

# Artificial stimulation of the peripheral nerves to generate natural-like activity in the Central Nervous System

V. Bonacasa, I. R. Cepeda, V. Makarov, F. Panetsos

Department of Applied Mathematics (Biomathematics), Universidad Complutense de Madrid, España

**Abstract**—In the present work we study how sensory inputs conveyed by nerve fibers in the form of spatiotemporal patterns generate different responses in the Central Nervous System (CNS) depending on the physical characteristics of the stimulus applied and then we reproduce similar responses by means of electrical stimulation of the nervous fibers.

**Keywords**—multielectrode recordings, nerve stimulation, rat, implants, DCN, dorsal column nuclei.

## I. INTRODUCTION

The objective in the present work focuses on how sensory inputs conveyed by nerve fibers in the form of spatiotemporal patterns generate different responses in the Central Nervous System (CNS) depending on the physical characteristics of the stimulus applied and then reproduce similar responses by means of electrical stimulation of the nervous fibers [1]. This is important when artificial members (i.e. hands) have to be connected directly to the peripheral nerves and be functionally equivalent to the natural ones. In the present communication we expose the results of our experiments on the somatosensory system of the rat (lemniscal pathway: dorsal column nuclei -DCN-, thalamus and cortex).<sup>1</sup>

The physical characteristics of peripheral stimuli applied to the skin are transformed into spatiotemporal and intensity patterns of electrical pulses. These patterns (varying with stimuli) are transmitted through the peripheral nerve to the DCN, the first relay station in the lemniscal pathway, where they are preprocessed and then transmitted to the upper stations of the CNS to produce sensations. Most neurons do not differ significantly in their electrical properties and they carry out different functions because of the individual afferent and efferent connections they make. That means that these neurons perform like dedicated processing devices whose output depends strongly on the spatiotemporal and intensity characteristic of the incoming signals. The perception of the external world by the CNS is the outcome of a constant interplay between incoming sensory signals and dynamically changing internal representations of the external world.

---

Work supported by Grants EU-IST-2001-34892, EU-IST-2001-34893, CICYT SAF2002-10935-E, CICYT SAF2002-10934-E, CAM 8.5/30/2003 and BEFI02/1767, University of Michigan Center for Neural Communication Technology.

Fiber activity depends on such characteristics and functionally is their replica. For a simple mechanical stimulus like those used in our experiments spatiotemporal pattern in the nerve has a limited duration (around 30 ms) and is relatively simple. In spite of this the activity recorded in the DCN is more extended suggesting a rich elaboration of the sensory stimuli and non trivial network reaction where firing events of different neurons occur synchronously or/and with a short time delay [2]. Coherent discharges observed in DCN also suggest the distributed over the neural network representation of the stimuli characteristics. When a sensory stimulus arrives, various functional neural sub-networks in the DCN pass through dynamical computation of the stimulus spike timing.

## II. METHODOLOGY

Experiments were carried out in accordance with the European Communities Council Directives (86/609/EEC), in female adult Wistar rats, weighing 200-300 g. The animals were anesthetized with urethane (1.6 g/kg, i.p.), supplementary doses were administered when necessary during long surgical procedure and the body temperature was maintained at 37°C.

1) *Sciatic nerve recordings and electrical stimulation*: Cuff microelectrodes with four recording/stimulating points located in complementary positions in two different places separated 5mm (Micro Probe, Inc) were used to record the electrical activity of the rat sciatic nerve and to deliver the electrical stimuli. The cuff was located in a silicone rubber tube (inside diameter of 1.5 mm) with four flexible wires to connect the electrodes to the preamplifiers.

2) *DCN recordings*: Single-tip tungsten with impedances in the range of 1-1.5 M $\Omega$  and multi-tip () needle electrodes were used to record multiunit activity from the DCN and the cortex (World Precision Instruments and Michigan University respectively). The small size and fine features permit multi-channel interaction with the tissue on a scale that approaches the size of neural cells. Michigan electrodes have 16 recording channels, ending in four tips (3mm long), separated each other for distance of 125  $\mu$ m, with four recording places each (separated by 50  $\mu$ m). To record neuronal activity in the gracilis nucleus rats were placed in a stereotaxic frame and artificially ventilated under control of the end-tidal concentration of CO<sub>2</sub>. To get an access to the DCN we made a cut at the dorsal midline at the level of the neck, separated the musculature and opened the

cisterna magna. Then electrodes have been introduced into the tissue. During the experiments the DCN were covered with mineral oil.

3) *Electrode implant procedure*: The rat sciatic nerve, was exposed under a chirurgic microscope and carefully liberated from the surrounding tissues. Cuff electrode was opened and rolled back around the sciatic nerve avoiding nerve compression and deformation. Then the cuff electrode was released and the whole nerve perimeter was covered and the end connector was plugged in the headset of the recording/ stimulating setup. The nerve was periodically wetted with saline solution to avoid drying.

4) *Stimulation procedure*: Mechanical stimuli lasting 200 ms were delivered to the glabrous part of the hindlimb by a solenoid (tip area 1 mm<sup>2</sup>) at 0.7 Hz. Electrical stimulation from the cuff microelectrode was performed by applying trains of stimuli of 0.01 mA at different frequencies resampling the recorded activity of the intact peripheral nerve.

5) *Data acquisition and analysis*: The commercially available apparatus Micro1401 by Cambridge Electronic Design, and PCI-6071E E Series data acquisition card from National Instruments were used with the accompanying software Spike2 and Recorder, respectively. Both of them also allows certain data analysis. Neuronal data in this study were derived from multi-unit recordings with subsequent spikes isolation. Then spike events were processed and compiled into peristimulus time histograms (PSTHs) and event correlation histograms (EvtCrl) with 2 and 5-ms bin width.

### III. RESULTS

Simultaneous recordings from sciatic nerve fibers and gracilis nucleus were performed with long-lasting (200 ms) mechanical stimulation on the hindpaw of the rats and different activity patterns were obtained depending on the stimulating places (fig 1). The different activity patterns recorded in the nerve fibers were analyzed and studied to generate a pattern of electrical stimuli that later were applied on the nerve and thus obtain a similar neural activity in the gracilis nucleus of the DCN (fig.2).

Neural activity recorded in the DCN (nucleus gracilis) was similar to that observed in previous electrophysiological studies [3]. In fig. 3 can be seen the peristimulus histogram of the response of a single neuron under stimulation of the skin. Its receptive field corresponded to a small part of the glabrous surface of the second digit. In fig. 4 can be seen the peristimulus histogram of the response of a the same single neuron of fig. 3 under electrical stimulation of the peripheral nerve using a stimulation pattern of 5 pulses at a frequency of 100 Hz.

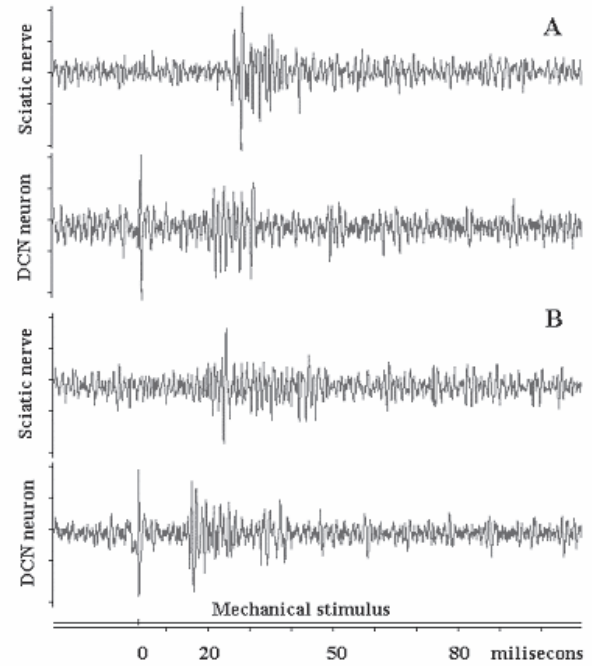


Fig. 1. Simultaneous recordings from the sciatic nerve and the DCN for mechanical stimuli in the second (A) and third digit (B).

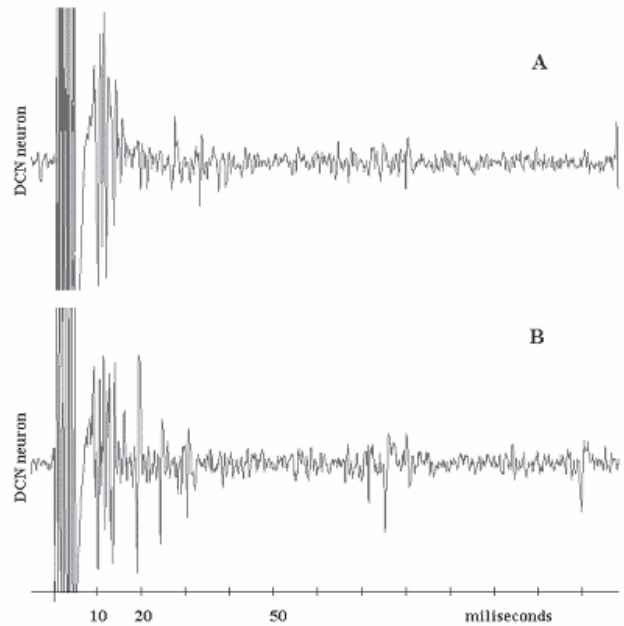


Fig. 2. Recordings from two different DCN neurons (A) and (B) under electrical stimulation of the sciatic nerve. The artifact of the electrical stimulus is recorded at 0 ms.

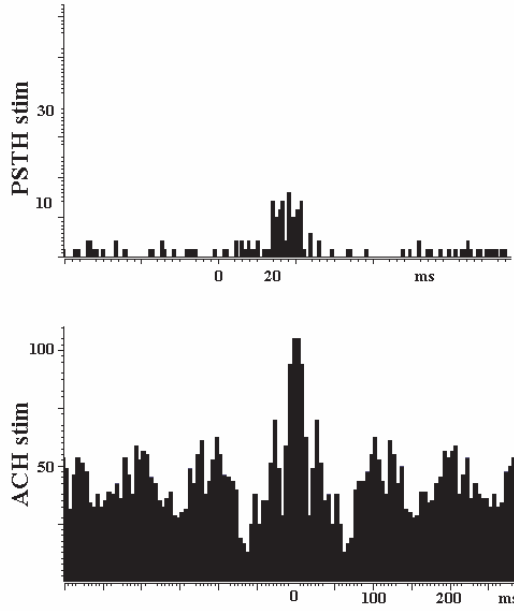


Fig. 3. PSTH of the response of a DCN neuron to mechanical stimulation of its receptive field (up) with a latency of 20 ms. ACH of the activity of the same neuron during the stimulation (down). It can be observed a clear 10 Hz oscillatory behavior.

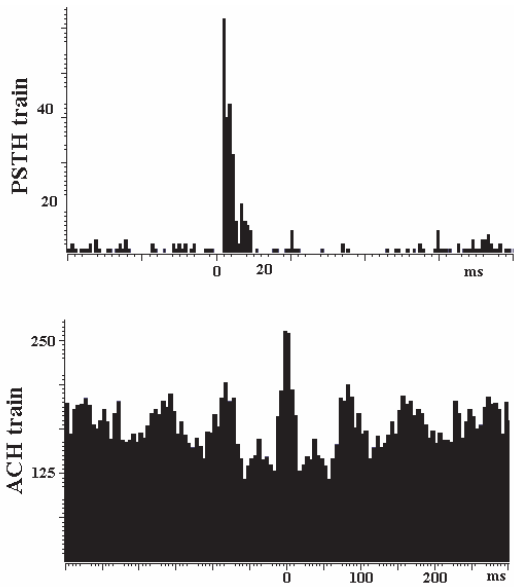


Fig. 4. PSTH of the response of the same DCN neuron of fig.3 to electrical stimulation of the peripheral nerve (up) with a latency of 5 ms. The difference in the latencies is due to the direct stimulation of the nerve in the second case that avoids the mechanical delays and the transduction of the signal through the first part of the nerve fibers. ACH of the activity of the same neuron during the stimulation (down). It can be observed a better 10 Hz oscillatory behavior as well as a new hill at 70 ms.

#### IV. DISCUSSION

It is very difficult to deliver artificial electrical stimuli and generate spatiotemporal and intensity patterns activity in the peripheral nerves very similar to those provoked by the natural stimuli. This is due to the fact that when we perform electrophysiological recordings of the sciatic nerve by means of the cuff electrodes we record the activity of some tenths of axons located in the periphery of the nerve while the greatest majority of information is carried out by a great amount of fibers mostly in the inner part of the nerve (and, consequently, inaccessible to the recordings). On the other hand, when we generate electrical activity by stimulating the same previously recorded fibers but not only them: every adjacent nerve axon is also stimulated. This double difference will originate difference to the neural responses in the DCN cells like those recorded by us.

Generally, electrical stimulation patterns reflecting the recorded characteristics of the spikes in the sciatic nerve are able to generate the desired neural activity. Among the non trivial differences we underline the better Autocorrelation Histograms (ACHs), both in the coherence and in the reduction of the noise. On the other hand persists the impossibility to selectively stimulate sensory fibers since they are distributed in the interior of the peripheral nerve.

#### V. CONCLUSION

Direct connections between CNS and electronic devices is possible but the use of cuff electrodes limits very much the field of the applications. To reproduce the desired spatiotemporal and intensity patterns in the peripheral nerve selective stimulation of the individual fibers is needed and, consequently, other solutions like sieve microelectrodes could be more promising.

#### ACKNOWLEDGMENT

Multielectrode probes were offered by the University of Michigan Center for Neural Communication Technology, sponsored by NIH/NCRR grant P41 RR09754.

#### REFERENCES

- [1] E. R. Kandel, T. M. Jessell, J. M. (Eds.) Principles of Neural Science. Elsevier, New York. 3rd Edition. 1994.
- [2] F. Panetsos, A. Nuñez, C. Avendaño, "Sensory information processing in the dorsal column nuclei by neural oscillators" Neuroscience, no. 84, pp. 635-639, 1998.
- [3] A. Nuñez, F. Panetsos, C. Avendaño, "Phytmic neuronal interactions and synchronization in the rat dorsal column nuclei" Neuroscience, no. 100, pp. 599-609, 2000.