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Neural Interfaces for Upper-Limb Prosthesis Control

Opportunities to Improve Long-Term Reliability

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Building on a long history of innovation in neural-recording interfaces, the Defense Advanced Research Projects Agency (DARPA) has launched a program to address the key challenges related to transitioning advanced neuroprosthesis technology to clinical use for amputated service members. The goal of the Reliable Neural Technology (RE-NET) Program is to develop new technology to extract information from the nervous system at a scale and rate needed to reliably control modern robotic prostheses over the lifetime of the amputee. The RE-NET program currently encompasses three separate efforts: histology for interface stability over time (HIST), reliable peripheral interfaces (RPIs), and reliable central nervous system (CNS) interfaces (RCIs).

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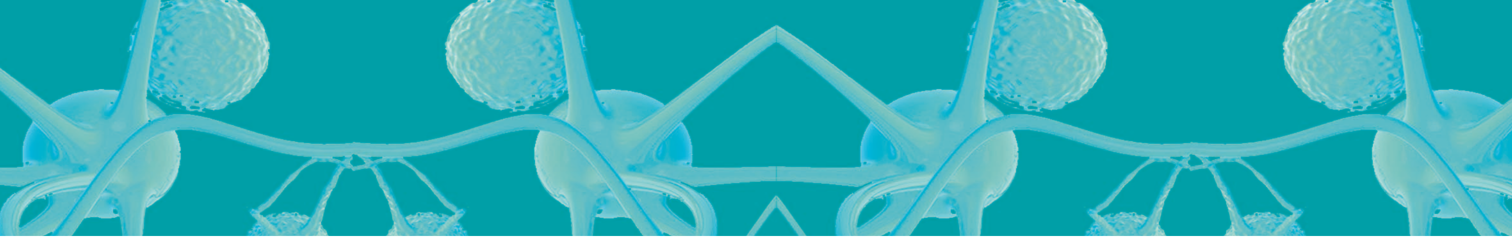
Chronic neural-recording technology promises to be able to extract adequate information from the nervous system so that it is useful for many types of patients, such as empowering amputees to control advanced prosthetic limbs.

Neural-interface technology, which has existed for recording neural activity since Du Bois-Reymond discovered the neural action potential more than 160 years ago [1], has been carefully refined over the past 70 years to better understand the function of the biological nervous system and to improve our ability to treat neurological injuries and disorders. Microelectrode technology of the 1940s and 1950s [2] enabled fundamental breakthroughs, such as the development of the Hodgkin-Huxley model, that describes how neural action potentials (or spikes) are generated and propagated. Microwire-array technology of the 1970s and 1980s [3] enabled the activity of neuronal populations to be observed and the movement of limbs to be decoded. Dense microelectrode arrays were demonstrated in the 1970s, using micromachining methods borrowed from the integrated-circuit industry [4]. Significant technological advances in micromachined electrode-array technology have occurred due to investments by the National Institutes of Health in the 1980s, 1990s, and 2000s, and the National Science Foundation in the 1990s. Leading probe-array technologies [5]–[7] were advanced in the 2000s by commercialization efforts that are still ongoing.

The goal of advanced neural-recording interfaces has been to support fundamental neuroscience activities, such as understanding how functions of interest are encoded in various neural signals [e.g., single-unit activity, multiunit activity, local field potentials (LFPs), and brain-wave activity]. However, since scientific experiments performed to date have typically been short term (i.e., on the order of months to a year or two), the emphasis of engineering activities supporting this work has not been directed toward improving the long-term reliability of neural-interface systems, but rather the development of real-time data acquisition and processing systems. As a result, it is not surprising that technologies presently used for neural interfaces have demonstrated an inability to maintain a consistently high level of performance for very chronic time periods in healthy and active animal models up to and including nonhuman primates. A clinical trial consisting of a single human patient with tetraplegia, caused by a brainstem stroke, demonstrated that it was possible to perform simple point-and-click control of a computer interface 1,000 days (2.74 years) after implantation [8]. Additional experiments performed in more test subjects will be needed to reveal the statistical significance of this and similar results.

Unlike many engineered system components that have dramatic failure modes, such as computer hard-disk drives, the definition of failure for brain–machine interfaces (BMIs) is not so clear-cut since performance of the system may simply degrade slowly over time. Therefore, a good metric of reliability is the duration of time that the BMI system is able to maintain a given level of performance, realizing that performance level can often be traded for increased operational lifetime. A generic metric of BMI performance and reliability will combine three important operational characteristics of BMIs: 1) rate of control information extracted ($R_{control}$, in total independent bits/second for all degrees of freedom), 2) rate of control error information generated (R_{error} measured in bits/second for all sources of error in all degrees of freedom), and 3) duration of individual real-time uninterrupted experimental tasks (t measured in seconds). An example of a combined generic performance metric is $(R_{control}/R_{error})t$, for which a larger number would correspond to greater performance when completing individual tasks. Plots of $(R_{control}/R_{error})t$ over chronic time periods would provide insight into and a means to illustrate the BMI reliability-performance tradeoff. Ultimately, applications using BMIs for motor control to complete specific tasks will have more operational and application-specific definitions of failure.

Another important factor, which is often not a significant consideration during basic preclinical experiments, is future



acceptance by human patients. There is a long history of well-intentioned prosthesis technologies that were ultimately not widely accepted by patients. Careful consideration of patient acceptance should be something that occurs during technology development, even at the early stages of scientific work. Unless appropriate functional targets are set beforehand much time, money, and effort could be wasted, and many more patients will go through life without enjoying the envisioned benefits.

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Defense Perspective

Since the American Revolution, soldiers of the United States have been wounded during line of duty. Far too often, the result of these injuries is amputation of one or more limbs and despite advances in medical and body-armor technologies, military limb amputation continues to occur at significant rates. Until recently, these wounded warriors have only had a few prosthesis options, including body-powered cable-driven claws or passive cosmesis and hooks. Advances in electronics, materials, and manufacturing have led to significant improvements in prostheses capable of restoring lost lower-limb function. As a result, injured warriors have already returned to the battlefield with powered prosthetic legs. Unfortunately, prosthetic upper-limb technology has accomplished far less. Although patients can use body-powered prostheses to regain two degrees of freedom (wrist rotation and claw actuation) and perform many activities of daily living, the limbs do not provide the dexterity and strength to enable warriors who are hurt to achieve their ultimate rehabilitative goal, which may be to return to active duty in the field. To accomplish this goal, they must be able to rapidly disassemble and reassemble their weapons. However, such a challenging functional task is well beyond the immediate goals of most clinicians, who are focused on rapidly addressing the needs of a far larger patient population that would benefit greatly from far less capability. Consequentially, DARPA, through its Defense Sciences Office (DSO), has made considerable investments to improve the capabilities and performance of upper-limb prosthesis technology. Through these efforts, tremendous breakthroughs have resulted in the development of lightweight 22 degrees of freedom prosthetic arms that can be controlled by BMIs. However, without addressing the fundamental reliability problems of chronic neural recording interfaces, the impact of these breakthroughs will be limited.

RE-NET

To overcome the problems limiting long-term reliability of chronic neural-recording interfaces, DARPA is making new investments. Specifically, the RE-NET program, managed through the Microsystems Technology Office (MTO), is supporting a number of competitive funding opportunities and advanced-study efforts aimed directly at these problems.

The first effort, DARPA-BAA-10-32: HIST, has four technical areas of interest: 1) identify the leading mechanisms of interface degradation and failure, 2) develop new invasive and noninvasive histology methods to gain greater insights in the assessment of neural-recording interface status and performance, 3) develop accurate predictive models of interface degradation and failure, which should reduce the time required to assess and develop new interfaces, and 4) develop methods to accelerate the degradation and failure of neural interfaces, which again should reduce the time required to assess and develop new robust interfaces. Seven primary and several smaller research teams have received funding from the HIST effort. These teams are investigating a wide variety of neural-recording interface failure mechanisms such as cell death, inflammation, blood–brain barrier disruption, microglia activation/deactivation, myelination, and abiotic faults. In addition, they are investigating the dependence of interface degradation and failure on probe geometry, mechanical stiffness, tethering, micromotion, materials, and implantation protocol. Teams are also developing new tools, such as multispectral morphological immunohistochemical three-dimensional (3-D) imaging, two-photon, electrical, spectroscopic, enzyme-linked immunosorbent assay, reactive-oxygen species, and genetic assessment methods. Although each team may develop their own failure-prediction models, each team has to take the lead to quantitatively assess high-dimensional heterogeneous datasets to predict interface performance. A few teams have developed novel approaches to accelerate interface degradation.

The second effort, identified as DARPA-BAA-11-08: RPI, has five technical areas of interest: 1) demonstrate peripheral-tissue interfaces that can reliably extract motor-control information, 2) demonstrate peripheral-tissue-interface electronics and packaging to facilitate reliable extraction of motor-control information, 3) demonstrate algorithms and subsystems that can reliably decode peripheral motor-control intent from recorded signals in real time, 4) combine the breakthroughs derived from efforts in technical areas 1–3 to demonstrate the effectiveness of the proposed RPI, and 5) demonstrate technology that can reliably provide direct sensory-feedback signal to the peripheral nervous system. A set of complimentary teams, which have been selected and are undergoing contract negotiations, plan to investigate a wide variety of reliable-peripheral interfaces strategies for recording motor-control information, such as nerve cuffs, penetrating probe arrays, regenerative interfaces, tissue-engineered biological constructs, and invasive electromyography systems.

DARPA has made considerable investments to improve the capabilities and performance of upper-limb prosthesis technology.

The third effort, identified as DARPA-BAA-11-37: RCI, has five technical areas of interest: 1) demonstrate CNS-tissue interfaces that can reliably extract motor-control information, 2) demonstrate CNS-tissue-interface electronics and packaging to facilitate reliable extraction of motor-control information, 3) demonstrate algorithms and subsystems that can reliably decode CNS motor-control intent from recorded signals in real time, 4) demonstrate amputee-relevant behavioral-testing methods to accurately evaluate the reliability of CNS-interface systems, and 5) demonstrate technology that can reliably provide direct sensory-feedback signals to the CNS. Several teams have been selected and are undergoing contract negotiations. Each team plans to investigate a different reliable CNS-interface approach for recording motor-control information from single units, LFPs, electrocorticograph, and electroencephalograph.

Conclusions

Despite decades of focused funding, more years of interest, and far more years of demand, high-performance neural interfaces for recording motor-control information are still not reliable enough for the demanding users of the technology. The investments of DARPA are directly addressing and solving the fundamental problems that limit the reliability of high-performance neural interfaces, to provide amputees with the ability to control state-of-the-art upper-limb prostheses and achieve their ultimate rehabilitative goals.

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