History of Lincoln Laboratory's Bioengineering Research

Edward C. Wack and Jeffrey S. Palmer

Lincoln Laboratory researchers began applying their considerable expertise in systems analysis, sensors, and signal processing to chemical and biological defense applications as early as 1995. This expertise, plus newer capabilities in synthetic biology and brain and cognitive sciences, has since been directed to include research into biotechnological solutions for identifying and remediating physiological, neurological, and cognitive problems impacting the health and performance of U.S. warfighters, veterans, and civilians.

Since 1951, MIT Lincoln Laboratory has remained at the forefront of technology development in support of national security. From the first integrated air defense system, the Semi-Automatic Ground Environment [1], that required advances in radars, communications, computing, and information theory to recent pioneering work in satellite optical communications [2], Lincoln Laboratory has developed cutting-edge scientific and technological capabilities and applied them to solve pressing national security problems.

As power generation and mechanization in the 19th century, and microelectronics technology and communications in the 20th century, created a host of new opportunities and challenges, the life sciences are poised to do the same in the 21st century [3]. The ability to read and write the fundamental code of life, the DNA letters of the genome, continues to increase exponentially. Understanding of the brain—its structure and function, injuries, and disease states—and the way this biological organ gives rise to the mind is accelerating each year. As scientists better understand the inner workings of life at all scales, they are able to cure diseases and repair injuries, and maintain optimal health and performance via the application of new technology. The human body attempts to keep itself in balance when confronted by changes in the environment or by injuries. From regulating internal temperature to blood glucose levels, the multiple physiological control systems strive to maintain homeostatic balance. When the bounds of the control system are exceeded, humans experience dysfunction, injury, or disease.

Technology enables an outer control loop to sense and respond to these "out of bounds" conditions. For example, continuous glucose monitors and insulin pumps are a technology-enabled solution to diabetes that keeps blood glucose levels in the proper physiological bounds. This integration of technologies to support human systems is enabled by the convergence of life sciences, physical sciences, microelectronics and nanoelectronics, and computer science. You will see examples of this technological convergence throughout this issue of the *Lincoln Laboratory Journal.* Our researchers at Lincoln Laboratory use speech signal processing with cutting-edge brain models of speech production to diagnose neurological conditions. We have developed novel wearable sensor technologies and detection algorithms to detect infection, prevent heat strain, and reduce lower-limb musculoskeletal injuries. And, we can create new genetic circuits to program cells to detect and destroy cancer cells in the body.

With the miniaturization and proliferation of technology, including biotechnology, we are working to achieve three important goals. We can intervene to restore health at multiple scales within the body, from the molecular and genomic level, to tissues and organs, to the entire human system, including social groups. Second, we can provide solutions that improve health not only in clinical or laboratory settings, but in regular living conditions at home and work. And finally, solutions can be tailored to personal needs, not based on population averages but on longitudinal data collected on individuals. The ability to measure and digitize human states, from the genome to blood chemistry and from physiology to cognitive states, enables the application of advanced computer science algorithms, artificial intelligence, and machine learning approaches to learn, analyze, and predict health states. It is an exciting time for developing bioengineering technology, and the convergence of these technical disciplines is accelerating innovation.

National Needs

It is fortunate that we are able to develop new approaches to solving health, performance, and security challenges as these challenges continue to grow in the complex environment in which we live. The U.S. military, in particular, faces multiple health challenges that affect soldiers' readiness and resilience, thereby impacting operational effectiveness. Such challenges create a fundamental national security risk if the United States is not able to field a physically, cognitively, and psychologically ready and resilient force. The threats come in many forms, internally and externally, as well as to individuals and populations.

Among the top concerns affecting the well-being of both soldiers and civilians are weapons of mass destruction, including novel and emerging biological threats. The Departments of Defense and Health and Human Services have done an outstanding job of developing sensors, medical countermeasures, and protective gear for traditional threats, such as *Bacillus anthracis* (the bacteria that causes anthrax disease), *Variola major* (smallpox), and *Yersinia pestis* (plague). However, the same biotechnology that allows genome editing to cure disease can be used to create new pathogen threats for which the world has no sensors or medical countermeasures. Novel sensors and rapid medical countermeasures are urgently needed to combat these novel threats [4]. Two articles in this *Journal* ("The Impact of Host-Based Early Warning on Disease Outbreaks" and "Synthetic Biology") describe work that begins to address these challenges. In fact, as this issue of the *Lincoln Laboratory Journal* goes to press, we are in the midst of refocusing multiple research efforts to support the nation's COVID-19 response. These initiatives include host-based early warning of infection, the use of speech to track disease symptoms, and the application of synthetic biology and bioinformatic tools to discover potential medical treatments.

Members of the U.S. services operate in challenging environments of high altitudes, extreme heat and cold, and increasingly in dense, urban megacities. These environments not only challenge service members' physical and cognitive capabilities, they also potentially present opportunities for servicepersons to confront near-peer adversaries who may contest the freedom of U.S. services to maneuver in the air, land, and sea and their ability to communicate. Such complex and dangerous environments have dramatic implications for battlefield medical care for those injured in combat. There is an expectation that the U.S. military will need to care for larger numbers of casualties and for longer time periods than were seen in the past 40 years [5–7]. No longer will U.S. field doctors be able to medivac the injured to medical treatment facilities within the "golden hour," the short period of time to sustain life until trauma surgeons can repair injuries. The military will require prolonged field care to sustain life and treat injuries, possibly longer than 24 hours, before medical evacuation is possible. This issue of the *Lincoln Laboratory Journal* presents research on technologies that will assist battlefield medicine ("Noncontact Laser Ultrasound for Biomedical Imaging Applications").

Even before deployment and potential battlefield injuries, U.S. service members perform rigorous training to master their operational roles. They enter service with a range of strengths and weaknesses that training raises and levels. However, some risk factors, such as genetic determinants of bone health or preexisting psychological trauma, can be exacerbated in training, reducing an individual's overall readiness. Quantifying baseline performance and tailoring nutrition, training, and support to maximize individual performance without injury will be necessary so that the United States can continue to have the most capable military in the world. Lincoln Laboratory is developing technologies to prevent injuries in training environments (see "Open Body Area Network Physiological Status Monitor," "Model and Personal Sensor for Metabolic Tracking and Optimization," "Biomechanical Sensing and Algorithms," and "Understanding Noise-Induced Auditory Damage").

The military's future operational environment will include humans teaming with autonomous systems. This new paradigm will potentially revolutionize the character of warfare, and the implications for individual performance are poorly understood. What are the optimal forms of communication between humans and machines? How is understanding and trust built in these teams? How do the series of interdependent tasks for complex missions get assigned and dynamically reassigned across team members? These difficult questions require that we gain a better understanding of how to measure and analyze human and machine physical and cognitive states, and develop models by which to characterize and predict individual and team performance (see "Fundamental Brain Research").

Service members work in complex human teams as well as with autonomous systems. Being able to measure and improve team dynamics will also be critical for future operational success. Social systems extend beyond operational settings into garrison, home, and civilian life. Today, U.S. adversaries are attempting to undermine civil and social society via disinformation operations. A better understanding of how our minds can be trained to detect and reject such attempts is important for national unity and citizenship.

Finally, many of these same threats affect veteran and civilian populations: infectious disease, trauma injuries, psychological health, and disinformation on social media platforms. The technology solutions developed for the military will have broad applicability in the homeland for civil society.

The Lincoln Laboratory Approach

Over the decades, Lincoln Laboratory has made multiple, important contributions to biomedical technology development. We were pioneering codevelopers (with MIT professors) of optical coherence tomography, known as OCT, a critical diagnostic tool used in ophthalmology, cardiology, and upper gastrointestinal endoscopy [8]. The Laboratory also developed RF-based thermotherapy for cancer therapy [9]. Early work in DNA microarrays utilized the Laboratory's microelectronics fabrication capability to build some of the earliest gene chips. Each of these technologies was successfully transitioned to commercial application via startup companies that spun out of Lincoln Laboratory.

In 2009, Lincoln Laboratory took a step back to understand what role it might play in the bioengineering and biomedical space in support of its national security mission. A panel of Boston-area luminaries in the medical and life science arenas was convened, and the study team mapped out a number of areas in which Lincoln Laboratory had unique capability combined with a strong mission pull. In 2010, the Laboratory began investing in internally funded research in the applied biomedical sciences and in 2012 formed a new group, the Bioengineering Systems and Technologies Group (recently renamed Human Health and Performance Systems), that joined the Chemical and Biological Defense Systems Group in the emerging human systems and biotechnologies mission area. In August 2019, the Laboratory created a new Biological and Chemical Technologies Group to expand research in these areas.

The articles in this issue of the *Lincoln Laboratory Journal* highlight some of the technical areas in which the Laboratory is working and the end-user applications of that technology. Building on decades of experience, we have been developing advanced sensors, algorithms, and systems, at all scales, to measure, model, and modify humans. These technologies are used to diagnose neurological conditions, quantify cognitive load, detect early onset of infections, measure biomechanical loads, and develop cell-based sensors to detect hazards in the environment and in the body. We work with civilian end users, military personnel, and clinicians in their respective environments to understand their critical and unique challenges. We conduct systems analysis and develop modeling approaches to identify the key variables through which advanced technology could enable orders of magnitude improvements in their missions. And, we transition the technologies to industry to enable the government to buy them, to improve the domestic economy, and ultimately to improve human well-being across our nation.

In the decade since we began to focus on this area, Lincoln Laboratory has won seven R&D 100 Awards for innovation in biomedical systems, has filed or been awarded 15 patents for its biotechnologies, and has seen one new biotech company spun off. Going forward, we will continue to solve current critical challenges in health, performance, and security in partnership with the government, academia, industry, and hospitals. We will continue to build unique infrastructure and technology to enable cutting-edge research and development that is both accessible and adaptable for tomorrow's needs.

Welcome to this special edition of the *Lincoln Laboratory Journal*. We hope you enjoy the articles and gain new insights into solving some of our nation's biggest challenges in health and performance. As our nation combats the current COVID-19 pandemic and its effects on our security, Lincoln Laboratory, with many other research organizations, is rapidly responding to urgent military and civilian needs. It is through our united effort we will innovate the solutions to bring the crisis to an end. ■

References

1. "SAGE: Semi-Automatic Ground Environment," MIT Lincoln Laboratory website, https://www.ll.mit.edu/about/history/sage-semi-automatic-ground-environment-air-defense-system, accessed 24 July 2019.
2. "Lunar Laser Communication Demonstration: NASA's First Space Laser Communication System Demonstration," NASA facts, https://www.nasa.gov/sites/default/files/llcdfactsheet.final_.web_.pdf, accessed 24 July 2019.
3. P. Sharp, T. Jacks, and S. Hockfield, eds., "Convergence: The Future of Health," 2016 Report to Convergence Revolution. Cambridge: MIT, June 2016, available at http://www.convergencerevolution.net/s/Convergence-The-Future-of-Health-2016-Report-55pf.pdf, accessed 24 July 2019.
4. National Biodefense Strategy. Washington, D.C.: White House, 2018, available at https://www.whitehouse.gov/wp-content/uploads/2018/09/National-Biodefense-Strategy.pdf, accessed 24 July 2019.
5. M. Kinney, "Evolving 'Golden Hour' Care to Mitigate the Treatment Gap," *Combat & Casualty Care*, spring 2018, pp. 4–6.
6. "Multi-Domain Battle: Combined Arms for the 21st Century," U.S. Army–Marine Corps White Paper, 18 January 2017, available at https://ccc.amedd.army.mil/PolicyPositions/Multi-Domain%20Battle%20-%20Combined%20Arms%20for%20the%2021st%20Century.pdf, accessed 24 July 2019.
7. A.S. Linde, "The Need for Pre-hospital Simulation Training Platforms in Battlefield Medicine," *Journal of Trauma and Rehabilitation*, vol. 1, no. 1, 2018.
8. J. Fujimoto and E. Swanson, "The Development, Commercialization, and Impact of Optical Coherence Tomography," *Investigative Ophthalmology and Visual Science*, vol. 57, no. 9, 2016.
9. A.J. Fenn, *Adaptive Phase Array Thermotherapy for Cancer*. Norwood, Mass.: Artech House, 2009.

About the Authors

Edward C. Wack is the assistant head of the Homeland Protection and Air Traffic Control Division at Lincoln Laboratory. In this role, he shares responsibility for research, development, evaluation, and technology transfer of advanced technologies and systems for chemical and biological defense, bioengineering, and biomedical systems. Prior to holding this position, he was the leader of the Bioengineering Systems and Technologies Group, which focused on innovative advanced technology programs in biodefense, forensics, and biomedical research. He was also Director of Future Acquisition at the Joint Program Executive Office for Chemical and Biological Defense (JPEO-CBD) within the Department of Defense. At JPEO-CBD, he was responsible for leading the office's future technology strategy and coordinating that strategy with the other members of the chemical and biological defense program, civilian government organizations, and international partners. Before joining the JPEO-CBD, he spent 13 years at Lincoln Laboratory, where, as an assistant leader of the Sensor Systems and Applications Group, he led a team working on standoff sensing, advanced detection algorithms, and system architectures. He has also been involved in various aspects of satellite remote sensing programs, including system architectures, sensor designs, sensor calibration, and requirements analysis and definition. He holds a bachelor's degree in mathematics from the College of the Holy Cross and a master's degree in bioinformatics from Brandeis University.

Jeffrey S. Palmer is the leader of the Human Health and Performance Systems Group at Lincoln Laboratory. He has oversight of multiple research programs that focus on health, human performance, objective neurocognitive analytics, and biosensing via wearable, ingestible, and implantable devices. In 2010, he helped to create the first Army War College Fellowship at Lincoln Laboratory and the MIT Security Studies Program. He has given presentations at international conferences and authored book chapters and technical articles on DNA biometrics and forensics, biomechanics, cell biology, materials science, soldier nanotechnology, biological-chemical defense, polymer science, high-energy lasers, microelectronics packaging, wearable biomedical sensing in extreme environments, and neurocognitive technologies. He has served on editorial boards for journals in biomechanics, molecular science, biomedical informatics, and biosensors. He has chaired technical conferences for the National Science Foundation, Department of Homeland Security, and the IEEE. Currently, he is the vice chair (and chair-elect) of the IEEE Engineering in Medicine and Biology Society's (EMBS) Technical Committee on Wearable Biomedical Sensors and Systems and the EMBS conference editorial board for tissue engineering and biomaterials. In addition, he has served as an advisor on senior military studies of enhancing health and performance, and led a multi-agency U.S. government effort to develop automated rapid human DNA analysis capabilities for field biometrics and forensics applications. Prior to working at Lincoln Laboratory, he worked at research laboratories at IBM and GE, and at the Physical Sciences Laboratory at New Mexico State University. He holds a bachelor's degree with a minor in mathematics from New Mexico State University, a master's degree from Rensselaer Polytechnic Institute, and a doctorate with a minor in bioengineering from MIT, all with majors in mechanical engineering.