Autonomous Control of Network Activity

Sreedhar Saseendran Kumar[1,2], Jan Wülfing[2], Samora Okujeni[1], Joschka Boedecker[3], Ralf Wimmer[3], Martin Riedmiller[3], Bernd Becker[4], Ulrich Egert[1,2*]

1 Biomicrotechnology, Institute of Microsystems Engineering, University of Freiburg, Freiburg, Germany
2 Bernstein Center Freiburg, Freiburg, Germany
3 Machine Learning Lab, University of Freiburg, Freiburg, Germany
4 Chair of Computer Architecture, University of Freiburg, Freiburg, Germany
* Corresponding author. E-mail address: egert@imtek.uni-freiburg.de

Abstract
Electrical stimulation of the brain is used to treat neurological disorders. Yet it is unknown how to find stimulation patterns that produce desired results with the least interference. Towards this goal, we tested a generic closed-loop paradigm that autonomously optimizes stimulation settings. We used neuronal networks coupled to a reinforcement learning based controller to maximize response lengths.

1 Background

High-frequency electrical stimulation is effective in managing the symptoms of neurological disorders (Parkinson's disease, dystonia). Major problems are: 1) stimulation settings do not adapt to the needs, 2) undesired network responses result in serious side effects, and 3) non-optimal energy consumption necessitates frequent battery replacement.

Closed-loop paradigms that autonomously learn could be useful to optimize stimulation settings. We present a proof-of-concept in a simple control task. A controller had to find the optimal timing of electrical stimuli applied to a neuronal network *in-vitro* at one electrode to maximize the response length at another electrode of a microelectrode array (MEA).

2 Methods

The full parameter space for such a controller currently cannot be scanned *in vivo*. To develop concepts and techniques, we stimulated neuronal networks on MEAs. We trained a controller with reinforcement learning techniques (Q-learning, Watkin, C.J., *Learning from Delayed Rewards*, PhD thesis, Cambridge University, 1989) (fig.1). Following each spontaneous burst (SB), a training episode began. It ended with the controller either stimulating (rewarded) or being disrupted by another SB (punished). During training (n = 5, 1000 episodes) the controller learned an optimal stimulation time. The learned controller was then tested in a 500 episode session.

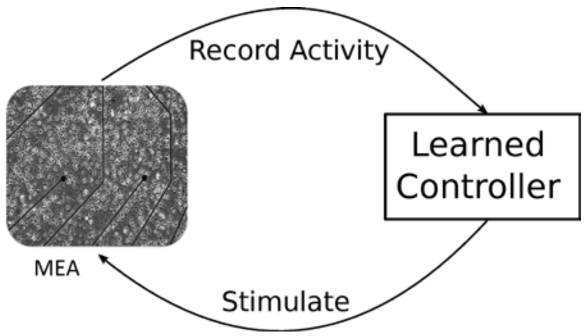

Fig. 1. Closed-loop experimental scheme

3 Results

Response length increases with the duration of pre-stimulus inactivity (fig. 2a, Weihberger et al. (2012), J.Neurophysiol 109:1764-1774). Our training data fits this exponential model indicating that the controller was able to identify this underlying relationship. Overall, the fit parameter *A* varied across cultures with the longest response, while the parameter λ stayed around $1.44 \pm 0.88\ s^{-1}$ (n = 5).

With increasing waiting periods SBs may occur before the stimulus. The controller learned the delay that minimized such disruptions. The ratio of the learned delay to the mode of the inter-burst interval (IBI) distribution of spontaneous activity was 0.98 ± 0.33 (n = 5), suggesting that the learned delay was always very close to the most frequent IBI (fig. 2 b-d).

4 Conclusion

Coupling closed-loop configurations with machine-learning techniques are promising strategies to adjust stimulation parameters autonomously. A simple controller was able to 1) identify stimulus-response relationships, and 2) balance stimulus timing between response lengths and the probability of disruptions by spontaneous bursts.

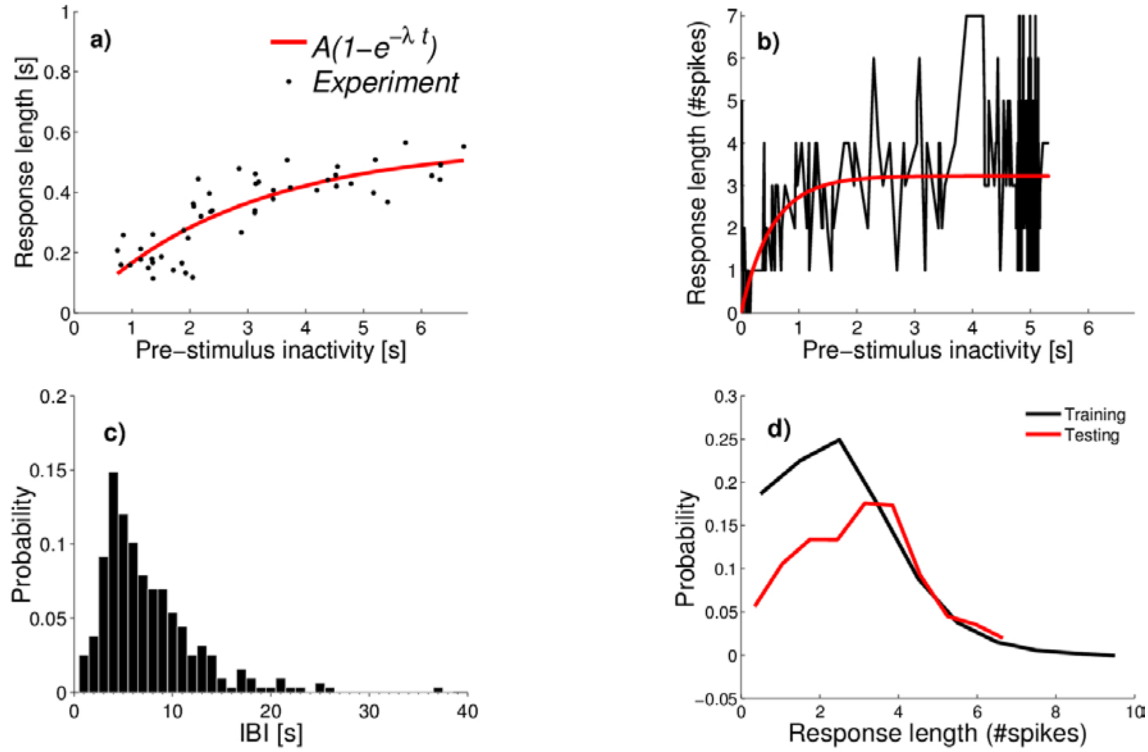

Fig. 2 a) Response length vs. pre-stimulus inactivity (Adapted from Weihberger et al. 2012). **b)** Stimulus-response relations learned by the controller for a culture. The controller 'chooses' to mostly stimulate at the peak of the spontaneous IBI distribution, ~5s **c)**. This improves the chances of evoking a consistent long response, without interruption by an intervening SB. At the same time, the shift in the peak of the response length distribution for the testing session towards a longer response suggests that the learned delay also improved the response lengths, **d)**.

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