Repairing Lesions via Kernel Adaptive Inverse Control in a Biomimetic Model of Sensorimotor Cortex*

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***Abstract*— In this paper we propose a kernel adaptive filtering (KAF) approach to repair lesions via microstimulation in a biomimetic spiking neural network of sensorimotor cortex. The fundamental challenge of designing neuroprosthetics and brain machine interfaces (BMIs) is the decoding of electrical activity of neurons and behavior. For injured or damaged brain, intracranial stimulation has the potential to modulate neural activity to match meaningful and natural response or behavior. In order to estimate the optimal microstimulation sequences, we construct an inverse model of the target system. However, to obtain sufficient data to learn the inverse, the neural system much be stimulated or probed repeatedly. For real brains, this is especially challenging and often unfeasible. Here, we demonstrate that by applying KAF to a biomimetic brain and realistic virtual musculoskeletal model, we are able to repair simulated lesion and drive the virtual arm to perform the correct motor task.**

I. INTRODUCTION

Brain machine interfaces (BMIs) connect the brain with external devices by establishing communication directly between the central nervous system and artificially engineered neural prosthetics. Cognitive, motor, and sensory BMIs for direct neural control have far reaching impact in rehabilitation and the understanding of brain functions [1]–[3]. At the core of the BMI framework is the decoding of brain processes involved in communication and control tasks, by learning the functional mapping between the electrical activity of neurons and behavior.

Intracranial stimulation can deliver information directly to the brain and drive neural response to match meaningful activity. Applying optimally designed low-power electrical signals (microstimulation) to intracranial microelectrodes may elicit motor behaviors mimicking the responses to natural sensory stimuli. This approach can be used to repair brain lesions by compensating for the missing activity or by inducing plasticity which can lead to recovery [4]–[6].

In [7], the kernel least mean square (KLMS) algorithm [8], specifically the quantized KLMS (QKLMS) [9], is used to estimate the dynamic nonlinear mapping from neural responses to the stimuli. This approach exploits the fact that linear signal processing in a reproducing kernel Hilbert space (RKHS) corresponds to nonlinear processing in the input space and can be used in the adaptive inverse scheme designed for controlling neural responses.

However, in order to obtain the optimal microstimulation sequences, it is necessary to construct an inverse model of the target system. For real brains, this is especially challenging, and often unfeasible, as it requires stimulating the neural system repeatedly to obtain sufficient probing data for reconstruction and depends on an unwarranted assumption of stationarity. In contrast, a biomimetic model (BMM) of the brain provides an attractive alternative testbed for understanding the interactions between ongoing neural activities and artificial stimulations. Unlike real brains, in silico brains can be probed extensively and precisely, providing access to detailed information of all the neurons and synapses in the network. Furthermore, different types of lesions and repair methods can be simulated and evaluated with ease.

In this paper we repair a simulated lesion by optimizing a set of microstimulation patterns that compensate for missing activity in a spiking network model of sensorimotor cortex, which controls a realistic virtual musculoskeletal arm to perform reaching tasks. Unlike [7] which continuously outputs a set of microstimulation, here, we wish to derive a short burst of repairing microstimulation in the early stage of each reaching task which corrects the lesioned trajectory.

The BMM of sensory and motor cortex consists of several hundred spiking model-neurons, as shown in Figure 1 [10], [11]. It is trained using spike-timing dependent reinforcement learning to drive a realistic virtual musculoskeletal arm in a motor task requiring convergence on a single target. The virtual musculoskeletal arm received input from the BMM signaling neural excitation for each muscle. It then feeds back realistic proprioceptive information, including muscle fiber length and joint angles, which were employed in the reinforcement learning process. Previous studies have shown that this BMM can be interfaced in real time with neurophysiological data from real brains [12], as well as with a robotic arm [13], potentially allowing for a full closed-loop prosthetic system.

Next, the trained network is perturbed by silencing 20 (10.42%) of its excitatory sensory (ES) cells in order to simulate a lesion. After perturbation, the virtual arm reach trajectory is severely impacted and the network is no longer capable of completing the original reaching task. The remaining ES neurons or cells in the BMM are probed using microstimulation pulse patterns. The network activity resulting from the probing sequences are then used to construct an inverse model of the BMM's motor layer kernel adaptive inverse control of neural spatiotemporal spike patterns. The

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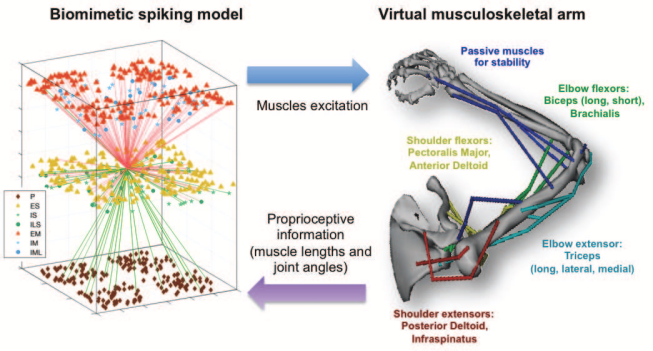

Fig. 1. Overview of the system interfacing the biomimetic spiking model and the virtual musculoskeletal arm. The virtual arm receives neural excitation from the biomimetic model and feeds back the joint angles, used in reinforcement learning algorithm, and the muscle lengths, used as part of the sensorimotor mapping. For the biomimetic model, all incoming (green) and outgoing (red) connections of a single ES neuron are shown. For the virtual arm, all muscles are labeled in their corresponding color.

inverse model is constructed using a kernel adaptive filtering technique and a tensor product kernel composed of individual spike train kernels. It tries to predict the microstimulation pulse pattern required to achieve a desired neural response at the BMM motor layer, i.e., the pre-lesioned activity.

Simulation results show that by applying kernel adaptive inverse control to the BMM we are able to optimize a set of microstimulation patterns to repair the simulated lesion in the model by restoring its correct reaching behavior. The rest of the paper is organized as follows. In Section II, we outline the kernel adaptive filtering algorithm in a spike train RKHS. Section III presents the experimental results, and Section IV concludes this paper.

II. Method

The kernel framework [14] has far reaching impact in classification, clustering, regression, and countless applications in machine learning, signal processing, and biomedical engineering. The theory of adaptive signal processing is greatly enhanced through the integration with the theory of RKHS. By performing classical linear methods in a potentially infinite dimensional feature space, kernel adaptive filtering (KAF) [15] provides general nonlinear solutions in the original input space.

In the family of kernel adaptive filters, the KLMS algorithm [8] is the simplest. A finite impulse response (FIR) filter trained in the RKHS using the least mean squares (LMS) algorithm, it can be viewed as a single-layer feedforward neural network or perceptron. For a set of n input-output pairs $\{(\mathbf{u}_1, y_1), (\mathbf{u}_2, y_2), \cdots, (\mathbf{u}_n, y_n)\}$, the input vector $\mathbf{u}_i \in \mathbb{U} \subseteq \mathbb{R}^m$ (where $\mathbb{U}$ is a compact input domain in $\mathbb{R}^m$) is mapped into a potentially infinite-dimensional feature space $\mathbb{F}$. Define a $\mathbb{U} \to \mathbb{F}$ mapping $\varphi(\mathbf{u})$, the feature-space parametric model becomes

$$\hat{y} = \hat{f}(\mathbf{u}) = \mathbf{\Omega}^T \varphi(\mathbf{u}) \tag{1}$$

where $\mathbf{\Omega}$ is the weight vector in the RKHS. Using the Nonparametric Representer Theorem [16] and the "kernel trick", Eq. (1) can be written as

$$\hat{f}(\mathbf{u}) = \sum_{i=1}^{n} \alpha_i \mathcal{K}(\mathbf{u}_i, \mathbf{u}) \tag{2}$$

where $\mathcal{K}(\mathbf{u}, \mathbf{u}')$ is a Mercer kernel, corresponding to the inner product $\langle \varphi(\mathbf{u}), \varphi(\mathbf{u}') \rangle$, and α_i are the coefficients. The most commonly used kernel is the Gaussian kernel

$$\mathcal{K}_a(\mathbf{u}, \mathbf{u}') = \exp\left(-a\|\mathbf{u} - \mathbf{u}'\|^2\right) \tag{3}$$

where $a > 0$ is the kernel parameter. To effective address the growth of the radial basis function structure in KAF, the QKLMS algorithm is used [9].

A. Reproducing kernel Hilbert space (RKHS) for spike trains

A spike train or sequence of M ordered spike times, i.e., $\mathbf{s} = \{t_m \in \mathcal{T} : m = 1, \cdots, M\}$ in the interval $\mathcal{T} = [0, T]$, can be viewed as a realization of an underlying stochastic point process with conditional intensity function $\lambda(t|H_t^i)$, where $t \in \tau = [0, T]$ denotes the time coordinate and H_t^i is the history of the process up to t. Spike trains can be mapped into a RKHS by defining a strictly positive definite kernel, the Schoenberg kernel, between the conditional intensity functions of two point processes [17] as

$$\mathcal{K}(\lambda(t|H_t^i), \lambda(t|H_t^j)) = \exp\left(-\frac{\int_\tau \lambda(t|H_t^i) - \lambda(t|H_t^j)^2}{\sigma^2}\right). \tag{4}$$

The intensity function can be estimated by convolving $s(t)$ with the smoothing kernel $g(t)$, yielding

$$\hat{\lambda}(t) = \Sigma_{m=1}^{M} g(t - t_m), \{t_m \in \mathcal{T} : m = 1, \cdots, M\}. \tag{5}$$

For simplicity the rectangular function $g(t) = \frac{1}{\mathcal{T}}\left(U(t) - U(t - \mathcal{T})\right)$ ($\mathcal{T} \gg$ the inter-spike interval) is used, where $U(t)$ is a Heaviside function. Let $s_i^n(t)$ denote the spike train for the ith sample of the nth spiking unit. The multi-unit spike kernel is taken as the unweighted sum over the kernels on the individual units

$$\mathcal{K}(\mathbf{s}_i(t), \mathbf{s}_j(t)) = \sum_n \mathcal{K}(\mathbf{s}_i^n(t), \mathbf{s}_j^n(t)). \tag{6}$$

As shown in Figure 2, the goal is to learn an inverse model of the plant **P**, which is the lesioned BMM motor layer, and then apply the pre-lesioned motor response to the trained multiple-input-multiple-output (MIMO) decoding model for a set of optimized repair microstimulation.

III. Results

A BMM of sensorimotor cortex, which controls a realistic virtual musculoskeletal arm, is trained to perform a one-second target reaching task. The trained network is then perturbed by silencing the first 20 (out of 192) excitatory somatosensory neurons, in order to simulate a lesion. After perturbation, the virtual-arm reach trajectory is severely impacted and the BMM is no longer capable of completing the original reaching task.

To construct the inverse model of the damaged neural system, each of the remaining 172 ES cells were probed

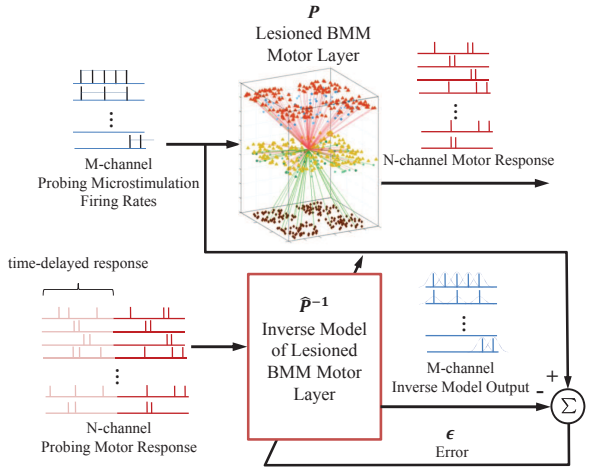

Fig. 2. System diagram of the adaptive inverse model of lesioned BMM.

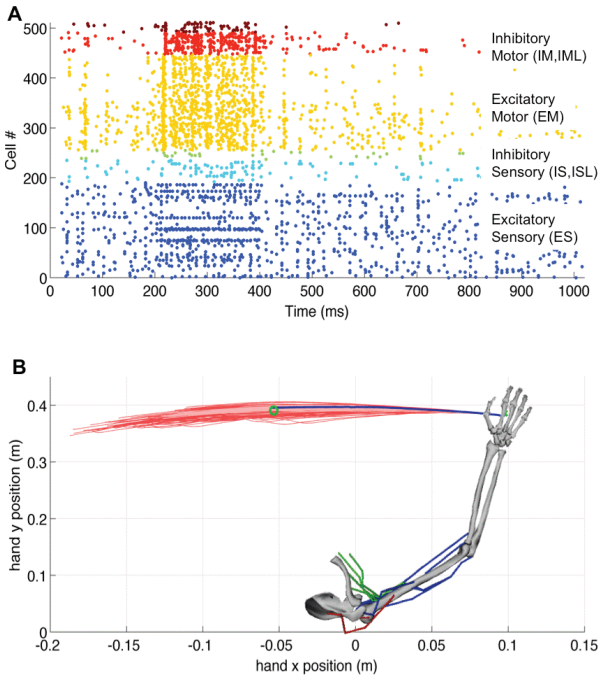

Fig. 3. A. Raster plot of a multiple-neuron microstimulation probing sequence. B. Virtual arm with superimposed hand trajectories for single-neuron (light red) vs. multiple-neuron (dark red) microstimulation probing sequences (original trajectory in blue; target in green).

individually and in small, random groups of 1-20 neurons, with a fixed-duration (200 ms) microstimulation sequence with pulse frequency of 250 Hz or 500 Hz for single cell stimulation and a range of 100-500 Hz for group stimulation. The BMM is stimulated starting at either the 200 ms or 400 ms mark of a 1 s trial. The combination of start times, stimulation sites (individual neuron or group), and pulse frequencies corresponds to a training set of 1376 unique microstimulation probing patterns. For each pattern, the output motor-neuron population activities and the virtual arm trajectories were recorded, as shown in Figure 3.

The 688 single-site stimulation sequences and their corresponding excitatory motor neuron population responses (which drive the virtual arm) are used to build an inverse model of the lesioned BMM using the QKLMS algorithm. After training, the 96-channel-input-172-channel-output decoding model takes shifting windows (in increments of 1 ms) of spike trains of duration 200 ms from the BMM's motor-neuron population and returns the estimated optimal microstimulation pattern: rates and starting times in a 400 ms window (from 200 ms to 600 ms). Since the system is time-variant, the past 200 ms of the motor layer response is used in a feedback, along with the current response, at the input of the inverse model.

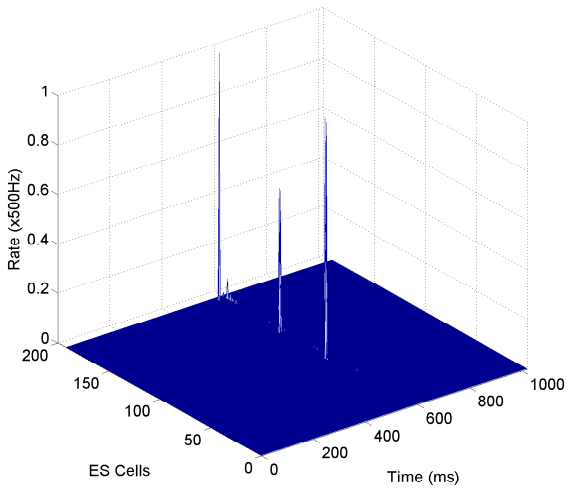

Fig. 4. Optimized microstimulation via an inverse model of the lesioned biomimetic spiking model, constructed from single-neuron probing sequence bases. This output shows that a judiciously selected set of spiking stimulation at the 500 ms mark (which is near the end of the allowed stimulation window of 200-600 ms) should be sufficient to repair the lesion, i.e., push the hand trajectory of the perturbed system onto the desired track.

Figure 4 shows the estimated optimal microstimulation by feeding the desired motor-neuron activity from the pre-lesioned BMM into the inverse model. We see that the estimated optimal microstimulation from the kernel adaptive inverse model can be decomposed into distinct single-neuron stimulation sites and pulse frequencies. Next, we applied the predicted microstimulation from the inverse model to the lesioned BMM. As shown in Figure 5, we are able to repair the damage and drive the virtual arm to the correct target. By judiciously selecting a sub population (3 neurons out of 172) of the excitatory sensory cells and stimulating them for only a short period of time (100 ms) in the early stage of a motor task, we are able to restore the correct reaching behavior in the lesioned spiking model of sensorimotor cortex.

IV. Conclusion

Using kernel adaptive filtering technique on spike trains, we are able to map a desired neural response into an set of repair microstimulation patterns for a lesioned biomimetic spiking network. This work demonstrates the potential of cortical prostheses to dynamically repair damaged brain regions

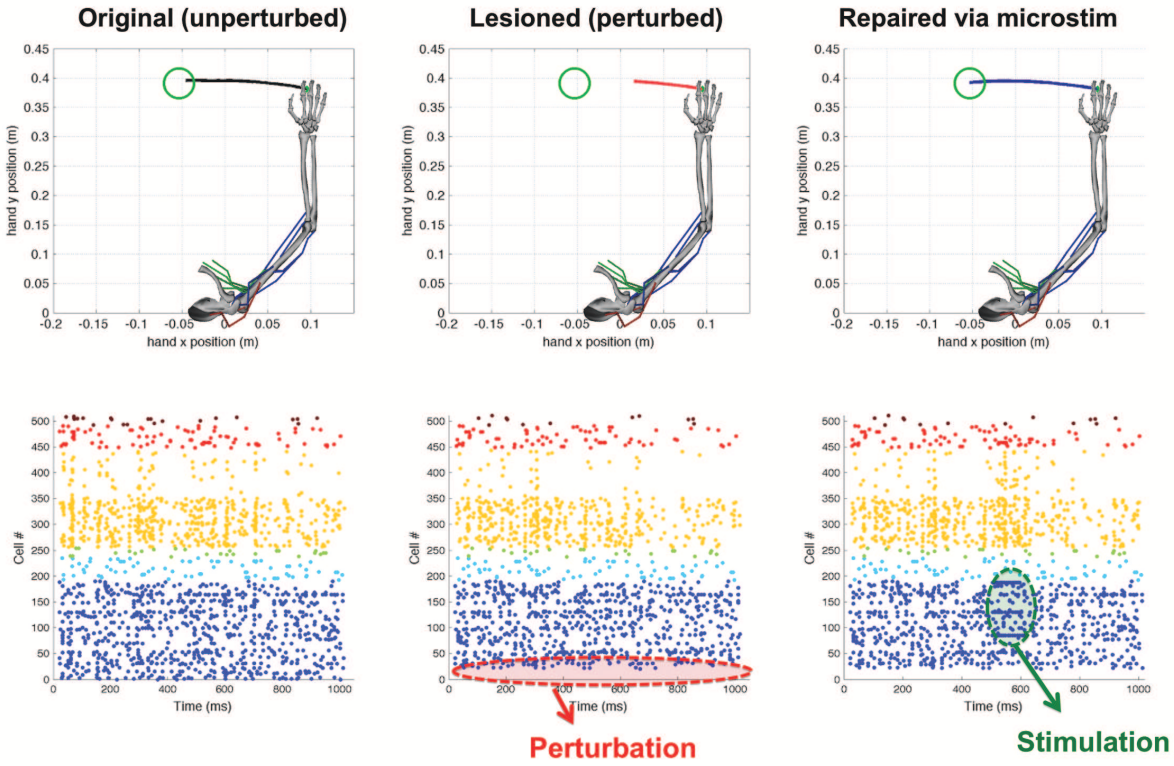

Fig. 5. A. Hand trajectory of the virtual arm and raster plot of the original (pre-lesioned) BMM trained using reinforcement learning. B. Hand trajectory of the virtual arm and raster plot of the lesioned BMM. C. Hand trajectory of the virtual arm and raster plot of the repaired BMM (target in green).

and the corresponding motor behaviors using biomimetic brain and musculoskeletal models. In the future, we will extend this research to more complex motor tasks involving multiple targets and different types of simulated lesions.

REFERENCES

[1] J. K. Chapin, K. A. Moxon, R. S. Markowitz, and M. A. Nicolelis, "Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex," *Nature Neuroscience*, vol. 2, no. 7, pp. 664?670, Jul. 1999.

[2] T.W. Berger, M. Baudry, R.D. Brinton, J.-S. Liaw, V.Z. Marmarelis, Y. Park, B.J. Sheu, and A.R. Tanguay Jr., "Brain-implantable biomimetic electronics as the next era in neural prosthetics," *Proc. IEEE*, vol. 89, no. 7, pp. 993?1012, 2001.

[3] M. S. Humayun, J. D.Weiland, G.Y. Fujii, R. Greenberg, R.Williamson, J. Little, B. Mech, V. Cimmarusti, G. Van Boemel, G. Dagnelie, and E. De Juan Jr., "Visual perception in a blind subject with a chronic microelectronic retinal prosthesis," *Vis. Res.*, vol. 43, pp. 2573?2581, Nov. 2003.

[4] A. Jackson, J. Mavoori, and E. Fetz, "Long-term motor cortex plasticity induced by an electronic neural implant", *Nature*, vol. 444, pp. 5660, 2006.

[5] S. Dura-Bernal, K. Li, A. Brockmeier, C. C. Kerr, S. A. Neymotin, J. C. Principe, J. T. Francis, and W. W. Lytton, "Modulation of virtual arm trajectories via microstimulation in a spiking model of sensorimotor cortex", *Computational Neuroscience*, July 2014.

[6] S. Dura-Bernal, K. Li, A. Brockmeier, C. C. Kerr, S. A. Neymotin, J. C. Principe, J. T. Francis, and W. W. Lytton, "Repairing lesions via microstimulation in a spiking network model driving a virtual arm", *Society for Neuroscience*, November 2014.

[7] L. Li, I. M. Park, A. Brockmeier et al., "Adaptive inverse control of neural spatiotemporal spike patterns with a reproducing kernel Hilbert space (RKHS) framework," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 21, no. 4, pp. 532?543, 2013.

[8] W. Liu, P. Pokharel, and J. Principe, "The kernel least mean square algorithm," *IEEE Transactions on Signal Processing*, vol. 56, pp. 543-554, 2008.

[9] B. Chen, S. Zhao, P. Zhu, and J. Principe, *Quantized kernel least mean square algorithm*, IEEE Transactions on Neural Networks and Learning Systems, vol. 23, no. 1, pp. 2232, Jan. 2012.

[10] S. A. Neymotin, G. L. Chadderdon, C. C. Kerr, J. T. Francis, and W. W. Lytton, "Reinforcement learning of two-joint virtual arm reaching in a computer model of sensorimotor cortex," *Neural Computation*, vol. 25, no. 12, pp. 3263-3293, 2013.

[11] S. Dura-Bernal, G. L. Chadderdon, S. A. Neymotin, Z. Xianlian, A. Przekwas, J. T. Francis, and W. W. Lytton, "Virtual musculoskeletal arm and robotic arm driven by a biomimetic model of sensorimotor cortex with reinforcement learning," *IEEE Signal Processing in Medicine and Biology Symposium*, SPMB13 (2014).

[12] G. Lee, A Matsunaga, S. Dura-Bernal, W. Zhang, W. W. Lytton, J. T. Francias, and J. A. B. Fortes, "Towards real-time communication between in vivo neurophysiological data sources and simulator-based brain biomimetic models," *Journal of Computational Surgery*, vol. 3, no. 12, 2014.

[13] S. Dura-Bernal, G. L. Chadderdon, S. A. Neymotin, J. T. Francis, and W. W. Lytton, "Towards a real-time interface between a biometic model of sensorimotor cortex and a robotic arm," *Pattern Recognition Letters: Special Issue on Multimodal Interfaces*, vol 36, no. 15, pp. 204-212, 2014.

[14] B. Scholkopf and A. J. Smola, *Learning with Kernels, Support Vector Machines, Regularization, Optimization and Beyond*, MIT Press, Cambridge, MA, USA, 2001.

[15] W. Liu, J. Principe, and S. Haykin, *Kernel Adaptive Filtering: A Comprehensive Introduction*,Wiley, 2010

[16] B. Scholkopf, R. Herbrich, and A. J. Smola, "A generalized representer theorem", in*Proc. 14th Annual Conference on Computational Learning Theory*, vol. 2111, pp 416-426, 2001.

[17] A. R. C. Paiva, I. Park, and J. C. Prncipe, A reproducing kernel Hilbert space framework for spike train signal processing, Neural Computation, vol. 21, no. 2, pp. 424449, 2009.