radiologist are ever involved in clinical trials and quantitative analysis. To address this situation, preclinical trials could be driven toward standardization by directly linking imaging stands development to the pharmaceutical industry's development cycle. With a change in basic radiological paradigms, regulatory pressures could then be used to drive the equipment toward quantitative assessment.

New imaging technologies, including microwave, chemical, and needle point imaging technologies, may be good for biomarker development; however, in order for these techniques to be used in clinical trials, only FDA approved systems may be used. The time lag for these new technologies may be quite significant, necessitating cross-vendor validation of imaging systems and algorithms to improve efficiency. Furthermore, phantoms or other references that allow each imaging device to be calibrated according to a common reference are required, so measurements are comparable.

(Sec. 2.2, Question 2) **What are the achievable goals, and what actions should we take to achieve these goals?**

The primary outcome from this breakout session is the determination that an activist community composed of radiologists, imaging scientists, engineers, pharmaceutical companies and imaging companies focused on quantitative radiology and standardization needs to be formed. This community should draw on the engineering community's infrastructure for creating standards. Through various conferences, tutorials, publications and other activities, we should drive the necessary paradigm shifts in the profession and practice of radiology, and thereby drive instrument re-engineering for repeatable quantitative analysis. This activist community can and should use professional societies (e.g. RSNA, ACR, IEEE) and government agencies (e.g. NIH, FDA) to assist education and to apply pressure for needed changes. The scientific community, with support from the NIH, will be used to define acceptable parameters and techniques needed to create open source reference implementations of measurement techniques. Furthermore, reference standard databases and atlases based on human phantoms, must be generated and made publicly available to the engineering and science communities. Beyond the focal issue of quantitative radiology, the engineering and biomedical communities should also establish stronger ties. This overarching goal can be accomplished through conferences focusing on standardization and new technologies, and efficient educational programs so the engineering community can better understand biomedical problems.

Additional open issues and questions in the biomedical imaging area were also identified: (i) the integration of imaging and biomarkers to form a comprehensive assessment package, (ii) the codification, standardization, and quantification of morphologic information, (iii) the feasibility of existing imaging tests as valid biomarkers in conjunction with tissue analysis techniques or usage as independent biomarkers, (iv) the positioning of imaging and image guided tissue analysis in the world of molecular diagnostics, and (v) the suitability of current imaging systems and radiologist expertise for detection tasks and more quantitative techniques used to study the identified lesions.

2.3 Bioinformatics for Biomarker Development

This break-out session was jointly chaired by Dr. Marc Rigas from CSR/NIH and Dr. Michael Hehenberger, and the following two questions were asked:

(Sec. 2.3, Question 1) **What are the challenges in the area?**

Modern biology is a data-driven science. The sequencing of the human genome and the associated data has given us clues as to how much information is contained in the genome, but scientists have only just begun to unlock and access this knowledge. Future discovery will be based as much on the integration of knowledge as it will be on the design of clever experiments. As biology becomes a more quantitative and information-driven science, there are a number of challenges ahead for developing informatics approaches to address biological questions and make an impact on health research and clinical medicine. These challenges will call on biologists, engineers, mathematicians, and computer scientists to work together to develop a better understanding in integrative biology. Some of the challenges that will require such close collaboration include developing robust tools for integrating data and knowledge from multiple sources, moving these tools from research applications to address clinically and medically relevant problems, and gaining acceptance of the informatics tools from both biomedical scientists and clinicians.

Another challenge is data integration in high-throughput biology. One of the basic technological tools in modern molecular biology is the DNA microarray, which allows the systematic measurement of the expression levels of thousands of genes in a single experiment. Of course, the single experiment generates thousands of data points. Clustering algorithms can allow biological researchers to analyze groups of genes with similar biological function. Genes work by

coding for the synthesis of proteins, the functional molecules in biology, and technologies such as liquid chromatography (LC) and mass spectrometry (MS) can be used in clinical or research proteomic experiments to identify the protein mix present in a biological sample. The integration of genomic and proteomic data can allow the development of models of gene regulatory networks—the control systems of cellular function. Pathologies can be traced to malfunctions of such regulatory networks, and drugs can be targeted to certain components within the networks. Certainly, clinical biomarkers can be developed that are the end products of some portions of these regulatory cascades; however, the development of such biomarkers requires a detailed knowledge of the system, which can only come from the careful integration of microarray data, proteomics data, and information obtained from gene annotations and ontologies of standard definitions and relationships.

The third challenge is portable tools for clinical use. One can envision clinical tools that can use genomic or proteomic tools developed for research applications. The ability to infer pathologies, based on some biological markers, either proteomic or genomic, would be of great clinical value. Of course, while this is an ultimate goal, our understanding of gene regulatory networks and quantitative understanding of the relationship between, for example, a genetic marker and a phenotypic response, is nascent. The clinical use of genomic and proteomic biomarker data will be accelerated by the development and acceptance of standards. Efforts such as the Cancer Biomedical Informatics Grid (caBIG) project of the National Cancer Institute are attempting to develop catalogs and repositories for tools and standards that can be used for both research and clinical molecular biology.

The last challenge is gaining acceptance. Informatics data and models will only be useful if they are understood and accepted by biomedical researchers and clinicians. This is an area where strong collaborations between biologists and computer scientists and engineers are necessary to develop the types of validations that will be rigorous and will be accepted by biomedical scientists. In terms of engineering approaches, it is noted that engineering approaches are already being applied to biomedical research and clinical medicine in areas such as systems biology (to better understand integrative physiology), in computational drug discovery and the simulation of clinical trials. However, the widespread acceptance of these techniques in biological research will be dependent upon close collaborations between biologists, computer scientists, engineers, and mathematicians. This requires in-depth collaboration and understanding among all types of scientists.

(Sec. 2.3, Question 2) **What opportunities exist for Interdisciplinary Collaboration?**
Critical issues for interdisciplinary collaboration between the engineering and biomedical domain include the availability of data and the ability to communicate across domains. Both barriers could be overcome by the development of seed grants for early-stage collaboration.

2.4 Opportunities for Biomarker Discovery, Detection and Application in the Environmental and Public Health Arena

This break-out session was jointly chaired by Dr. David Balshaw from NIEHS/NIH and the invited session speaker, Dr. Ian A. Blair, and the following four questions were asked:

(Sec. 2.4, Question 1) **What are the major challenges in the area of environmental and public health?**
Nearly every human disease is either caused or exacerbated by environmental exposures and an interaction between genetic susceptibility and environmental factors. Through a combination of 'basic science' mechanistic research, clinical studies and population based epidemiological studies, the field of Environmental Health strives to understand how these environmental factors influence normal biological function and increase individual and population risk of disease. Application of this research has typically been in the important area of primary prevention—preventing disease before it occurs—through public health practices including community education and risk reduction.

One of the challenges in the area of environmental health is that real world exposures are complex. Unfortunately, much of the mechanistic research that has been conducted so far uses animal models with acute high dose exposure to a single analysis. Scientifically, this is justified as it presents a clear picture of the hazard associated with that particular toxicant; however, there are few tools which allow for accurate extrapolation across dose, species, and mixtures to predict the risks of these exposures. An alternative strategy has been proposed that identifies critical common pathways altered by the classes of environmental toxicants that underlie disease, and measurement of perturbations of these pathways. This approach enables a prediction of biological risk based on mechanistic information that does not rely on direct knowledge of the underlying environmental exposures. This knowledge can be used to drive therapeutic interventions. This methodology represents a massive challenge that can only be

addressed by cross-disciplinary efforts. Initial efforts will rely on the development of compendia of responses to individual exposures in relevant model systems and can be facilitated by collaborations across the engineering and biological domains.

An even greater challenge exists in how to utilize this knowledge once we understand the mechanisms of exposure induced disease. Throughout recent history, there have been successes with translating understanding of environmental influences into improved public health. Among the greatest successes has been the understanding that the chemical element "Lead" in paint and gasoline was contributing to neurological problems in children. This brought public policy changes and a drastic reduction in lead exposures with accompanying health benefits. In contrast, cigarette smoking is widely acknowledged to be the predominant cause of lung cancer and emphysema. The decade-worth of public health policy changes geared towards reducing the burden of these diseases has lead to only minor decreases in incidence. Potential strategies to strengthen these approaches could relate to earlier identification of biological effects, individual risks and strategies to intervene early in the exposure-disease process.

(Sec. 2.4, Question 2) **What are the short-term (two-year) and mid-term (five-year) goals that we would like to achieve?**

Although NIH initiated the Genes, Environment, and Health program, significant effort is being expended on the development of sensors that can assess individual exposure and identify biomarkers of biological response. These efforts will not be able to overcome all of the previously mentioned challenges, but they and similar efforts will lay a foundation over the next four to five years. The development of additional programs in biomarker identification and informatics strategies to enable improved risk assessment based on mechanistic information could have substantial public health impact.

The long-range goals of improved public health rely on a foundation of strong research and can be facilitated by the development of technologies for improved exposure assessment, biomarker discovery and biomarker detection. The reality of a modern world is that everyone is exposed and that exposures come in the form of complex mixtures and chronic low-level accumulation of toxins. For instance, cigarette smoke is known to be a mixture of over 4,000 chemicals, many of which are known toxins; this obviously complicates the assessment of risks for exposure to these mixtures as the biological effects of these individual components are often synergistic or antagonistic with each other. In contrast, exposures to many toxins such as polychlorinated biphenyls or heavy metals occur over a lifetime at very low levels; this poses a distinct set of challenges in identifying disease conditions that occur based on exposures that may have occurred decades before. Identification of biomarkers of exposure, such as direct measurement of toxicants in human tissues or of protein or DNA adducts can provide a picture of the chemical milieu which influences individual risk. As with genetic variability, though, it is evident that simply being exposed is not sufficient to determine the appearance of a disease. Therefore, it is vital that we understand the indicators of biological response to those exposures and to determine if those responses are compensatory, adaptive or deleterious. These biomarkers take the form of other biomarkers that relate directly to disease processes and may include transcript, protein or metabolite changes or phenotypic measures of altered organ function. As these biomarkers are identified and validated, it then becomes imperative that tools are developed for the detection and analysis of these markers of exposure and response.

(Sec. 2.4, Question 3) **What opportunities exist for Interdisciplinary Collaboration?**

Critical issues for interdisciplinary collaboration between the engineering and biomedical domain include the availability of data and the ability to communicate across domains. Both barriers could be overcome by the development of seed grants for early stage collaboration.

Through tutorials and research presentations, and several highly interactive breakout sessions, the participants of the workshop explored biomarker development from the realm of nanomedicine to medical imaging and environmental health and identified a set of challenges confronting the research community. A formal theory of biomarker development is lacking, which makes the field somewhat fluid. It was concluded that a broad "shotgun approach" to biomarker discovery does not work, nor is there very often a single, "silver bullet" measurement. This is illustrated by the upward trend of tens of thousands scientific papers published every year in the field of biomarkers during the past decade and yet a paucity of biomarkers was actually approved by the Food and Drug Administration (FDA) during the same period (see Figure 1). The focus for effective biomarker development must rather be on panels or motifs of attributes and new mathematical techniques for combining these multiple measures in an intuitive manner. There is a growing dichotomy between researchers working in the *in-vitro* assays of genes, proteins, cells and tissues and those developing *in-vivo* techniques to apply in animals and humans. Scientists working in *in-vivo* systems expressed concerns that the prevalent bottom-up, high throughput, reductionist approach adopted in systems biology

renders the scientific findings not scalable beyond the cellular level. One area that was highlighted was the use of quantitative imaging techniques to iteratively provide targeted genomic, proteomic and metabolomic measures in order to converge to an optimal and scalable solution for *in-vivo* systems under investigation. This approach, in a way, is similar to the 'trial-and-error' method that engineers have been practicing for centuries. Furthermore, the validation of candidate biomarkers is a critical issue. Validation is very difficult and time-consuming due to the lack of standards and common protocols to generate and quantize data. There is a growing need for new tools and approaches for validation. To encourage students, including high school ones, to enter the field, an attendance grant has been established for future LiSSA workshop.

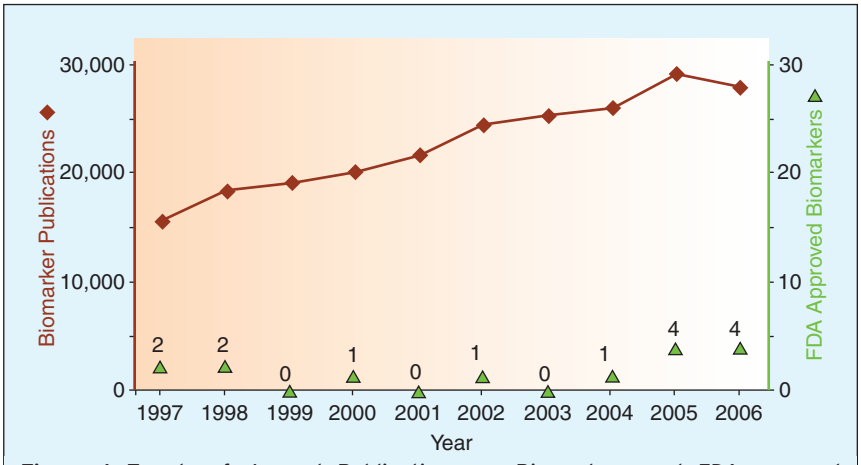

Figure 1. Trends of Journal Publications on Biomarkers and FDA-approved Biomarkers. Triangles (green) represent the number of FDA-approved markers per year (data from FDA and Nat Rev Can 2005). Red squares and circles indicate publications under the Medline medical subject heading biomarker (courtesy of Dr. Hong Zhao, Systems Biology Laboratory, Center for Biotechnology and Informatics, The Methodist Hospital Research Institute, Weill Medical College, Cornell University).

3. Open Forum for Discussing Possible "Research Opportunities"

Perhaps more important than the scientific results presented at the workshop was the existence of the workshop series itself and the underlying theme of bridging the wide and growing chasm between biomedical research on the one hand and the engineering disciplines on the other. The LiSSA workshops represent the initiation of a dialog between these two communities, which is made difficult by the lack of a common language. In response to the challenge of linking the engineering and biomedical communities, the workshop also included an open forum that was jointly chaired by Dr. Joseph Chang from Nanyang Technological University, Singapore, and Dr. Robert Newcomb from the University of Maryland. The forum included presentations on roadmaps by the Office of Portfolio Analysis and Strategic Initiatives (OPASI) and was followed by a delineation of the BEACON (Biomedical Engineering Alliance and Consortium/ Biomedical Information Science and Technology Initiative) as a model possibly to be emulated.

The IEEE (http://www.ieee.org) community with its 370,000-strong membership and highly diversified and specialized societies has immense potential and bandwidth to contribute to the abovementioned roadmap and initiatives. Although there are some common interests and interactions between the IEEE and NIH at the level of individual members or societies, a systematic conduit through which the IEEE might make contributions is lacking. Conversely, life-science and biomedical researchers who already appreciate the importance and applications of engineering to many life science and biomedical problems, argue for more such interactions. It is the intent of the LiSSA program committee to help bridge this gap. Likewise, the IEEE presented her roadmap and 'Mission Statement', followed by a review of the eight IEEE diversified and specialist societies (Circuits and Systems Society, Signal Processing Society, Engineering in Medicine and Biology Society, Communications Society, Man, Systems and Cybernetics Society, Solid-State Society, Computational Intelligence Society and Instrumentation and Measurement Society) that have supported and have representatives at the workshop.

We had an interesting, stimulating Open Floor discussion, which serves as a good working model for collaboration and symbiosis between IEEE and NIH. A NASA engineer reported that the workshops inspired him to tackle a life science problem for the first time and that his efforts had resulted in a patent filed for a gene expression device conceived by adapting technology he had developed in aeronautical projects. An electrical engineer from Canada changed his field of research after attending the first workshop and quickly generated good results to obtain funding in nanomedicine using his microelectronics background.

Multi-disciplinary workshops such as LiSSA are, however, rather rare and often difficult to organize. The papers presented at LiSSA cover a wide range of interrelated topics including (1) Biochip design in novel

life and health science applications, (2) Biomedical image computing and informatics, (3) Biomedical automation and control, (4) Biosystems and miniature instruments, (5) Biosensors and biosensor networks, (6) High-throughput devices and systems in life science, (7) Image-guided diagnosis, biopsy, and therapy, (8) Micro-nanoelectronics in life science applications, (9) Modeling and simulation of systems biology, (10) Multi-scale signal processing and imaging, (11) Nanotechnology in life science, (12) Novel architecture and applications of large-scale bio-systems, (13) Systems and applications in biosciences, drug discovery, personalized medicine, and public health, (14) Genomic, proteomic, metabolomic, and imaging biomarkers, (15) Impacts in predictive, preventive, and personalized medicine, (16) Predictive modeling and simulation of biomarkers, and (17) Regulatory issues of bioscience devices and systems.

It was also the first time where Best Student Papers were awarded, and they were (a) "A Novel Floating-Gate Biosensing Device with Controlled Charge-Modulation" by Chengwu Tao, Baozhen Chen, S. William, and S. Pandey from Iowa State Univ. at Ames; (b) "Biomarker Identification by knowledge-Driven Multi-Scale Independent Component Analysis" by Li Chen, Jianhua Xuan, R. Clarke and Yue Wang from Virginia Tech. at Arlington; (c) "Surface Modifications of Gold-nanoparticles to Enhance Radiation Cytotoxicity" by Tao Kong, Jie Zeng, Jing Yang, Yao Yao, Xiaoping Wang, Pen Li, A. Yang, W. Roa, J. Xing and Jie Chen from the University of Alberta, Canada; and (d) "Extraction of Breast Cancer Related Biomarkers in T1 Weighted MR Images of a Rodent Model" by Bin Wang, Jianhua Xuan, M.T. Freedman, P.G. Shields, and Yue Wang from Virginia Tech. at Arlington. The selected winning papers were presented in a "Best Student & Postdoc Paper Awards" session.

4. Conclusions

Critical issues for interdisciplinary collaboration between the engineering and biomedical domains include the availability of data and the ability to communicate across domains. Both barriers could be overcome by the development of seed grants for early stage collaboration. Similarly, a greater emphasis on joint funding opportunities between NIH and other more engineering-friendly funding agencies, such as NSF, DOE and DOD, would help to emphasize the need for multi-disciplinary interactions.

Scientific research and medical practice changes with the arrival of new technology, with examples spread throughout history: the arrival of antibiotics in combating infectious disease, the development of the fields of microbiology, and the proactivity of pathology with the advent of microscopy, the creation of radiology with the discovery of X-rays, the birth of the vast biotech industry following the development of recombinant DNA; and the list goes on and on. Now with the advent of genomics, proteomics, many other '-omics', molecular imaging, nanotechnology, and fast computers, we stand at the threshold of another golden era of biological discovery and progress. However the specializations and creation of silos in the traditional engineering and biomedical science disciplines stand as obstacles to the advance of biomedical research and human. Fundamental changes in conducting cross-disciplinary research are required if we are to step forward—cutting down 'silos' and breaking down walls of traditional scientific boundaries, and embracing 'team work' or 'team science,' concepts that are so alien to traditional academic communities. If the engineering and biomedical science communities refuse to see the need for change, this golden era of biological discovery may never come.

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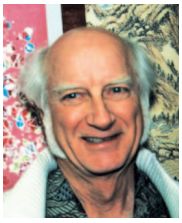

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