Biomedicine at APL: Guest Editor's Introduction

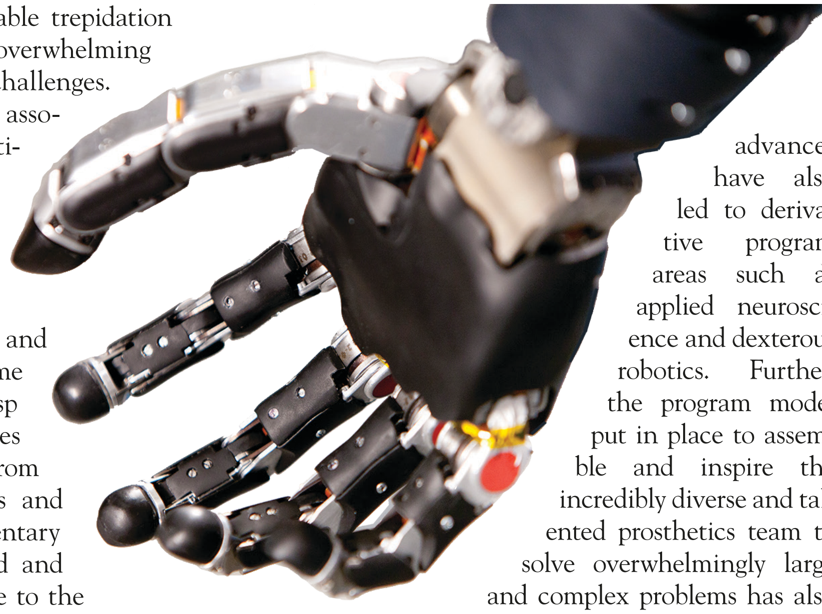
John D. Bigelow

APL has a rich heritage in research and development in biomedical and biological sciences. Building on earlier successes and complementing them with sound systems engineering principles, APL continues to address challenges of ever-increasing size and complexity. The Revolutionizing Prosthetics program has been a model for integrating scientific research and advanced development across an expansive multidisciplinary and multiorganizational team. This proven capability has led to significant advances in applied neuroscience, dexterous robotics, biomechanics and injury mitigation systems, patient-centered precision care, advanced explosive ordnance disposal robotics, systems engineering for improved patient safety, and many other areas. This issue of the Johns Hopkins APL Technical Digest *provides an overview of several significant and exciting advances in the biological sciences.*

INTRODUCTION

> "In January 2006, more than 100 engineers, scientists, researchers, and clinicians from government, academia, and industry met in Jekyll Island, Georgia, with an extreme and compelling challenge—to engineer a system to seamlessly integrate with a patient and replace a lost upper limb."[1]

So began the saga of the Revolutionizing Prosthetics program, detailed in the December 2011 issue of the *Johns Hopkins APL Technical Digest*.[2] This program continues today, now in its third phase, advancing and applying innovative neural integration technologies for amputees, as well as capitalizing on research in direct cortical control to restore functionality to those with high spinal cord injury or neurodegenerative disease. Indeed, this current issue includes an article discussing Phase 3 of the program, as well as a technical article on human sensory feedback and haptics. Equally important, this issue begins to round out the tremendous impact and staggering potential of biomedicine and the biological sciences at APL. Interestingly, when the nascent Biomedicine Business Area won the Defense Advanced Research Projects Agency (DARPA) Revolutionizing Prosthetics program award, there was considerable trepidation regarding APL's ability to rise to the overwhelming scientific, technical, and management challenges. However, in retrospect, the challenges associated with this multidisciplinary, multi-institutional, highly complex system are ideally suited to APL, as its holistic systems view, discipline, and rigor are essential ingredients for the program's success. Furthermore, as APL explores other aspects of its biomedicine and biological sciences portfolio, these same themes emerge. As we stand on the cusp of the "Century of Biology," these themes resonate again, with the progression from reductionism to higher-order synthesis and the integration of multiple complementary disciplines. APL is uniquely positioned and qualified to capitalize on and contribute to the revolution in biological sciences—to drive the underlying science when necessary; to apply research and technology from academia, government, and industry; and to fill the necessary gaps to provide deployable solutions for our national security and interests.



Over many years, biomedicine has been chronicled in the *Digest*.[1–9] As detailed in the December 2011 issue of the *Digest*,[2] APL's contributions to biomedical research and systems engineering date back to the early 1960s, with significant accomplishments in neurology, ophthalmology, radiology, cardiology, and biomedical devices. In late 2004, the Biomedicine Business Area was established, with the challenge of developing a solid and sustainable funding base through impactful efforts, working in concert with the entire Johns Hopkins enterprise. The vision and emergent strategy focused on warfighter protection, sustainment, and performance spanning predeployment through combat casualty care and finally to long-term rehabilitation. Within that first year, DARPA announced its desire to develop a neurally integrated upper extremity prosthetic device that would mimic human performance in terms of appearance, function, and natural control. Despite competition from the world's leading organizations in prosthetics, neuroscience, and neuroprosthetics, APL was awarded the program, due in large part to its strength in systems engineering and a proven track record of executing large, complex, multidisciplinary development efforts. Almost every department in the Laboratory, the Johns Hopkins School of Medicine, the Whiting School of Engineering, the Bloomberg School of Public Health, and more than 30 other world-renowned organizations contributed to the program.

In its own right, the Revolutionizing Prosthetics program has been and continues to be an enormous success story in scientific research and advanced development. Significantly, and with forethought, many of these technological advances have also led to derivative program areas such as applied neuroscience and dexterous robotics. Further, the program model put in place to assemble and inspire the incredibly diverse and talented prosthetics team to solve overwhelmingly large and complex problems has also been mirrored in programs such as Biomechanics and Injury Mitigation Systems, Patient-Centered Precision Care, Advanced Explosive Ordnance Disposal Robotics, Applied Neuroscience, Systems Engineering for Improved Patient Safety, and many others.

In 2011, the Laboratory reorganized into sectors and enterprise departments. The resultant Research and Exploratory Development Department (REDD) blends the talents from the Milton Eisenhower Research Center, the Biomedicine Business Area, and its advanced design, modeling, and fabrication organizations. From a biomedicine and biological sciences perspective, this creates a strategic critical mass to address emerging challenges and provide disruptive solutions to issues of critical national and global significance. The prevailing themes underpinning the anticipation for the Century of Biology are the fundamental knowledge of the building blocks from the 20th century reductionist biology (think genomes, cell biology, and synthetic biology)—new technologies, concepts, and methods for discovery and analysis; integration of the physical sciences, mathematics, computational sciences, and engineering; and a holistic systems perspective and approach for realizing complex systems. This model should sound familiar from the above examples. This is truly a remarkable period for the biological sciences, poised for extraordinary advances in genetics, molecular biology, synthetic biology, neurobiology and cognitive science, bioinformatics, and biomaterials. Applications in APL's traditional sponsor domains include biological sensing and mitigation of chemical threat agents, biological systems engineering for materials synthesis surveillance, forensics, security, and development of advanced countermeasures for existing, emerging, or engineered biological threat agents. Broader issues affecting our national security, economy, and global community include sustainable food production, renewable energy, environmental protection, and human health. Within REDD, APL, and the Hopkins enterprise lie the competencies in the core biological sciences, materials science, physical sciences, and information/computational science; the engineering discipline, rigor, and wherewithal to conceive, model, design, and fabricate solutions from the nano- to the macro-scale; and experience in the integration of multidisciplinary, multiorganizational teams to solve complex problems. As such, APL stands ready to confront the challenges before it and to continue to provide innovative solutions.

THE ARTICLES

In the first article, Merkle et al. discuss the efforts across our core Biomechanics and Injury Mitigation Systems (BIMS) program area. Our warfighters are threatened by blast events, ballistic impacts, and transportation accidents. APL has developed novel computational and physical models of the human system to measure the body's mechanical response to dynamic loading, providing insights into future injury mitigation strategies. These models are critical tools in the evaluation and development of personal protective equipment and vehicle safety systems to ultimately reduce the risk of human injury.

Blast-induced neurotrauma, i.e., traumatic brain injury, is often cited as a signature wound of recent conflicts and currently represents one of the highest research priorities in military medicine. In the second article, Cernak discusses research into the blast–body–brain interactions, attempting to understand the complex, interconnected physiological and molecular alterations that can lead to long-term neurological deficits. APL has developed a research model replicating major types of military-relevant traumatic brain injury (blast-induced, penetrating, and blunt trauma), with the aim of increasing understanding of these injuries, leading to development of improved diagnostics, treatments, and mitigation strategies.

In the next article, Benson et al. take a look at APL's contributions to the Army's Medical Communications for Combat Casualty Care (MC4) program. APL supported the program for more than 10 years in the areas of researching, developing, testing and evaluating, and fielding information technology systems supporting the medical care provided to deployed forces.

Similarly, APL supported the analysis and development of an integrated data management system for the Joint Trauma Analysis and Prevention of Injury in Combat (JTAPIC) program, whose mission is to collect and analyze theater operational data to improve warfighter survivability. The article by Cain et al. discusses the analysis and initial concept development of the JTAPIC Data Management System (JDMS).

The article by Johannes et al. discusses research concepts, derived from the Revolutionizing Prosthetics program, of human capabilities projection, the manifestation of human-like dexterity and sensory perception through robotic telemanipulation. Human capabilities projection requires advances in robotic manipulation technologies, intuitive operator control modalities, immersive visual feedback, and effective haptic feedback. The goal of human capabilities projection is to leverage robotic systems to accomplish tasks that may not be practical or safe for human execution.

Building on the pioneering application of neuroscience to human capabilities restoration from the prosthetics program, the article by Vogelstein begins to explore the application of neuroscience to much broader problem domains. Information superiority, defined as the capability to collect, process, and disseminate an uninterrupted flow of information, is the pillar upon which the United States will build its future military and intelligence dominance. Although the nation's ability to collect and disseminate information has dramatically increased, its ability to process information has remained roughly constant, limited by the bandwidth of human sensory perception. Advances in neuroscience and neurotechnology afford the opportunity to correct this imbalance. This article provides an overview of APL's efforts in applied neuroscience research and development and highlights ways in which these advances can provide critical contributions to critical national security challenges.

Personal genomic information is poised to revolutionize medicine and provide patients with increasingly individualized medical care. However, moving forward, the effective integration of genomic information into clinical care will pose many logistical, ethical, and legal challenges. In response to this rapidly evolving health care revolution, the U.S. Air Force has established the Patient-Centered Precision Care Research (PC2-Z) program, with the aim of evaluating the clinical impact of genome-informed care and to begin to lay the foundation for its implementation. The article by Bradburne et al. discusses APL's role as the program integrator responsible for bringing together governmental, academic, and industry partners to implement focus areas in research, bioinformatics, education, and policy.

Despite the introduction of technology in medicine, there remain challenges related to patient safety and quality health care delivery, and the economic and personal costs associated with these challenges are enormous. The article by Ravitz et al. discusses the partnership of APL, Johns Hopkins Medicine, and the Whiting School of Engineering's Systems Institute. The goal of the collaboration is to couple systems engineering principles and best practices with clinical expertise to develop innovative approaches to the socio-technical dynamics involved in health care, with the ultimate aim of improving outcomes.

The next article, by Armiger et al., delves deeper into an essential research and technology area supporting the Revolutionizing Prosthetics program. Specifically, the article asserts that the need for a "closed-loop" system, i.e., a system including sensory feedback, is critically important to achieve a highly functional dexterous upper limb prosthesis. This article describes the need for sensory feedback systems in upper extremity prosthetic limb systems, the system design components including the native human sensory system, prosthetic sensors, and actuators for providing feedback, as well as the software algorithms used to control the system.

Finally, we close the issue with an update on the Phase 3 activities of the Revolutionizing Prosthetics program. Specifically, the article by Ravitz et al. begins to detail the efforts to provide upper-extremity functionality to people who have no ability to control their native arms, such as those with high spinal cord injury or neurodegenerative disease. Clinical activities during this phase have involved a subject successfully demonstrating multi-degree-of-freedom control of the Modular Prosthetic Limb (MPL) via cortical control in a laboratory setting.

CONCLUSION

APL is particularly poised for dramatic breakthroughs as it peers into the future of the Century of Biology. Whether developing advanced biosensors, countering biological threat agents, or providing innovative advances to human health, APL offers the capabilities to conceive, model, design, and fabricate solutions at all levels and is experienced in the integration of multidisciplinary, multi-organizational teams to solve complex problems. This issue of the *Digest* provides a retrospective overview of several significant and exciting advances in the biological sciences portfolio in just the last couple of years. Since we began this issue, several other significant collaborative programs have started, and the potential is limited only by imagination. When we started the Revolutionizing Prosthetic program, there were many participants, including renowned neuroscience researchers on the program, who thought the goals were impossible to achieve. As illustrated in a *60 Minutes* vignette of a paralyzed young woman using the MPL to feed herself a candy bar, "possibility" is difficult to assess from one's current vantage point; this is an important lesson to remember as we contemplate the future in biological science.

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The Author

John D. Bigelow is a member of APL's Principal Professional Staff, the acting Branch Supervisor for REDD, and the Group Supervisor for the Biological Sciences Group in REDD. His prior position was as the Biomedicine Business Area Branch Supervisor and acting Program Area Manager within the National Security Technologies Department (NSTD). On the Revolutionizing Prosthetics program, he was the Assistant Program Manager responsible for structuring and executing Phases 1 and 2 of this dynamic and challenging program. His e-mail address is john.bigelow@jhuapl.edu.

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