A compact integrated system for neural signal acquisition and stimulation

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Abstract

The mechanism by which the neural networks communicate and the understanding of these processes remains the fundamental issue of neuroscience. Long-term brain activity registration and stimulation is the main ally to analyze and interpret data coming from the brain. Several materials and microelectronics techniques have been pursued to obtain reliable and long lasting implantable devices from intracortical electrodes to soft epicortical arrays. Among them, ultra-flexible interfaces result particular appealing for their superior conformability and intimate contact with the brain tissue, especially for epicortical devices, thus achieving higher signals and reducing brain injuries. By other side, also external electronics is important properly to treat the signal, filtering the artifacts and minimizing the noise. In this paper, a novel compact integrated system for both brain stimulation and recording is presented. The device consisted in an ultra-flexible polyimide 32-channel microelectrodes array (8 um thick) connected to a miniaturized PCB able to amplify, filter and digitalize the neural signals. The size of this acquiring board is 60x45 mm and it provides an amplification of 200x with a sampling rate greater than 1 MSamples/s. The system has been successfully tested both in-vivo and in-vitro experiments on Wistar rat demonstrating that it could be a good candidate for a further miniaturization of the measurement equipment.

Introduction

Understanding the relationship between neurons communication and the corresponding human action or the emerging thought remains a key challenge for neuroscience. The main tool to investigate the brain electrical activity, that is the language with which the neurons interact is the Brain Machine Interface (BMI). This device is generally constituted by a matrix of microelectrodes (MEAs) capable to record and even stimulate a specific part of the brain [1-2]. After the rise of the first single intracortical microelectrode four decades ago [3], the recent progress in microelectronics and material science made available diverse technologies to miniaturize the testing devices, to minimize the damage to the living tissue, to increase the material biocompatibility, to produce flexible and soft electronic platform, etc.

We are assisting to the spreading of a large variety of recording devices, typically constituted by several electrodes, which can be implanted directly on the cortical surface or inserted in the brain tissue (epicortical and intracortical MEAs respectively). The usefulness of the MEAs has been shown in studies that provided fundamental insights in the processing strategies during encoding of the brain [4-7]. However, the neural interfaces currently available have still to improve their reliability and need bulky amplification or analysis system to be used in human medical applications. Indeed, although some prototypes permit the local amplification of the signal by using crystalline TFTs technology embedded into flexible substrate, the yield of these devices is far from a possible application in an industrial perspective.

Another appealing feature of some BMIs are related to the implementation of telemetry system to allow the free movement of the animal during the experiment [8-9]. Unluckily, these devices are still big in size and weight and they are inherently unreliable since they lack of a safety communication protocol that can manage the large amount of data incoming from the real time acquisition of multiple channels (up to 256).

A possible compromise between a fully embedded BMI with high cost and low yield and a commercial thick MEAs connected to a standard electronic equipment is the fabrication of a customizable ultra-thin electrode array equipped with new commercial chip able to directly acquire, amplify and digitalize the data in real time. To obtain this kind of device a series of issues need to be addressed: the choice of a biocompatible and flexible substrate and its handling during the process, the

reduction of the mechanical stress of the entire ultra-flexible tool, the interfacing of this device with the custom PCB, the heating dissipation effect, etc.

To simplify the fabrication process of ultra-flexible polymeric MEAs and properly handle the device a wise choice is the usage of polyimide film directly deposited on a rigid carrier such as a wafer or a corning glass by spin-coating technique. Under specific surface conditions, it is possible to limit the adhesion of the polyimide layer on the carrier and detach it at the end of the process together with the devices. To minimize the mechanical stress the metallic tracks can be embedded into a second polyimide foil with the same thickness. Polyimide is biocompatible and it can be lithographically defined, moreover, it is normally used in the microelectronics process. A drawback of the very thin polymer layer is the difficulty of bonding, so a flex-to-flex interconnection is preferred, adopting solution like zero force connector or anisotropic tape film.

In this work, the design of a compact system, composed of UltraFlexible MicroElectrode Arrays (UF-MEAs) connected to a recording/stimulating board (NeuroDaq) is presented.

Microelectrode array

UF-MEAs were fabricated by embedding a metal bi-layer of Cr/Au (250 nm thick) into 2 Polyimide (HD2611, HD MicroSystems) layers, reaching a final thickness of 8 μm [10]. The array is composed by 28 electrodes of 50 μm, with 2 group of 4 electrodes in rhomboidal shape (d=10 μm) and 4 stimulation pads on the border limit of the MEA. Furthermore via-holes have been made through the PI in order to oxygenate the surface and achieve a better surface adhesion. These apertures have been fabricated by a novel method on standard polyimide. We avoid utilizing polymeric conductive tracks since the low conductivity respect to metals like gold or copper. The polyimide roughness has been increased by means reactive ion etching to improve the metal adhesion.

Different MEAs design have been custumized according to the different requirements imposed by in-vivo and in-vitro requirements. Figure 1a and 1b shows two examples of MEA designs.

Acquisition Board

An acquisition board (NeuroDaq) has been specifically designed to match the impedance of the passive microelectrode array (MEA) previously described. It is able to acquire, filter, amplify (up to 200x) and digitize the signal recorded over 32 channels using a low noise technology (Amplifier Input Reference Noise = 2,4 μVrms) thanks to a 16 bits analog to digital interface. Finally, the neuronal signal can be sampled up to 1MSample/s.

The board is equipped with a microcontroller, that integrates USB communication (High Speed USB) directly on board and extends computational capabilities (80 Mips @ 200MHz). In addition, the board exposes general purpose IO and standard communication protocols (I2C, UART, SPI) to easily control other external devices, it is provided with a RAM and can be powered by a Li-ion battery. A picture of the board is shown in figure 2.

The board is endowed also with independent stimulation channels that allows locally to stimulate through two independent output channels by means of AC or DC voltage and currents applied by an external source. In this way, it is possible to stimulate during the recordings in order to investigate and develop closed loop control algorithms. The close integration of the hardware will allow simultaneously recording and stimulating brain activity to develop closed loop control algorithms also directly on board providing a fully integrated acquisition/stimulation system.

Acquisition Software

The system is controlled by a software interface developed in Matlab. Each channel can be selected independently or in combination with other channels (**Errore. L'origine riferimento non è stata trovata.**a) and viewed through the visualization window (**Errore. L'origine riferimento non è stata trovata.**b). Channels can be visualized and recorded selectively. A filter panel allows select BETA, GAMMA and MUA bands or alternatively a custom pass band filter.

Results

Preliminary tests has been performed at the "Institut d'Investigacions Biomèdiques August Pi i Sunyer" (IDIBAPS) of Barcelona in order to validate the MEA-NeuroDaq acquisition system. With the aim to investigate possible noise introduction, simultaneous recordings from a tungsten depth electrode and a MEA grid lied over the cortex surface of a Wistar rat have been compared. A sinusoidal stimulus at 100 Hz for 3 seconds was applied trough a saline (0.9%). The grid successfully recorded the stimulation wave, and the presence of the device did not increase the noise level in the tungsten recording (Figure a).

In the second experiment, the Local field Potential (LFP) from the left motor-somatosensory cortex have been simultaneously recorded with a tungsten electrode placed into infra-granular layers and a MEA grid lied on the surface of the cortex, the signal are shown in Figure b. The power spectrum (Figure c) of the acquired data shows that MEA grid recorded the slow oscillations, moreover, the heart rate of the rat was also recorded at 5-7Hz by the MEA.

Conclusions

In this work, a compact standalone low noise amplification system for measuring ECoG signals in-vitro or in-vivo has been shown. The miniaturized system is composed of UltraFlexible MicroElectrode Arrays (UF-MEAs) connected to a recording/stimulating board (NeuroDaq). This device can be a keep point for fabrication of portable miniaturized ECoG system.

Acknowledgement

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Figure 1: a) a snapshot from the cad software of the in-vivo MEA. b) a detail of the MEA dedicated to in-vitro measurements
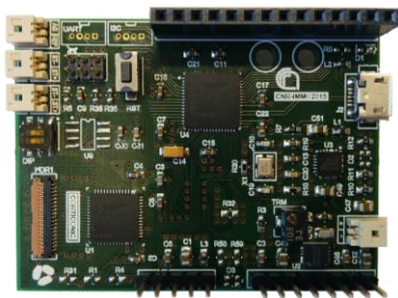

Figure 2: A picture of the board prototype.
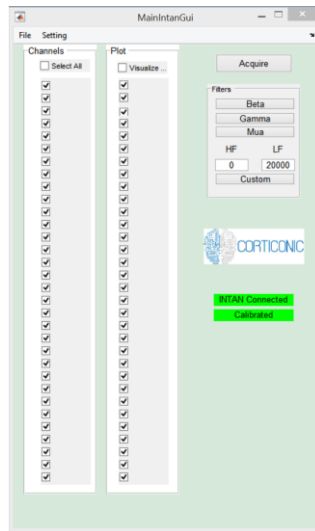
a)   b)
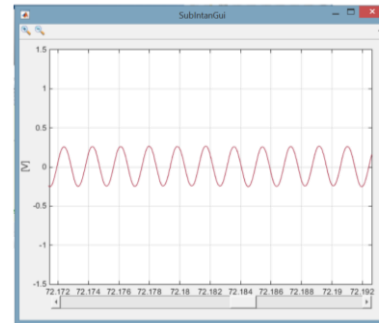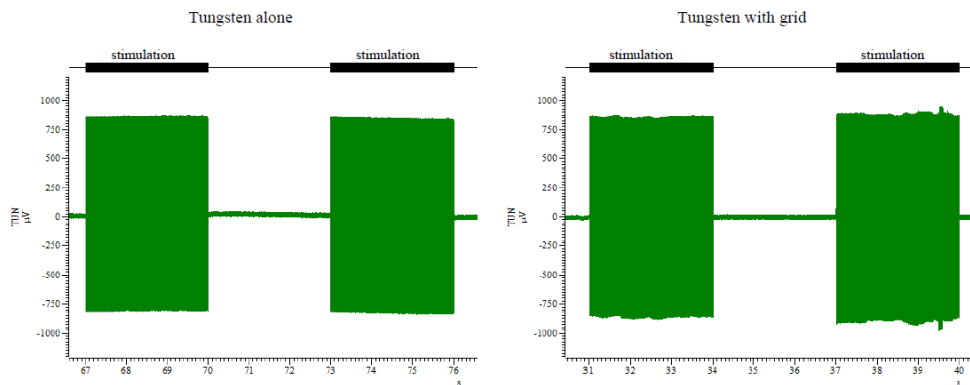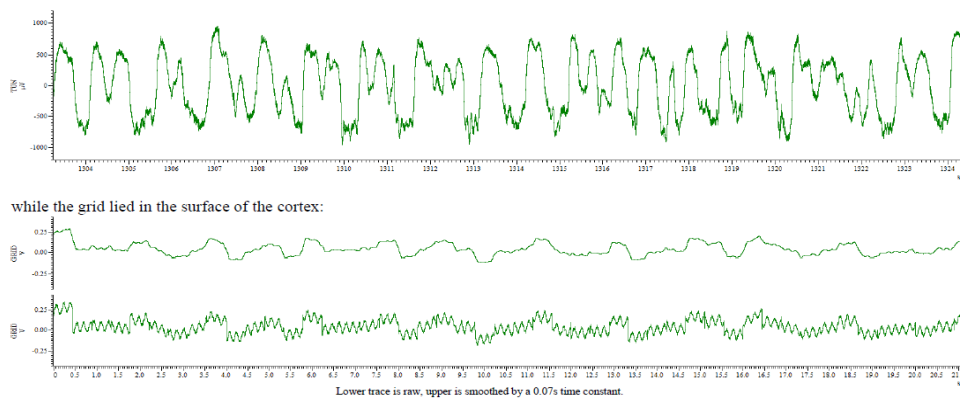

Figure 3: a) Channel selection panel of the Matlab software interface. It is possible to see the selectable channels and filters. b) A snapshot of the visualization windows during a signal acquisition.
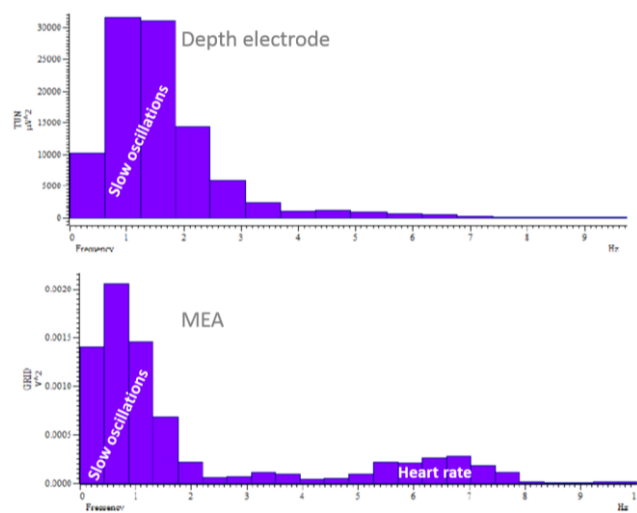
a)

b)

c)

Figure 4: a) Noise test in saline, the NeuroDaq board do not introduce noise; b) Slow oscillations recorded during in-vivo test c) power-spectrum emphasizing slow oscillations activity and heart rate of the mouse.