

# Hippocampal CA3-CA1 Neural Ensembles in Nonhuman Primates Encode Spatial and Object Features Relevant for Neural Prosthetics

Ioan Opris, Dong Song, *Member, IEEE*, Greg A. Gerhardt, *Member, IEEE*, Vasilis Z. Marmarelis, *Fellow, IEEE*, Robert E. Hampson, *Member, IEEE*, Theodore W. Berger, *Fellow, IEEE*, and Sam A. Deadwyler, *Member, IEEE*

The primate hippocampus has been postulated to play a critical role in encoding, representing and retrieving cognitive information. Effective nonlinear multi-input, multi-output (MIMO) model extracted electrical stimulation patterns have been applied online to the prefrontal cortex (PFC) to facilitate performance of monkeys trained to perform a complex cognitive delayed match to sample (DMS) task, and reverse the effects of pharmacological agents that impair performance of the task [1].

The extension of the application of this model to hippocampal areas CA1 and CA3 is demonstrated using the same MIMO model and applying stimulation to the hippocampus during performance of the task. These results confirm prior findings in rodents [2] in that they show facilitation of task performance by stimulation during the time of memory encoding in the Sample phase of the task. The results also verify prior work in the rodent showing that the extracted patterns of activity during high performance levels reflected the firing of task specific cells conditioned to fire only to certain trial-specific events and conditions [3], and that those cell types were responsible for controlling task performance [4-5].

The MIMO model-derived stimulation mimicked such trial-type cell firing in the same task contexts to facilitate memory encoding in the same type of memory task in primates. An additional feature of this study was the finding that individual hippocampal cells also encoded visual stimuli only on a specific type of trial [6] in which retention of either 1) the image (object) or 2) the spatial position of the Sample image on the screen were required. Thus, cell types were recorded which showed differential firing in the Sample phase of the task with respect to type of trial (object vs. spatial response) as well as successful encoding of information critical for completion of the task. This MIMO stimulation was capable of enhancing the encoding of trial-dependent information in hippocampus, resulting in facilitated performance and decreased impact of length of memory retention or trial complexity.

## REFERENCES

- [1] R. E. Hampson, Gerhardt GA, Marmarelis VZ Song D, I. Opris, L.M. Santos, T. W. Berger, S. A. Deadwyler Facilitation and Restoration of Cognitive Function in Primate Prefrontal Cortex by a Neuroprosthesis that Utilizes Minicolumn-Specific Neural Firing. *J Neural Eng.* Vol. 9(5) pp. 056012, 2012
- [2] T. W. Berger, R. E. Hampson, D. Song, A. Goonawardena, V.Z. Marmarelis , S. A. Deadwyler A cortical neural prosthesis for restoring and enhancing memory *J. Neural Eng.* Vol. 8 pp. 046017, 2011
- [3] Hampson RE, Song D, Chan RHM, Sweatt AJ, Riley MR, Goonawardena AV, Marmarelis VZ, Gerhardt GA, Berger TW, Deadwyler SA. "Closing the Loop" for memory prostheses: detecting the role of hippocampal neural ensembles using nonlinear models. *Trans Neural Syst Rehabil Eng.* 2012; 20:510-525.
- [4] S. A. Deadwyler, T. Bunn, and R. E. Hampson, "Hippocampal ensemble activity during spatial delayed-nonmatch-to-sample performance in rats," *Journal of Neuroscience*, vol. 16, pp. 354-72, 1996.
- [5] R. E. Hampson, J. D. Simeral, and S. A. Deadwyler, "Distribution of spatial and nonspatial information in dorsal hippocampus," *Nature*, vol. 402, pp. 610-4, 1999.
- [6] I. Opris, J.L. Fuqua, P. Huettl, G.A. Gerhardt, T.W. Berger, R.E. Hampson, S.A. Deadwyler (2012) Closing the loop in primate prefrontal cortex: Inter-laminar processing. *Front. Neural Circuits.* Vol. 6 pp. 88.

This work was supported by The Defense Advanced Research Projects Agency (government contract N66601-09-C-2080 to S.A.D. and N66601-09-C-2081 to T.W.B.). 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. This work was also supported in part by grants NSF EEC-0310723 to USC (T.W.B.), NIH/NIBIB grant No. P41-EB001978 to the Biomedical Simulations Resource at USC (V.Z.M. and T.W.B.) and NIH R01 DA06634, DA023573, DA026487 (S.A.D.).

I. Opris, R. E. Hampson and S. A. Deadwyler are with the Department of Physiology & Pharmacology, Wake Forest University, School of Medicine, Winston-Salem, NC 27157 USA (e-mail: ioopris@wfubmc.edu; rhampson@wfubmc.edu, sdeadwyl@wfubmc.edu).

G.A. Gerhardt is with the Center for Microelectrode Technology, University of Kentucky, Lexington, KY, USA (e-mail: gregg@uky.edu).

D. Song, V. Z. Marmarelis, and T. W. Berger are with the Department of Biomedical Engineering, University of Southern California, Los Angeles, CA 90089 USA (e-mail: dsong@usc.edu, vzm@bmsr.usc.edu, berger@bmsr.usc.edu).