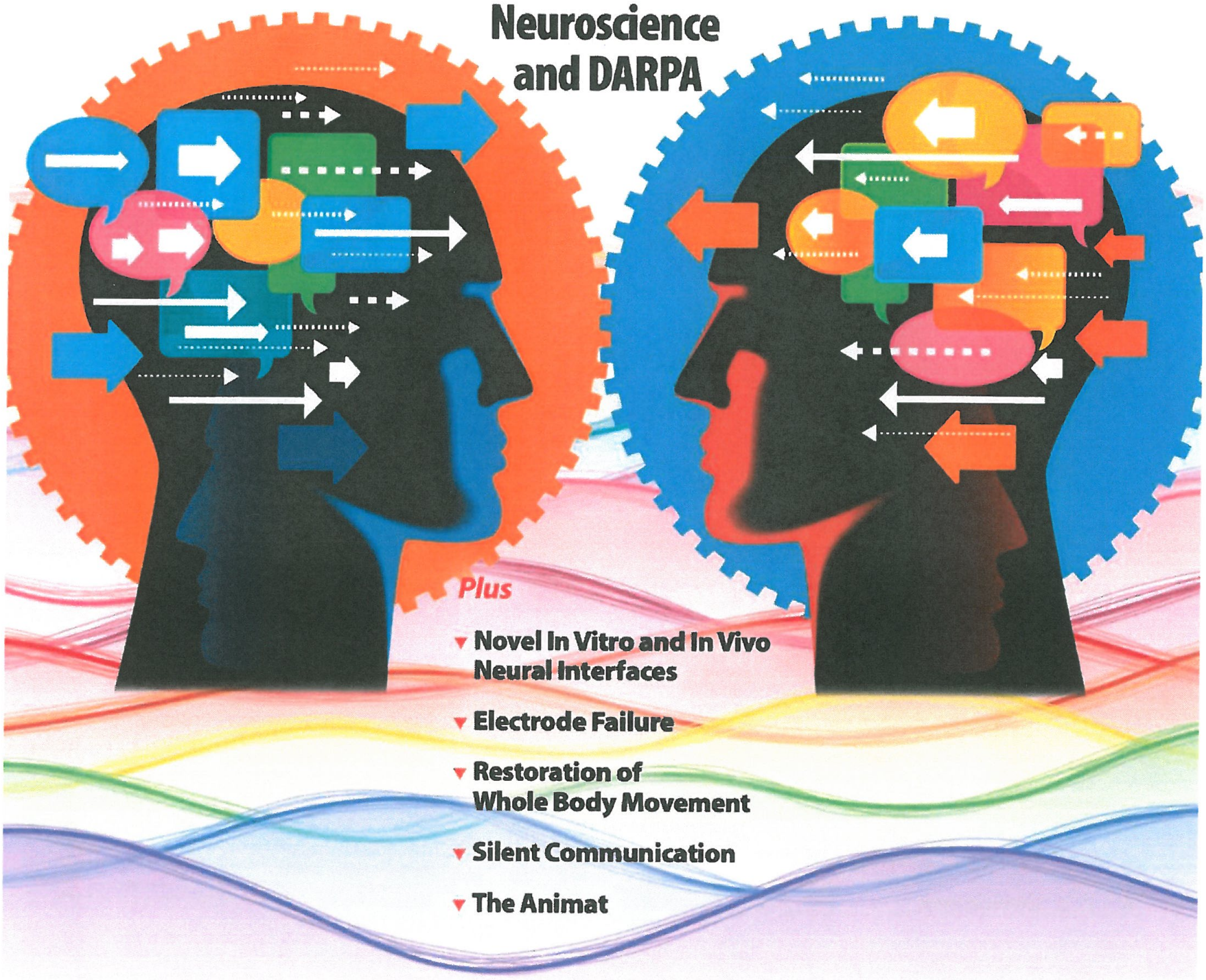
January/February 2012
Volume 3 ▾ Number 1
http://magazine.embs.org

IEEE PULSE
A MAGAZINE OF THE IEEE ENGINEERING IN MEDICINE AND BIOLOGY SOCIETY

Pushing the Horizon

Neuroscience and DARPA



Plus

- Novel In Vitro and In Vivo Neural Interfaces
- Electrode Failure
- Restoration of Whole Body Movement
- Silent Communication
- The Animat

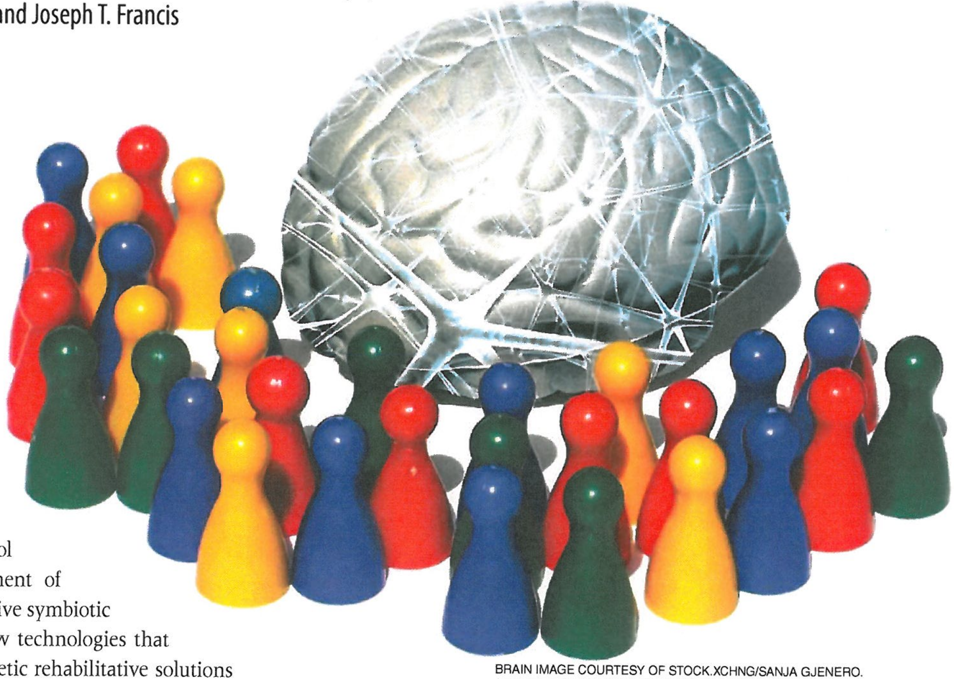
Indexed in PubMed® and MEDLINE®, products of the United States National Library of Medicine

PubMed MEDLINE U.S. National Library of Medicine

EMB IEEE

Dynamically Repairing and Replacing Neural Networks

By Justin C. Sanchez, William W. Lytton, Jose M. Carmena, Jose C. Principe, Jose Fortes, Randall L. Barbour, and Joseph T. Francis



BRAIN IMAGE COURTESY OF STOCK.XCHNG/SANJA GJENERO. NEURAL NETWORK COURTESY OF STOCK.XCHNG/GERARD79

The debilitating effects of injury to the nervous system can have a profound effect on daily life activities of the injured person [1]. In this article, we present a project overview in which we are utilizing computational and biological principles, along with simulation and experimentation, to create a realistic computational model of natural and injured sensorimotor control systems. Through the development of hybrid in silico/biological coadaptive symbiotic systems, the goal is to create new technologies that yield transformative neuroprosthetic rehabilitative solutions and a new test bed for the development of integrative medical devices for the repair and enhancement of biological systems.

Using Hybrid Computational and Biological Tools

The damage imposed on neural tissues disrupts the normal activation needed to produce the substrates for expressing the intent of communication and control. An analysis on the generation of sensorimotor programs in the nervous system reveals that there are an intricate set of synergies among the hierarchical activation of multiscale signals in the brain [2], temporal dynamics of their interaction [3], and interplay among subsystems related to motor, sensory, and reward signaling [4]. While great strides are being made in medical practice to restore communication and control functions, the approaches that are typically employed lack the tools needed to assess the coordinated and time-varying properties of systems of neurons. In essence, the clinical perspective in how to diagnose and treat injuries is limited by the tools used to probe the system, which are often static and unable to contend with the perturbations that have been imposed by injury. A prime example of these limitations can be observed in the neurosurgery theater where real-time assessment of neuronal function in cases of traumatic brain injury is difficult or often impossible to quantify or predict [5]. One aspect of our team's efforts is the production of multiscale neural analysis through tools, such as electrophysiology and functional tomographic, near infrared imaging [6] that allows tracking of dynamic changes at a high temporal resolution that could be used in the near future to help aid the clinician.

The road map for developing the next-generation therapies for repairing and replacing neuronal networks in the brain injury requires a novel integration of neuroscience and engineering approaches that can be used to understand, assess, predict, and respond to perturbations of the nervous system. The new focus is on symbiotic (biological in silico) systems that exploit neuroscience knowledge and engineering methods to raise the combined system performance to levels comparable to the intact biological system. Our work moves beyond purely observational studies and seeks to investigate functional relationships between computational and biological systems that coadapt with each other. We have

Digital Object Identifier 10.1109/MPUL.2011.2175640
Date of publication: 6 February 2012

2154-2287/12/$31.00©2012 IEEE

recently assembled a team of scientists to develop a transformative experimental and computational approach capable of deriving and modeling sensorimotor intention and somatosensory feedback in real time from perturbed neural systems, facilitate the incorporation of artificial neural substrates into biological signaling, and adapt the context of a rich real-time environment for functional control. The fundamental scientific approach is to utilize computational and biological principles, along with simulation and experimentation, to create realistic computational models of the sensorimotor system of the brain. The work leads to the creation of hybrid in silico/biological symbiotic systems relying on real-time error and reward feedback, which by design are capable of interacting with the reduced functional dynamics of the perturbed neural systems that we seek to repair, replace, or assist in injury. In our endeavor, we hope to create new engineering design procedures based on cognitively inspired dynamical models, new technologies that yield transformative neuroprosthetic rehabilitative solutions, and a new test bed for the development of integrative medical devices for neural repair and enhancement.

The restoration of communication and control to injured networks is the primary goal of our work. Brain–machine interface experimental test beds are used as a platform to study the hierarchical dynamics of sensory, motor, and reward systems in the context of injury and real-time environments. As shown in Figure 1, experiments are designed to advance our understanding of system-level neural information processing and the robustness of decoding through novel in silico models. Next, we will introduce each of the key components of our work and report on our progress and future goals.

In Silico Models for Testing Perturbation

It has been noted for the past 80 years that a major feature of brain function is the tendency for dynamics and oscillation. The implications of this basic property have been debated almost since its discovery: are oscillations and dynamics an epiphenomenon or are they really central to brain functioning? We have focused on the broad spectrum of cortical oscillations with the idea that the different frequency bands may be a key to the capacity of cortex for multiplexing. Our models replicate the spectrum of activity in a representative area of cortex. What is the use of these oscillations? To answer this, we draw findings from recent investigations in reservoir computing. Discoveries in this area demonstrate the possibility of developing active systems based on large sets of active units such as neurons. These systems can produce an enormous repertoire of dynamics that are stored in these dynamical reservoirs. We can then use these repertoires to study perturbations in representation and behavior. In addition, since our experimental test beds are hybrid biological–computational in nature, the real neural networks that are being modeled can actively be probed in vivo using small electrical perturbations to induce neural activity. The modulation can be tracked through the real neural substrate, and we can ensure that our in silico model has the same properties. The difficulty lies in selecting the proper subset of neurons to produce the dynamics that are suited for a particular case. We are looking at reward-learning mechanisms that would allow us to appropriately select the proper set of activities. To deal with the exigencies of real-world interaction, we develop our systems within the context of the perception–action–reward (PARC) cycle. Note that this cycle can start at any point: the system acts, observes the results of its action, and is then either rewarded or punished for its efficacy or lack thereof.

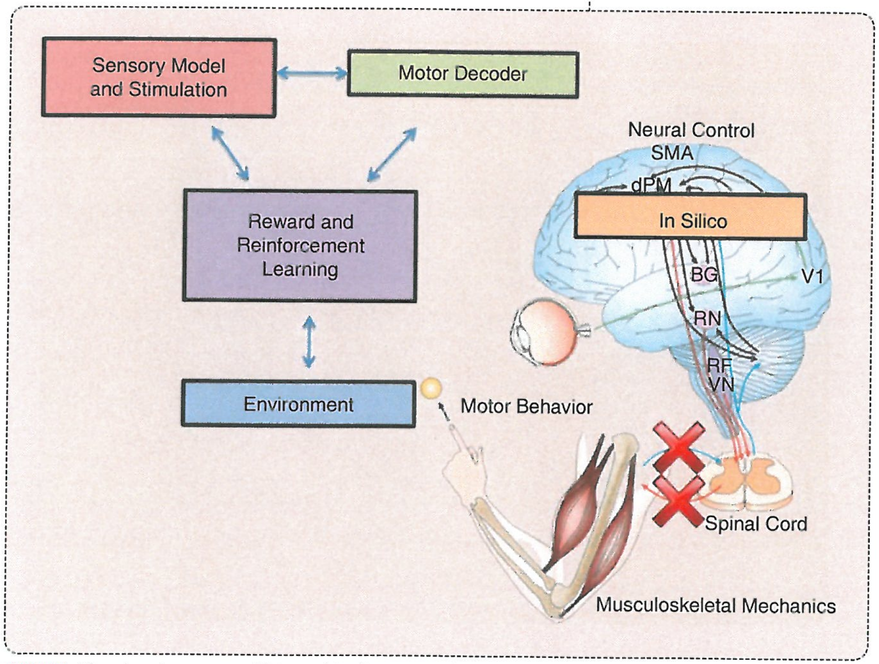


FIGURE 1 The development of hierarchical, systems-based in silico models for sensory, motor, and reward systems. The ability to predict and assess function under perturbed conditions leads to improved communication and control in the environment. (Adapted from [7].)

Reward Learning

Within the PARC, we are using reinforcement learning (RL) as a guiding principle to link in vivo physiology with computational modeling during dexterous tasks in dynamical environments. Unlike other learning principles, RL enables our networks to learn and consolidate knowledge through experience as the natural network would. This computational and biological framework offers a method of neural interfacing that uses goal-directed, experience-based learning to relate neural modulation to behavior through an accumulation of rewards and interaction with the environment. Collectively, in this framework, sensorimotor subsystems naturally contribute to forming a

PARC, which plays a critical role in organizing behavior in the nervous system. We have directly interfaced the nervous systems of behaving animal subjects with symbiotic computational models and shown that two-dimensional [8] and three-dimensional [9] reaching control with RL is possible. During the process, we have also discovered that modulation in the reward centers can affect the performance of communication and control decoding models [9]. Changes in the state of this primary RL signal is a useful diagnostic tool to assess and affect the dynamics and speed of adaptation of the full system [9].

Multiscale Analysis

Within these biological and in silico systems, we are studying the nature of neuronal mechanisms subserving local cortical computation and long-range communication in the brain. In this regard, a promising but poorly understood aspect of cortical dynamics that may lead to new decoding techniques is the dependence of spike timing in single neurons upon the spontaneous local field potential (LFP). While neurons in early sensory or motor areas respond to external factors such as visual orientation or the direction of movement with systematic changes in their spike rate, a large amount of jitter or spike-timing variability remains in neural recordings. This spike-timing jitter has long been dismissed as noise, but the advent of simultaneous recordings using multiple microelectrodes provided the opportunity to record spontaneous ongoing activity in the form of the LFP and measure the degree of statistical dependence between spikes and the ongoing population activity. Once this internal receptive field of the neuron is estimated, investigators can account for the spike-timing variability due to internal dynamics alone. This can amplify the fidelity with which the external receptive field can be estimated, improving decoding performance. In particular, we have shown that neural spiking depends upon large-scale, frequency-specific LFP patterns occurring in multiple brain areas [10]. This type of information adds another reference point for us to pin down our large-scale simulations in our effort to develop novel in silico models.

Summary

There is a great need to establish key foundations and knowledge for the understanding and treatment of the millions of individuals suffering from the effects of nervous system injury. The development of new medical therapies hinges on the ability to understand the dynamics of hierarchical brain activity because the current tools used to probe these systems are unable to contend with the perturbations that have been imposed by injury itself. We describe novel experimental test beds and computational methods for tracking and modeling dynamic brain activity at the multiscale level, as well as the creation of symbiotic biological/in silico interfaces that lead to deeper insight into how behavior is functionally generated and organized in the nervous system. In short, we are developing next-generation tools that allow scientists and physicians to probe and predict the ongoing interaction between neural systems and behavior under natural and perturbed conditions. We expect this approach to allow us to produce truly realistic models for the diagnosis and restoration of communication and control.

Acknowledgment

This work was supported by DARPA REPAIR project N66001-10-C-2008.

The views, opinions, and/or findings contained in this article are those of the author and should not be interpreted as representing the official views or policies, either expressed or implied, of the Defense Advanced Research Projects Agency or the Department of Defense.

Justin C. Sanchez *(jcsanchez@ miami.edu) is with the Departments of Biomedical Engineering, Neuroscience, and the Miami Project to Cure Paralysis, University of Miami, Coral Gables, Florida.* ***William W. Lytton*** *(bill@neurosim.downstate.edu) is with the Graduate Program in Neural and Behavioral Science, The Robert Furchgott Center for Neural and Behavioral Science, Department of Physiology and Pharmacology, Graduate Program in Biomedical Engineering, and Department of Neurology, State University of New York (SUNY) Downstate Medical Center, Brooklyn, New York.* ***Jose M. Carmena*** *(carmena@eecs.berkeley.edu) is with the Department of Electrical Engineering and Computer Sciences, Helen Wills Neuroscience Institute, and Program in Cognitive Science, University of California, Berkeley.* ***Jose C. Principe*** *(principe@cnel.ufl.edu) and* ***Jose Fortes*** *(fortes@ufl.edu) are with the Department of Electrical and Computer Engineering, University of Florida, Gainesville, Florida.* ***Randall L. Barbour*** *(randall.barbour@downstate.edu) is with NIRx Medical Technologies, Glen Head, New York, and Department of Pathology, SUNY Downstate Medical Center, Brooklyn, New York.* ***Joseph T. Francis*** *(joey199us@gmail.com) is with the Graduate Program in Neural and Behavioral Science, The Robert Furchgott Center for Neural and Behavioral Science, Department of Physiology and Pharmacology, and Graduate Program in Biomedical Engineering, SUNY Downstate Medical Center, Brooklyn, New York.*

References

[1] V. D. Chase, *Shattered Nerves: How Science Is Solving Modern Medicine's Most Perplexing Problem*, 1st ed. Baltimore, MD: The Johns Hopkins Univ. Press, 2006.

[2] M. Botvinick, Y. Niv, and A. Barto, "Hierarchically organized behavior and its neural foundations: A reinforcement learning perspective," *Cognition*, vol. 113, pp. 262–280, Dec. 2009.

[3] M. D. Mauk and D. V. Buonomano, "The neural basis of temporal processing," *Annu. Rev. Neurosci.*, vol. 27, pp. 307–340, 2004.

[4] J. Fuster, "Upper processing stages of the perception-action cycle," *Trends Cogn. Sci.*, vol. 8, no. 4, pp. 143–145, 2004.

[5] D. S. Plurad, "Blast injury," *Military Med.*, vol. 176, pp. 276–282, Apr. 2011.

[6] R. L. Barbour, H. L. Graber, Y. Pei, S. Zhong, and C. H. Schmitz, "Optical tomographic imaging of dynamic features of dense-scattering media," *J. Opt. Soc. Amer. A, Opt. Image Sci.*, vol. 18, pp. 3018–3036, Dec. 2001.

[7] S. H. Scott, "Optimal feedback control and the neural basis of volitional motor control," *Nature Rev. Neurosci.*, vol. 5, pp. 532–546, July 2004.

[8] J. C. Sanchez, A. Tarigoppula, J. S. Choi, B. T. Marsh, P. Y. Chhatbar, B. Mahmoudi, and J. T. Francis, "Control of a center-out reaching task using a reinforcement learning brain–machine interface," presented at the IEEE Int. Neural Engineering Conf., Cancun, Mexico, 2011.

[9] B. Mahmoudi and J. Sanchez, "A symbiotic brain–machine interface through value-based decision making," *PloS One*, vol. 6, no. 3, pp. 1–14, 2011.

[10] R. T. Canolty, K. Ganguly, S. W. Kennerley, C. F. Cadieu, K. Koepsell, J. D. Wallis, and J. M. Carmena, "Oscillatory phase coupling coordinates anatomically dispersed functional cell assemblies," *Proc. Nat. Acad. Sci.* USA, vol. 107, pp. 17356–17361, Oct. 2010.