Brain-Machine Interface Paradigms for Neuroscience and Clinical Translation

Samantha R. Santacruz, Vivek R. Athalye, Ryan M. Neely and Jose M. Carmena*
Department of Electrical Engineering and Computer Sciences
Helen Wills Neuroscience Institute
University of California, Berkeley
Berkeley, CA 94720-3370
(*) jcarmena@berkeley.edu

The brain-machine interface (BMI) is a novel technology that holds great potential to aid large numbers of people with sensory, motor and cognitive disabilities. The goal of cortically controlled BMIs is to reliably, accurately, and robustly convey enough motor control intent from the central nervous system (CNS) to drive multi-degree-of-freedom (DOF) prosthetic devices by patients with amputated, paralyzed, or otherwise immobilized limbs for long periods of time (decades). To achieve this goal, two main challenges remain: 1) how to make viable neural interfaces that last a lifetime, and 2) skillful control and dexterity of a multi-DOF prosthetic device comparable to natural movements. In a BMI system, neural signals recorded from the brain are fed into a machine that transforms these signals into a motor plan. This is the subject's "intention of movement", which is then streamed to the prosthetic device. A closed control loop is established by providing the subject with visual and sensory feedback of the prosthetic device. BMIs provide also a framework for examining basic neuroscience questions, especially those related to the understanding of how neural plasticity relates to the acquisition and consolidation of skills.

In the first part of this talk I will postulate that achieving skillful, natural control of a multi-degree-of-freedom BMI will entail synergizing two different types of adaptation processes: natural (brain plasticity) and artificial (decoder adaptation), as well as providing realistic sensory feedback from the prosthetic device. I will present recent work showing that 1) neuroplasticity facilitates consolidation of neuroprosthetic motor skill in a way that resembles that of natural motor learning; 2) corticostriatal plasticity is necessary for neuroprosthetic skill learning, and 3) closed-loop decoder adaptation (CLDA) techniques can expedite the learning process by adapting the decoder parameters during closed-loop BMI operation (i.e., while the subject is using the BMI). The design process of a CLDA algorithm requires important decisions not only about *which* parameters of the decoder should be adapted and *how* these should be adapted, but also *when*, (i.e. how often), as the rate at which the decoder changes can influence performance. We believe that BMI systems capable of exploiting both neuroplasticity and CLDA will be able to boost learning, generalize well to novel movements and environments, and ultimately achieve a level of control and dexterity comparable to that of natural arm movement.

Next we will discuss how to use BMIs to study skill learning and consolidation. In addition to holding great therapeutic potential as assistive and rehabilitation technology, BMIs provide also a powerful framework for examining basic neuroscience questions, especially those related to the neural correlates of learning behavior as it offers researchers the unique opportunity to directly control the causal relationship between neuronal activity and behavioral output. In particular, we focus on the question of how neuroplasticity relates to the acquisition and consolidation of skills. The importance of this question is paramount as it impacts both brain function and dysfunction. We examine the question of how a task-relevant neural population explores and consolidates spatiotemporal patterns supporting neuroprosthetic skill learning? In the early stages of motor skill learning, movements are variable from attempt to attempt. This variability can be beneficial to learning, permitting the motor system to explore actions and their consequences. Gradually movement variability decreases as the motor system consolidates

particular movements which lead to success. Neurophysiological motor learning studies have found neural activity in various species and brain areas follows a similar trend, exhibiting high variability in early training and reducing variability as particular activity patterns are consolidated in late training. These studies have focused on overall changes in neural variability. Given the large dimensionality of possible activity patterns available to a neural population, and the possibilities for interaction among cells, it is critical to understand how different sources of neural variability contribute to motor learning. If the variability in a neural population is driven mostly by private independent inputs, then each neuron produces independent activity, and the population fully explores high dimensional activity space. On the other hand, if cells receive coordinating inputs (input activity which drives multiple cells simultaneously), then activity becomes constrained to a co-activation manifold.

Because the motor system is a distributed and redundant dynamical system, with parallel degenerate pathways and many more neurons than muscles, a fundamental challenge of neuroscience has been to ascertain the causal relationship between observed neural activity patterns and motor output. This apparent complexity and degeneracy makes the question of how neural plasticity changes movement production difficult to answer. We therefore took advantage of a paradigm in which we could identify the output neurons that control behavior and identify the explicit transformation between output neuron activity and behavior. We used an operant learning BMI paradigm in which stable recordings from ensembles of primary motor cortex neurons in macaque monkeys are fed through a constant mathematical transform (hereafter referred to as decoder) to transform neural activity into prosthetic movements. The BMI provided a closed-loop feedback system operating within the natural motor system, hereafter referred to as the “neuroprosthetic circuit”. Under the condition of a fixed decoder and fixed neural population over training, subjects acquire proficient neuroprosthetic control which is stable and readily-recalled over days. This neuroprosthetic skill learning paradigm is uniquely advantageous to investigate how task-relevant neural populations explore and consolidate activity patterns that support skill learning. By selecting the stable cells whose activity is fed through the decoder (hereafter referred to as “direct cells”), we define the direct cells to be task-relevant. By designing the decoder and task goals, we define a priori the neural activity space that is relevant for behavioral output as well as the possible activity patterns that can lead to success. By holding the neuroprosthetic circuit fixed, we can investigate how variability from different sources in a task-relevant neural population evolves with training, contributes to the consolidated activity and neuroprosthetic patterns, and ultimately drives neuroprosthetic learning.

We used Factor Analysis to model independent and coordinated sources of variability in a neuroprosthetic skill learning task, and revealed that population dynamics became more coordinated and low-dimensional with training. We leveraged the decoder structure to interpret the observed changes in dynamics, finding that task-relevant coordinating input signals were consolidated. Previous studies have shown that motor learning is accompanied by a decrease in total trial-to-trial neural variability. Here, we uncovered that private and shared sources of variability evolve differently over training. While private variability is important early in training and decreases over training, shared variability slowly consolidates to produce faster and straighter movements. Hence, our findings describe neuroprosthetic skill learning as a process of spatiotemporal neural pattern consolidation whereby the strengthening of task-relevant input signals coordinates initially variable, high-dimensional activity. A greater understanding of the neural substrates of neuroprosthetic skill learning can provide insight into the mechanisms of natural sensorimotor learning as well as help guide the development of neurobiologically-informed neuroprosthetic systems designed to aid people suffering from devastating neurological conditions.

Finally, in the last part of the talk I will discuss the emerging field of "mind prosthetics", with applications to mental health. The current paradigm for the treatment of neuropsychiatric disorders, such as addiction and depression, relies heavily on pharmacological and behavioral therapies. This paradigm is inherently limited by its palliative rather than curative approach. Prospective corrective therapies must target the etiology of neuropsychiatric disorders and this approach can be realized using neurotechnologies that are capable of leveraging neurofeedback to construct targeted mechanisms that ameliorate pathological activity. BMI technologies are ideal for neuropsychiatric treatment therapeutics. In combination with new physiological biomarkers and animal models, future BMI neurotherapeutic devices will have the potential to cure people suffering from psychiatric and mood disorders. Towards this goal, we have developed a novel animal model for assaying correlates of acute anxiety and closed-loop strategies for mood modulation with strong anxiolytic effects.