Coding and decoding of information in a bi-directional neural interface

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Abstract

We report on an experiment in which a population of rat cortical neurons, cultured on a micro-electrode array, was connected bi-directionally to a mobile robot. Bi-directional communication between a neural population and an external device requires to translate time-varying signals into spatio-temporal patterns of neural activity, and back. Here we describe the experimental set-up and the computational modules of the neural interface, and describe our work of characterization of the 'transfer function' of the neural preparation, as it emerges from closed-loop experiments.

Keywords: cultured neurons, micro-electrode arrays, neural interface, neural coding

Introduction

Several researchers have proposed to study learning and memory by connecting nervous tissue, kept alive *in-vitro*, bi-directionally to an external device, i.e. an actual physical body. For instance, Reger & al. [1] connected a lamprey brain, isolated and kept alive *in-vitro*, bi-directionally to a mobile robot. The robot was presented light stimuli and the brain reacted to them inducing the robot to follow or escape the light source. Similar experiment were performed by DeMarse & al. [2], who interfaced a neuronal network cultured on a micro-electrode array to a computer-simulated animal, moving inside a virtual world. Following this approach, and with the aim of establishing general interfacing techniques and computational

methods [3], we interfaced a mobile robot with a population of neurons, extracted from rat embryos and cultured on a micro-electrode array.

In-vitro cultured neurons form a bi-dimensional physical model of the brain and, in spite of their simplified level of organization, are an useful framework to study information processing in the nervous system. One peculiar feature of this preparation is the possibility to stimulate and/or record from multiple sites at the same time. To establish a neural interface between cultured neurons and an external device, at least three issues need to be addressed: (i) how to optimally translate time-varying, multi-dimensional sensory information into spatio-temporal stimulation patterns; this is a kind of reverse of the neural coding problem - synthesis rather than analysis; (ii) how to efficiently translate spike trains, recorded from multiple neurons, into time-varying 'control commands' for the external device; and (iii) how to induce selective changes in the input-output behavior of the neural preparation; i.e. sensorimotor learning. Embodiment places constraints on the latter, in the sense that puts learning in relation to behavior; i.e., learning has to be aimed at the emergence of a specific behavior. Embodiment also implies that, to preserve efficiency (i.e., optimality) of the neural 'interface', during learning the processes of coding and decoding should adapt as well. Here we describe the experimental set-up and the computational modules of the neural interface; we show the results of our initial closed-loop experiments, and propose simple techniques for analyzing the responses of multiple recording sites to sustained multi-site stimulation.

Materials and Methods

Experimental set-up. Primary cultures of cortical neurons, extracted from rat embryos (17-18 days), were plated on planar arrays of 60 TiN/SiN electrodes, arranged along a square grid (MEA60, Multichannel Systems, Reutlingen, Germany), and equipped with an integrated 60-channel pre-amplifier. The diameter of the electrodes and the inter-electrode spacing were, respectively, 30 μm and 200 μm. Experiments started after 18-34 days in-vitro (DIV), i.e.

when these preparations reportedly display maximum spontaneous activity [3]. Stimulation consisted of monopolar, biphasic stimuli (peak-to-peak amplitude 1.5 V, duration 250 μs), generated by a custom stimulator under computer control. The external body consists of a miniature mobile robot (Khepera II, K-team, Préverenges, Switzerland), equipped with two wheels and eight infrared proximity sensors. For each preparation, we identified two sets of channels to be, respectively, the recording and stimulation sites, i.e. the 'motor' and 'sensory' areas of the model brain. The sensory area simply consisted of two channels, which coded the average activity of the proximity sensors on, respectively, the left and the right side of the robot. Two separate sets of recording sites, eight sites each, were selected to control the left and right wheels of the robot.

Computational architecture. A block diagram of the computational architecture is depicted in Figure 1A.

<center>Figure 1 near here</center>

The time-varying signal which comes from the robot proximity sensors, $u(t)$, is sampled at 10 Hz and averaged into 'left' and 'right' sensor activities, $s_L(t)$ and $s_R(t)$ – this corresponds to having defined two receptive fields – and is translated into, respectively, a left and right instantaneous rate of stimulation, $r_s(t)$. For these experiments, we used a proportional coding scheme, i.e. the rate of stimulation is proportional to sensor activity, and the maximum rate of stimulation, r_s^{max}, is only attained when the robot hits an obstacle. This value should be as large as possible for accurate coding of the temporal structure of the sensory signal [4], but on the other hand there is an upper limit on the energy per unit time that can be delivered to the preparation without damage. In these experiments, we conservatively used r_s^{max} = 2-5 Hz. The instantaneous rate of stimulation directly modulated a perfect integrate-and-fire module. This allows optimal coding accuracy, and a coding fraction of about 30%; see [4].

As regards the decoding part of the interface, the raw signals recorded from the sixteen 'Output' sites are sampled at 10 kHz, and individual spikes are detected on-line through a

simple peak-to-peak thresholding algorithm over a 4 ms sliding window. Stimulus artifact is suppressed on each recorded signal by blanking a 8 ms window following each stimulus on either input site.

The istantaneous firing rates, $r_y(t)$ are then estimated on-line from the recorded spike trains, $y(t)$, through a 1st order low-pass filter, with $\tau = 100$ ms. Finally, these resulting spatio-temporal patterns of neural activity have to be translated into a pair of motor commands for the two wheels of the robot. In these experiments, we simply chose to take the average neural activity of the Left and Right portions of the Output region:

$$\omega(t) = \omega_o - h\frac{1}{N}\sum_{j=1}^{N}r^y{}_j(t) \tag{1}$$

where $\omega_o = 3$ rad/s is the average angular speed, h is an arbitrary constant, and N is the number of recording channels for each portion of the Ouput region (as above stated, here we used $N = 8$). The resulting speed commands were finally low-pass filtered (4th-order Butterworth filter, cut-off frequency 5 Hz), sampled at 10 Hz and delivered to the robot.

Real-time control. The above described computational architecture was mapped into two P4 PCs. A first PC is responsible for the most computation-intensive portion of the calculations, i.e. acquisition of raw neural data (at a 10 kHz sampling rate) and on-line spike detection. A second PC is responsible for spike decoding, communication with the robot and generation of the patterns of stimulation. This part of the architecture runs at 250 Hz (communication with the robot runs at 10 Hz). An additional PC is used as experiment front-end, and a fourth PC, outside the control loop, is used for monitoring and logging the raw recorded neuronal data.

Closed-loop experiments. As the target behavior, we focused on a simple obstacle avoidance task, i.e. a 'Braitenberg vehicle' [5]. The robot was placed inside a circular arena (0.8 m diameter) containing a number of cylinder-shaped obstacles. A total of 4 neural preparations

were used in these experiments. Each experiment consisted of four closed-loop trials, each lasting 10 min, separated each other by periods of rest.

Results

Figure 1B-G shows a 10-s portion of a typical experiment. The sensory signal tends to switch between two extreme values (no obstacles, or obstacle hit), reflecting the short range of action (about 5 cm) of IR proximity sensors (Figure 1E).

I/O neural 'transfer function'. To derive a more synthetic description of the input-output behavior of the neural preparation, as it emerges from these experiments, for each input-output pair of channels we estimated the post-stimulus time histogram, i.e. the average output firing rate in response to an individual stimulus on one of the input channels:

$$PSTH(\tau) = \left\langle r_y(\tau - t_i) \right\rangle \qquad (2)$$

The resulting PSTH curves for one of our experiments are displayed in Figure 2A.

Figure 2 near here

A typical feature of the observed PSTHs is a peak at about 100 ms following the stimulus; the latency of the peak varies little at the different recording sites.

To test stability of the input-output response of the neural preparation during an individual experimental trial, we repeated the computation of the PSTH by using the first half and the second half of the trial. We found that the PSTHs change little with time across the same trial; see Figure 2.

I/O connectivity. To assess the relationship between the observed 'transfer function' and the patterns of 'functional' connectivity between input and output regions, we substituted the neural preparation in the closed-loop system with a simulated network

of 100 leaky integrate-and-fire neurons, with connectivity dominated by inhibitory cross-lateral connections (i.e., left input connected to right output, etc), which is close to an ideal Braitenberg vehicle (i.e., perfect obstacle avoidance); see Figure 3.

Figure 3 near here

We then estimated the PSTH from the simulated firing patterns for each individual input-output pair, and displayed, for each output site, the peak PSTH values in response to either left or right stimulation. Figure 3A shows that, for simulated data, left and right output sites (depicted in black and white, respectively) are arranged into two clearly separated clusters. This suggests that peak values of PSTH may be taken as measures of 'functional connectivity' between inputs and outputs. In contrast, Figure 3B shows no clear separation between the response of left and right output sites, at least for that experiment (same as that of Figure 2). This implies a much more random connectivity between input and output sites.

Discussion

We have described a computational architecture, and its real-time implementation, for interfacing a population of cultured neurons to an external device (a mobile robot). We suggested that the PSTH, estimated for each individual input-output pair, may provide useful information on the input-output behavior of the preparation and in particular on its 'functional I/O' connectivity. PSTH is relatively stable with time, and may be an useful tool to assess changes in the input-output behavior induced by adaptation protocols.

Acknowledgements

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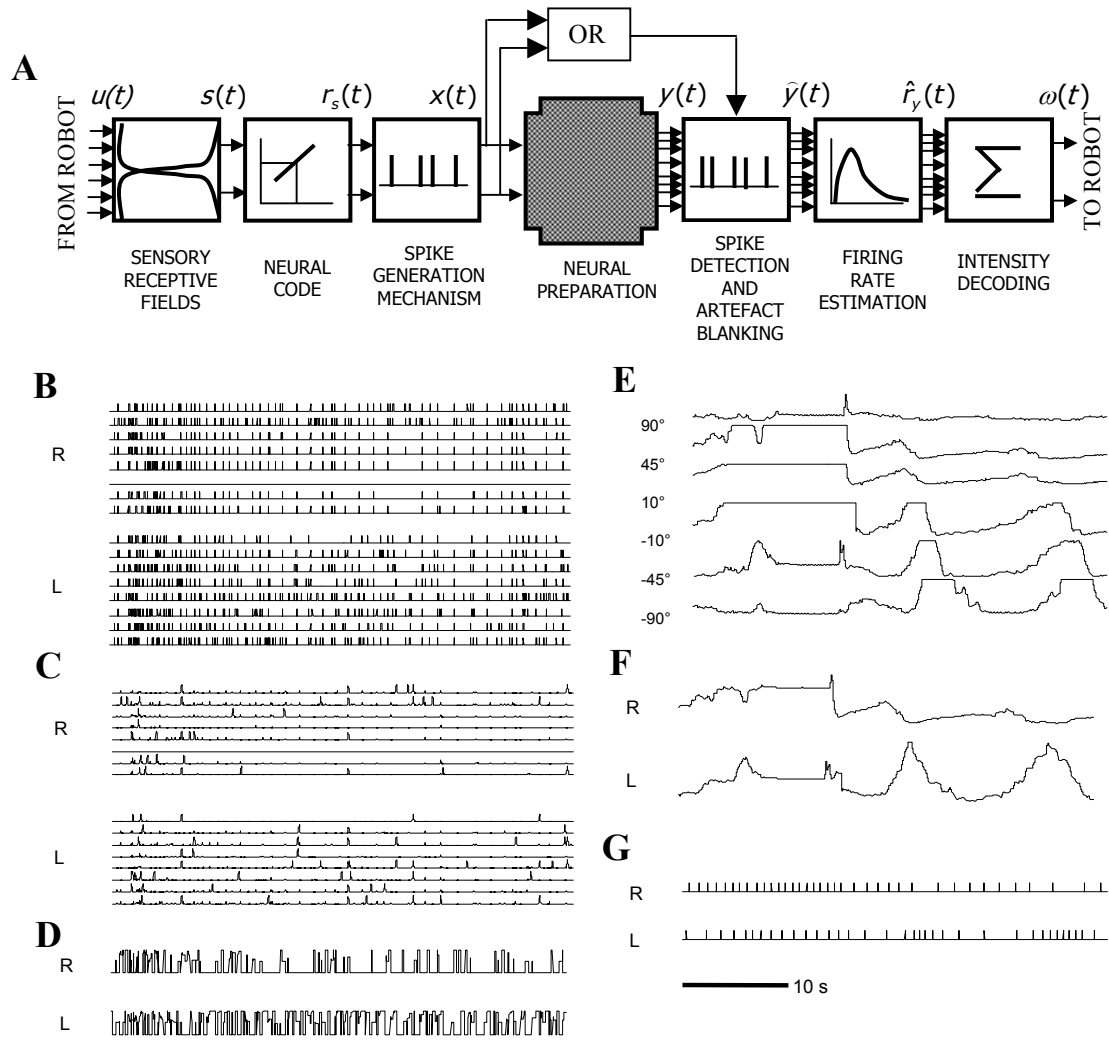[5]   Braitenberg V (1986) Vehicles – Experiments in Syhthetic Psychology. MIT Press.

Figure 1 A: Block diagram of the bi-directional neural interface. B-G: A 10-s portion of a typical closed-loop experiment: recorded spike trains (B) and instantaneous firing rates (C) from the 16 output sites, motor commands (D) and, on the right, the corresponding activity of the IR sensors (E), the average Left and Right sensor activity (F) and the corresponding pattern of stimulation (G).
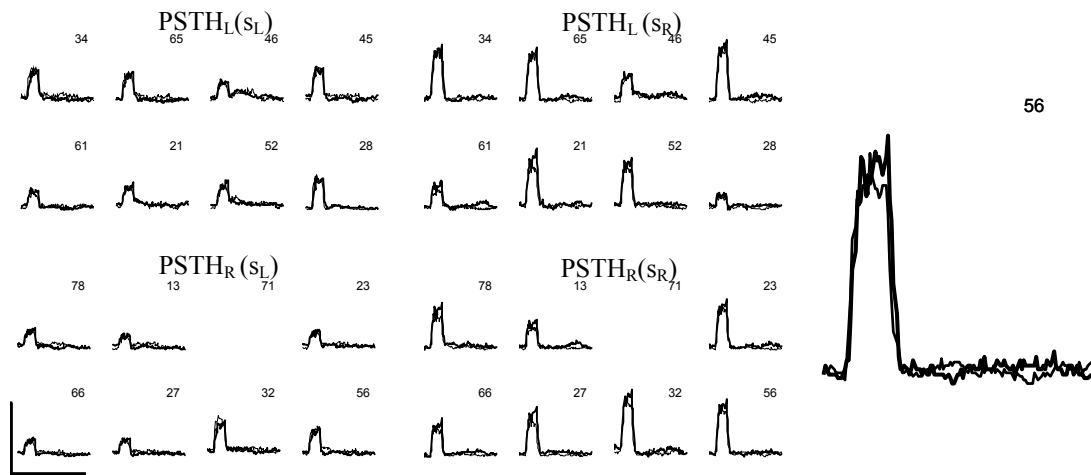
Figure 2 Post-stimulus time histograms for each input-output pairs (bin size: 4 ms)**.** Left, from top to bottom: Responses to stimulation of Left channel. Center, from top to bottom: Responses to stimulation of Right channel. Each PSTH is estimated from the first half (thin lines) and the second half of the data (thick lines). Channel 71 does not respond to stimulations on either side. Right: magnification of the PSTH of channel 56 (R output region, stimulation of R side). Scale bars: 0.5 s, 100 spikes/s.
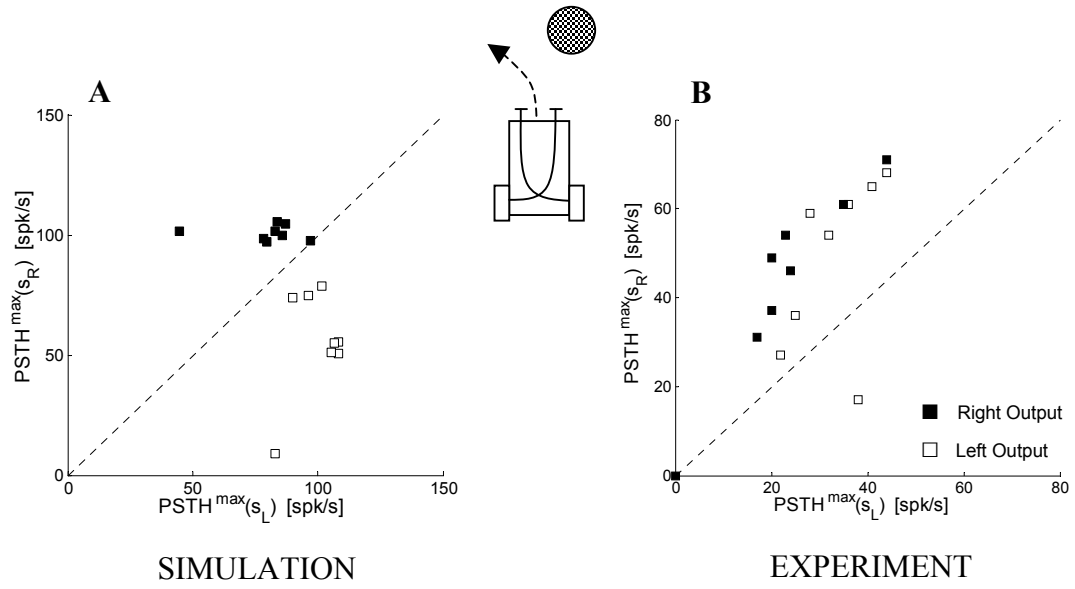
Figure 3 Peak PSTH of left (white) and right (black) output sites in response to stimulation of left vs right input channels. A. Simulated neural network of 100 leaky integrate-and-fire neurons, controlling a Braitenberg vehicle (top). B. Experimental data.