BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Miller, Lee Eugene

POSITION TITLE: Distinguished professor of neuroscience

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Goshen College, Goshen, Indiana	B.A.	April, 1980	Physics
Northwestern University, Evanston, Illinois	M.S.	June, 1984	Biomedical Eng.
Northwestern University, Evanston, Illinois	Ph.D.	Dec,1990	Physiology
University of Nijmegen, The Netherlands	Post-Doc	1991, 1992	Medical Physics

A. Personal Statement

For most of my academic career, I have done work that addresses basic properties of the neural control of reaching and grasping. My early training in Physics and Engineering has very much influenced my approach to these problems, which tends strongly to the quantitative. The recent growth of neural engineering has provided a productive avenue for the transformation of my basic research into a more applied, translational line of work. We have developed a very successful efferent interface that restores hand use to temporarily paralyzed monkeys using Functional Electrical Stimulation of the paralyzed muscles that is controlled in real time by motor cortical (M1) recordings. We are also developing novel interfaces to control reaching movements. One uses a control system for a prosthetic limb based on a simplified musculoskeletal model, rather than the kinematic controllers that are currently used. Another embodies a novel “dual-state” kinematic decoder that recognizes the monkey’s intent to reach toward a target, or maintain its position within a target.

At the same time, we have begun to approach the opposite problem: Informing the spinal cord injured patient about limb state by stimulating the somatosensory cortex (S1). This has required that we study proprioceptive signals within areas 3a and 2 of the primary somatosensory cortex (S1). Using this knowledge, we hope to engineer a highly biomimetic approach to restoring sensation through multi-electrode stimulation within S1. We have shown that electrical stimulation can be used to evoke a sensation that the monkey’s hand

My lab group currently numbers 17 graduate and undergraduate students, post-docs, interns, and technicians. I have mentored about 20 graduate students, 15 post-docs, and 55 interns and rotating students. Most of my graduate students have done on to pursue academic post-doctoral fellowships, but an increasing number have turned recently to industry. Most summers we have one or two undergraduate interns working in the lab. The highly multidisciplinary nature of our work offers a unique and quite compelling atmosphere in which to be exposed the neurosciences.

B. Positions and Honors

Positions and Employment

1983-1989	Graduate Student / Research Assistant, Physiology Dept, Northwestern University
1990-1992	Post-Doc. Res., Dept of Biophysics and Med. Physics, Univ. of Nijmegen, The Netherlands
1992-1993	Research Associate, Physiology Department, Northwestern University
1993-1995	Research Assistant Professor, Physiology Department, Northwestern University
1995-2003	Assistant Professor, Physiology Department, Northwestern University
1997	Appointed to the faculty of the Northwestern University Institute for Neuroscience
2003-	Associate Professor, Physiology Department, Northwestern University
2006-	Associated faculty member, Biomedical Engineering Dept., Northwestern University
2008-	Associate Professor, Physical Medicine and Rehabilitation, Northwestern University
2009-	Professor

2011- Appointed Edgar C. Stuntz distinguished professor of neuroscience

Honors and Awards

1981-1982	Murphy Fellowship, Northwestern University
1990-1992	European Community ESPRIT II Post-Doctoral Fellowship
1996-1998	Co-PI, NATO Collaborative Research Grant
2002	Senior Visiting Fellow, Institute of Neurology, University College London
2007	Best podium presentation, 10th Int. Conf Rehab Robotics
2016	Elected Fellow in the American Institute of Medical and Biological Engineers

Professional and Scientific Activity

2003-2007	SMI study section, National Institutes of Health
2007-	Board member, Society for the Neural Control of Movement
2010-	International BCI Meeting Steering Committee
2013-2015	Development officer, Society for the Neural Control of Movement
2015-	President of the Society for the Neural Control of Movement

Society Memberships

American Institute of Medical and Biological Engineers
American Physiological Society
Engineering in Medicine and Biology Society
Institute of Electrical and Electronics Engineers
Society for Neuroscience
Society for the Neural Control of Movement

C. Contribution to Science

http://scholar.google.com/citations?hl=en&user=24i8cx8AAAAJ

Control of limb movement by populations of sensorimotor cortical neurons

Recent and accelerating technical developments provide the experimental tools for monitoring the activity of large numbers of neurons, as well as the statistical and modeling tools for analyzing how these neural populations perform the computations necessary to plan and execute movement. These methods allow us to capture the statistical interactions among the neurons and to infer something about the function of the networks. Reliable patterns of covariance within these networks permit the use of dimensionality reduction methods that can provide low-dimensional, denoised “latent signals” opening a window onto detailed neural processing on the single-trial level. We have successfully applied these experimental and analytical tools to a variety of problems in the somatosensory, motor, and premotor cortices.

Stevenson, I. H., J. M. Rebesco, L. E. Miller and K. P. Kording (2008). "Inferring functional connections between neurons." Curr Opin Neurobiol **18**(6): 582-588.

Gallego, J. A., M. G. Perich, L. E. Miller and S. A. Solla (2017). "Neural Manifolds for the Control of Movement." Neuron 94(5): 978-984.

Dekleva, B. M., K. P. Kording and L. E. Miller (2018). "Single reach plans in dorsal premotor cortex during a two-target task." Nature Communications 9(1): 3556.

Perich, M. G., J. A. Gallego and L. E. Miller (2018). "A Neural Population Mechanism for Rapid Learning." Neuron 100(4): 964-976.e967.

Development of a cortically-controlled neuroprosthesis to restore limb movement in spinal cord injury

My study of the relation between M1 and muscle activity provided the natural basis for the development of a BMI that uses the concurrently recorded activity from large numbers of M1 neurons to predict EMG. We have been able to use these real-time EMG predictions to control the intensity of electrical stimulation applied to muscles, a technique called Functional Electrical Stimulation (FES). This novel FES BMI restores voluntary hand movements to monkeys whose forearm muscles are temporarily paralyzed by a peripheral nerve block. The methods have direct application to patients with spinal cord injury, and may also be appropriate to control a prosthetic limb by implementing a simple musculoskeletal model of joint torques and limb impedance.

Pohlmeyer EA, Solla SA, Perreault EJ, Miller LE (2007) Prediction of upper limb muscle activity from motor cortical discharge during reaching. Journal of Neural Engineering 4: 369-379. PMC2586074.

Pohlmeyer EA, Oby ER, Perreault EJ, Solla SA, Kilgore KL, Kirsch RF, Miller LE (2009) Toward the Restoration of Hand Use to a Paralyzed Monkey: Brain-Controlled Functional Electrical Stimulation of Forearm Muscles. PLoS ONE 4: e5924. PMC2691481.

Ethier, C., Oby, E.R., Bauman, M.J., and Miller, L.E. (2012). Restoration of grasp following paralysis through brain-controlled stimulation of muscles. Nature 485, 368-371. PMC3358575

Sachs, N. A., R. Ruiz-Torres, E. J. Perreault and L. E. Miller (2015). "Brain-state classification and a dual-state decoder dramatically improve the control of cursor movement through a brain-machine interface." Journal of neural engineering 13(1): 016009.

Development of an afferent neuroprosthesis to restore proprioception

Although the great majority of BMI development work has been directed toward the development of efferent interfaces that effect movement, there is increasing recognition of the need to develop afferent interfaces as well. A number of groups have begun to develop interfaces that use intracortical microstimulation (ICMS) to restore the sense of touch. On the other hand, proprioception, the sense of limb position and movement, has received much less attention. We have used microelectrode arrays, chronically implanted in proprioceptive areas of S1, to investigate its encoding of limb state, and our ability to cause sensations of directed limb movement by stimulating one or more electrodes. We are working to develop a neuroprosthesis that will cause a sensation of time-varying limb state intended to restore proprioceptive awareness, and to provide the information needed by the motor system to plan and execute reaching movements.

Weber DJ, London BM, Hokanson JA, Ayers CA, Gaunt RA, Torres RR, Zaaimi B, Miller LE (2011) Limb-State Information Encoded by Peripheral and Central Somatosensory Neurons: Implications for an Afferent Interface. Neural Systems and Rehabilitation Engineering, IEEE Transactions on 19: 501-513. PMC3694199

London BM, Miller LE (2013) Responses of somatosensory area 2 neurons to actively and passively generated limb movements. Journal of neurophysiology 109: 1505–1513. PMC3774588.

Zaaimi B, Ruiz-Torres R, Solla SA, Miller LE (2013) Multi-electrode stimulation in somatosensory cortex increases probability of detection. Journal of Neural Engineering 10:05601. PMC3821924.

Tomlinson T, Miller LE (2016) Toward a proprioceptive neural interface that mimics natural cortical activity. In: Laczko J, Latash ML (eds) Progress in Motor Control: Theories and Translations. Springer

Encoding of muscle activity by brainstem and cortical motor areas

The primary motor cortex (M1) was identified 150 years ago based on the ability to elicit limb movements through electrical stimulation of the cortical surface. For nearly as long, there has been a debate over whether this part of the brain is organized to specify high-level aspects of movement or the more intimate details of muscle activation necessary to effect movement. My work has made pivotal contributions to this discussion. This work has shown that the activity of individual neurons in M1, the red nucleus, the superior colliculus and the reticular formation is well correlated with the EMG measured from small groups of synergistically-related muscles. In addition to the impact of his work on models of M1, it profoundly impacts the implied role of spinal networks in the production of independent limb movements. It also has formed the basis for more recent work in my lab directed toward the development of Brain Machine Interfaces (BMIs).

Miller LE, van Kan PLE, Sinkjaer T, Andersen T, Harris GD, Houk JC (1993) Correlation of primate red nucleus discharge with muscle activity during free-form arm movements. J. Physiol. London 469: 213-243. PMC1143869

Stuphorn V, Hoffmann K-P, Miller LE (1999) Correlation of primate superior colliculus and reticular formation discharge with proximal limb muscle activity. *Journal of Neurophysiology* 81: 1978-1982

Holdefer RN, Miller LE (2002) Primary motor cortical neurons encode functional muscle synergies. Exp Brain Res 146: 233-243

Morrow MM, Jordan LR, Miller LE (2006) A direct comparison of the task-dependent discharge of M1 in hand-space and muscle-space. J Neurophysiol 97: 1786-1798. PMC2586084.

Use of precisely-timed stimulation to alter function and functional connectivity in the CNS

Plastic adaptations in the nervous system show great promise for restoration of function following spinal cord injury or stroke. There is increasing evidence in both animal and human studies, that carefully timed electrical stimulation can be used to evoke Hebbian plasticity and guide beneficial adaptive changes. We are able to use multi-electrode arrays implanted in the cortex, together with intramuscular or nerve electrodes, to effect changes in computed functional connectivity in the intact animal, as well as effects on sensorimotor function. We are working to develop these approaches for application to animal models of spinal cord injury or stroke.

Rebesco JM, Stevenson IH, Koerding K, Solla SA, Miller LE (2010) Rewiring neural interactions by micro-stimulation. Frontiers in Systems Neuroscience 4: 39. PMC2936935

Rebesco JM, Miller LE (2011) Enhanced detection threshold for in vivo cortical stimulation produced by Hebbian conditioning. Journal of Neural Engineering 8: 016011 (Selected for inclusion among the highlights of 2011 issue). PMC3056083

Ethier, C., J. A. Gallego and L. E. Miller (2015). "Brain-controlled neuromuscular stimulation to drive neural plasticity and functional recovery." Current Opinion in Neurobiology **33**(0): 95-102. PMC4523462

Ethier C, Miller LE (2015) Brain-controlled muscle stimulation for the restoration of motor function. Neurobiology of Disease 83:180-190 doi: http://dx.doi.org/10.1016/j.nbd.2014.10.014

D. Research Support

Ongoing Research Support

IIS-1835345 (Pandarinath) 10/1/2018 - 9/30/2021
National Science Foundation
"Discovering dynamics in massive-scale neural datasets using machine learning"
In the fifty years of recorded from neurons in M1, great effort has been devoted to understanding the relation between these individual signals, and movement-related signals collected during highly constrained motor behaviors performed by over-trained monkeys. In parallel, theoreticians posited that the computations performed in the brain depend critically on network-level phenomena: lawful “dynamics” within brain circuits that constrain the activity, and dictate how evolves over time. Our primary goal is to develop a powerful new suite of analysis tools based on cutting-edge machine learning techniques that can reveal these dynamics at unprecedented temporal and spatial scales.
Role: Co-I

R01 NS104344 (Cogan) 09/01/2018 – 08/31/2023
NIH/NINDS
"Scalable Electrode Technology for High Resolution Chronic Recording of Brain"
There is a need in neuroscience research for arrays of very small electrodes that are implanted in the brain to provide stable long-term recording and stimulation of neural electrical activity. The neural recordings are used to understand normal brain functions such as learning, adaption, and behavior, as well as to investigate neural dysfunction. We are proposing to develop an electrode technology that meets these needs and uses scalable fabrication processes that will promote dissemination of the technology to the neuroscience community and eventually for clinical applications in brain-computer interfaces for individuals with spinal cord injury, amputation, stroke, and other major neurological deficits.
Role: Co-PI

R01NS053603-11A1 09/1/2017 - 07/31/2022
NIH /NINDS
“A primate model of an intra-cortically controlled FES prosthesis for grasp”
Brain machine interfaces (BMIs) offer remarkable opportunities to study how the brain learns, and to restore function to paralyzed patients, but existing BMIs are usable only intermittently, in highly constrained lab settings. We have developed a novel BMI that will restore hand use to monkeys with nerve-block paralysis, 24 hours a day, in their home cage as well as in the lab. This BMI offers a novel tool to study motor learning, and is a critical bridge to clinical translation of this technology to human patients.
Role: PI

R01 NS095251 (Miller) 06/012016-05/31/2021
NIH /NINDS
“Biomimetic Somatosensory Feedback through Intracortical microstimulation”

Spinal cord injury causes both paralysis and loss of feeling from the limbs (somatosensation); brain machine interfaces (BMIs), which record signals directly from the brain, can be used to control prosthetic devices, computers, or environmental controls. However, BMIs currently do not restore somatosensation, a critical component of normal limb movement. We propose to develop a new type of brain interface that will mimic the somatosensory brain activity generated during movement and provide natural and informative artificial sensation for people with paralysis or limb amputation.
Role: PI

R01 NS095162 (Bensmaia) 09/012015-08/31/2020
NIH /NINDS
"Probing somatosensory representations in the cuneate nucleus of awake primates"
The cuneate nucleus (CN) receives input from somatosensory afferents that innervate the skin, joints and muscles as well as descending input from sensorimotor cortex, but virtually nothing is known about its response properties. We propose to lay a foundation for this by studying, for the first time, the tactile and proprioceptive response properties of neurons in CN in awake, behaving primates.
Role: co-PI

#340943 (Miller) 09/30/2015 – 08/29/2018
Neilsen Senior Research Grant
"Development of an FES neuroprosthesis for rehabilitation following SCI"
This project seeks to restore locomotion in rats following spinal cord injury using functional electrical stimulation of hindlimb muscles driven by cortical recordings. We propose test the extent to which locomotion can be restored and whether training rehabilitation with the neuroprosthesis provides faster of more complete recovery of motor function that rats receiving a similar amount of treadmill training without the neuroprosthesis.
Role: PI

Completed Research Support
R01 NS074044 (Kording) 07/01/2011-04/30/2017 (NCE)
NIH /NINDS
"The representation of uncertainty in the sensorimotor system"
The sensorimotor system must deal with uncertainty in its estimates of information received via the senses, and uncertainty in our internal models of our limbs and movement experiences, acquired slowly over time. However, there is a fundamental gap in our understanding of how this uncertainty is represented in the brain and used for movement planning. The goal of this project is to test the predictions of a number of prominent models using signals recorded from various visuomotor areas during reaching movements.
Role: co-PI

R01 NS048845 (Miller) 05/01/2005 - 04/30/2016
NIH/NINDS
"Development of a bidirectional brain machine interface"
This grant is a biomedical research partnership involving collaborators at 5 different institutions. The goals are to develop a BMI that incorporates realistic musculoskeletal dynamics into the control pathway, and a feedback BMI that delivers artificial proprioceptive to the CNS by electrical stimulation of the somatosensory cortex.
Role: PI