

COMPUTER-CONTROLLED NEUROSTIMULATION FOR A VISUAL IMPLANT

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Keywords: Artificial vision, electrical neurostimulation, microelectrodes, active implants, phosphene, neuroprosthesis.

Abstract: Current research in therapies for restoring a functional form of sight to the blind includes interfacing electronic neurostimulators with some point of the visual pathway. This approach requires controlling a number of waveform parameters which might vary for every implanted patient and for every channel in an interface that may have hundred or thousands of electrodes. Therefore, the clinical, acute research stage of the implant should be controlled in a flexible and easy way, in order to obtain the information that will lead to a chronic implantable device. We describe such a system, based on a PC connected to an electronic neurostimulator, which delivers bi-phasic pulses to a set of implanted microelectrodes. This platform performs an automated patient-driven procedure to find stimulation thresholds. The system implements a set of psychophysical tests in order to determine the properties of the elicited visual perceptions, and applies an automatic re-mapping of the electrodes to obtain better recognizable patterns of percepts. Our platform can interface some other tools oriented to obtain, in a next research stage, a portable and chronic version of the visual implant.

1 INTRODUCTION

World Health Organization estimates that about 37 million persons are completely blind, while those affected by low vision sum up to 124 million (WHO, 2005). These numbers are increasing due to the ageing of population in developed countries, and to a variety of pathologies and accidents affecting one or more of the components of the complex visual system.

Major causes of blindness are age-related macular degeneration (AMD), diabetic retinopathy, glaucoma or traumatic damage.

Therapeutic choices for blindness might be as varied as its causes. Clinical treatments are available for some kinds of visual impairments, as the ones caused by cataracts. However, a strong research is

undergoing for other types of visual pathologies, for which no clinical solutions are available yet.

These research lines include retinal cell transplantation, the use of growth factors, or gene therapy, mainly applied to retinitis pigmentosa (RP).

Apart from biological approaches, a number of research groups are working towards the development of visual prostheses, which would replace one or more of the damaged stages of the visual pathway, providing a rudimentary, but functional, form of visual perceptions.

Depending on the point of the visual pathway on which the neurostimulation interface is placed, we can classify visual neuroprostheses as retinal (Humayun, 2003), optic nerve (Veraart, 1998), or cortical implants (Dobelle, 2000; Troyk, 2003; Fernández, 2005).

In retinal prostheses, the set of electrodes are implanted below or onto the retina, in order to replace the role of photoreceptors, or ganglion cells, respectively. In the case of optic nerve implants, a cuff electrode is placed around the bunch of axons of the ganglion cells connecting the output of the retina to the next stage of the visual pathway. In cortical implants, electrical pulses are directly delivered to the visual area of the brain cortex, by using surface planar electrodes, or penetrating tips.

Whatever is the selected interface for visual neurostimulation, the employment of this kind of devices implies a high degree of complexity.

The amount of channels in the different prototypes used in research range from 16 to 100 electrodes (Normann, 1999), although some studies have shown that a number between 600 and 1000 electrodes would be required to obtain an adequate performance in basic tasks, such as object discrimination, recognition of big characters or pedestrian navigation (Cha, 1992).

The signal delivered to every electrode is a bi-phasic charge-balanced pulse, and includes a set of parameters such as phase width, pulse duration, pulse current amplitude, number of pulses in a train, inter-pulse interval, inter-train interval, etc. The set of values for these parameters might vary from channel to channel, and are expected to be different for every implanted individual (see Fig. 1).

This way, the process of tuning all the parameters for the prosthesis after safe implantation is a complex and lengthy task, which is unavoidable in the research to determine the feasibility of a neurostimulation-based visual prosthesis.

In this paper, we describe a computer-based set of software and hardware conceived for research with visual neuroprostheses. Our platform is mainly oriented to test cortical implants, but it is easily extendable for other types of implants.

The purpose of the research platform is to provide automated and patient-driven procedures for prosthesis parameter tuning and psychophysical testing. The computer-controlled neurostimulator serves as an abstraction layer to hide the complexity of handling such an intricate implant.

The platform is part of a set of tools designed to cover different needs in the development of a full visual prosthesis, such an artificial retina model, or an automated synthesizer for embedded circuits to obtain a portable, low power consumption controller for the stimulator.

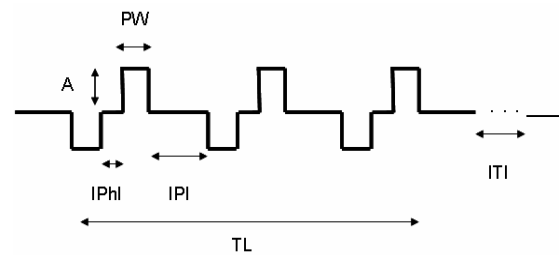


Figure1: Biphasic pulse train for cortical neurostimulation. Pulse trains contain a number of parameters that can be selected, as amplitude (A), pulse width (PW), inter-phase interval (IPhI), interpulse interval (IPI), train length (TL), and inter-train interval (ITI).

2 A VISUAL PROSTHESIS MODEL

The platform described in this paper has been developed to assist in the post-implantational stage of research of a visual neuroprosthesis project. The whole project, known as CORTIVIS (Cortical Visual Neuroprosthesis for the Blind) (CORTIVIS, 2002), has been carried out by a consortium of seven research labs and a small company under European funding (see Fig. 2).

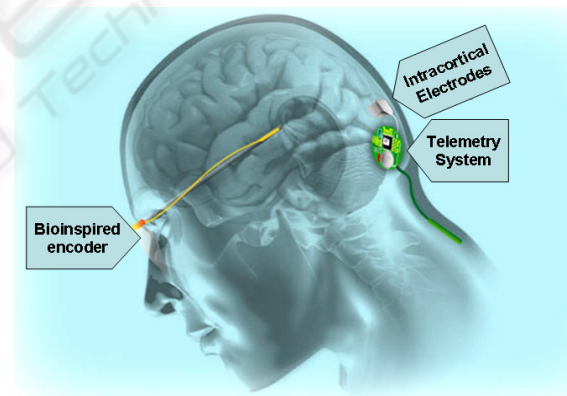


Figure 2: Scheme of the visual prosthesis proposed by CORTIVIS. A camera grabs images, which are processed by a bioinspired encoder. The encoder sends stimulation commands wirelessly to the intracranial telemetry system. Finally, the array of microelectrodes stimulates the visual cortex of the subject.

The model selected for the CORTIVIS prosthesis includes one or two cameras, as input, which feed a bio-inspired retinal encoder, which partially replaces the role of the visual processing taking place at the retina, and determines the moment in which specific implanted electrodes should be activated. The output

of this stage is an address-event representation (AER) indicating the number of electrode which will be stimulated. This stream of addresses is sent through a wireless link to the implanted section of the prosthesis. The RF link also provides energy for the implanted stimulator. This neurostimulator is finally connected to an array of microfabricated electrodes, which are inserted into the visual area of the brain cortex. In our case, the Utah Electrode Array (Normann, 1999), bearing 100 electrodes, has been selected as the neuroelectrical interface.

3 RESEARCH PLATFORM

In this section, we describe the organization, operation modes and capabilities of the research platform we have developed for the testing and tuning of cortical visual neuroprostheses.

3.1 System Architecture

Fig. 3 shows the building blocks that integrate the experimenting station. A PC which runs the software required to control the platform is connected to an electronic neurostimulator. The connection is made through one of the computer ports. Initially, we employed the LPT port. However, the second version of the neurostimulator is using a USB port to exchange information with the PC. An optocoupling stage protects the patient against electrical risks, as required for biomedical instruments.

The second stage of the platform is an electronic equipment which receives and decodes commands from the PC, according to a pre-established protocol. This neurostimulator can receive configuration, stimulation and test commands. Whenever a configuration word is received, it stores the waveform parameters for the corresponding channel in a configuration memory. If a stimulation command is sent from the PC, the equipment selects the corresponding output channel through a demultiplexer, and drives a Digital-to-Analog converter so that a biphasic waveform is sent to the output, according to the stored parameters for the corresponding channel. Test commands just check the state of the electronics, in order to detect malfunctioning electrodes (due to encapsulation, breakage during insertion, etc.).

The last block in the platform is the intra-cranial implant, which is connected to the output of the neurostimulator. In our case, we have selected the Utah Electrode Array, which is a microfabricated array of 10x10 microelectrodes (Fig. 4). This array

is pneumatically inserted into the brain cortex, so that the tips of the electrodes are expected to reach layer IV of the visual cortex. Previous experiences have shown that electrical stimulation of cells in this layer evoke visual percepts, similar to stars in the night, which are called “phosphenes” (Schmidt, 1996).

In this acute clinical version of the CORTIVIS prosthesis, a set of wires is used to connect the stimulation equipment to the implant, discarding for later use the radio-frequency link.

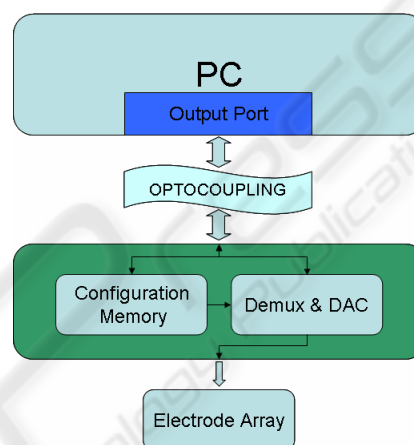


Figure 3: Structure of the research platform. A PC runs a control software, and sends configuration and stimulation commands through a PC port. An optocoupling stage protects the patient against electrical risks. The next block is the neurostimulation electronics. A configuration memory stores the waveform parameters for every channel, and a demultiplexing and digital-to-analog conversion block issues the corresponding waveform, and sends it to the proper electrode in the array.

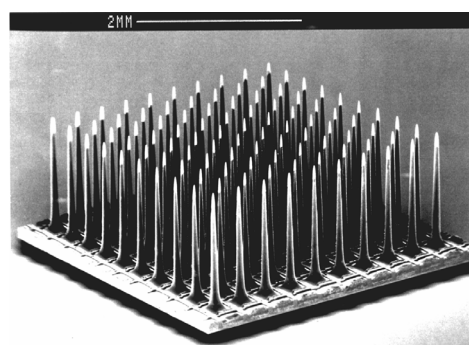


Figure 4: the Utah Electrode Array (UEA). It is a 10x10 electrode matrix, bearing 1.5 mm tips, separated by 400 microns. It is microfabricated in silicon and platinum (Normann, 1999).

3.2 Operation Modes

The experimental set-up can present two different configurations, called “stimulation” and “simulation/training” modes.

The neurostimulation configuration corresponds to the set described in section 3.1, that is, a PC controlling a neurostimulator, which delivers pulses to an implanted array of electrodes. The purpose of this set is to allow researcher tuning the set of parameters required to elicit phosphenes in the visual field of the patient, and then, run a series of psychophysical tests, in order to characterize the evoked perceptions.

However, an alternative configuration is available for debugging and training purposes (with sighted volunteers). In this second choice, the electronic neurostimulator and the implanted array of electrodes are replaced by a second PC with head-mounted displays. The first PC plays the same role as in the previous configuration. The commands sent through the communication port are received by the second PC, which implements simulation rules including random values for current threshold, and phosphene location in the visual field. The simulator in the second PC leads to a representation of a set of phosphenes in a head mounted display, according to the information obtained in similar experiences with human visual intra-cortical microstimulation.

4 SOFTWARE CONTROL

The platform described in the former section runs a program written in C++, under Microsoft Windows, which controls all the automated procedures to be carried out for stimulation parameter tuning and psychophysical testing.

The control application, named “V1 Cortistim” has a graphical user interface that allows the experimenter to select every stimulation parameter for the waveform, and run or stop every test. However, in order to accelerate the lengthy process of tuning the stimulation parameters for each implanted electrode, and executing an extensive set of psychophysical essays, every of these procedures have been automated. This way, the patient becomes the operator of the system, setting the pace of the experimenting steps, and avoiding verbal interaction, so the feedback given by the implanted individual by means of the computer input mechanisms, is automatically recorded, launching the next action of the process. In the following sections, we detail the

procedures that are implemented in the research platform.

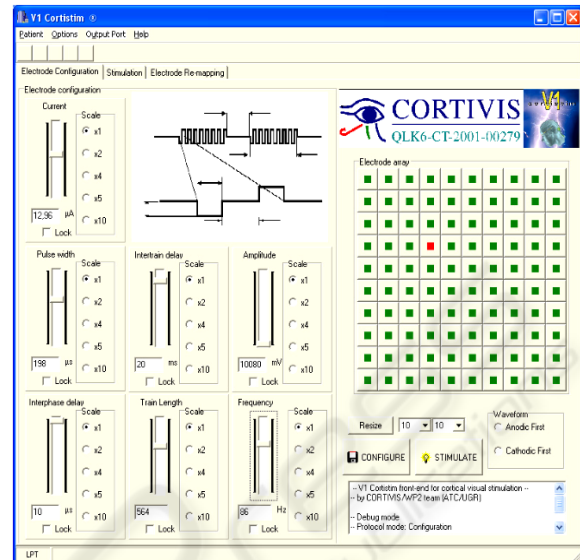


Figure 5: V1 Cortistim Graphical User Interface, allowing to control every waveform parameter for every channel in the microelectrode array.

4.1 Current Threshold Finding

The first task after the patient has been safely implanted is finding the lowest current amplitude required to evoke a phosphene. This procedure has to be done for every channel of the implant. This way, the objective is to have as many phosphenes as possible forming patterns of percepts, but injecting a minimum amount of charge into the cortical tissue.

As mentioned before, this procedure is patient-driven, so the response of the patient triggers the next step of the process. The basic algorithm selects every channel, and issues pairs of configuration and stimulation commands to the stimulator with increasing current amplitude, until the patient signals the occurrence of a phosphene in his/her visual field, by clicking a mouse button. Then, the process is repeated for the next electrode.

We have included two modifications to this basic search algorithm to reduce the number of total steps required to complete the process. We have to take into account that in a near future, next generations of implants might include an amount of electrodes over the thousand, and for each electrode a set of current values should be tested, leading to a very tedious and lengthy process. The first modification is employing a binary search scheme, instead of a linear model, reducing the complexity of the problem. The second enhancement takes into

account that current thresholds are expected to gather around a mean value. Having this, we set the starting point for the binary search for a channel to the threshold found for the previous channel.

Applying this procedure, a set of 100 electrodes can be configured in less than 5 minutes (for a step of 1 second between consecutive stimulations).

A similar scheme can be applied to the rest of parameters of the stimulation waveforms, although most experimental implants take amplitude as the main parameter. In any case, all the parameters are interrelated, as they influence the amount of charge injected, which is the main responsible for phosphene evocation.

Experimental results of using the platform to generate biphasic stimulation pulses are exposed in Fig. 6 and in Fig. 7.

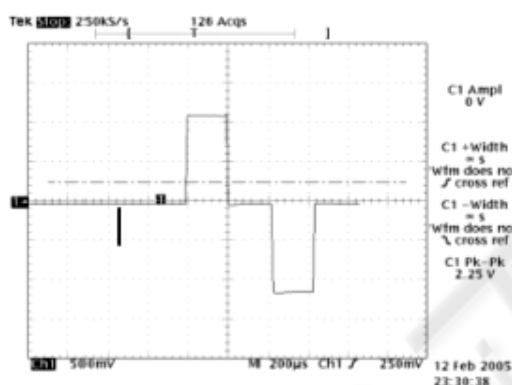


Figure 6: Example of biphasic pulse obtained with the experimental neurostimulation platform (vertical scale: 500 mV/div; horizontal scale: 200 microsec/div).

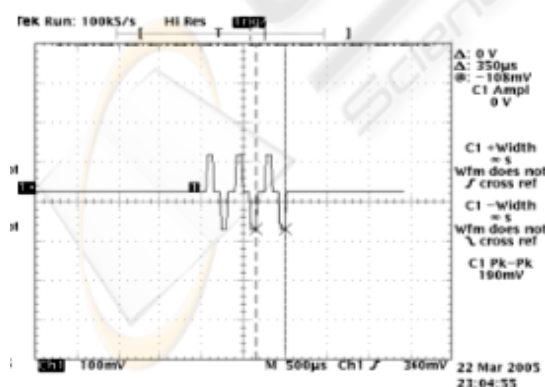


Figure 7: Example of pulse train obtained with the experimental neurostimulation platform (vertical scale: 100 mV/div; horizontal scale: 500 microsec/div).

4.2 Psychophysical Tests

After the threshold current has been determined for every channel, a set of tests is required to be carried out in order to characterize the psychophysical properties of the evoked percepts.

This way, an extensive set of perceptual tests has to be run, which again requires making this process as easy and agile as possible. Following the same philosophy as for the threshold finding procedure, a patient-driven automated scheme is again employed.

The V1 Cortistim platform provides the following set of psychophysical essays:

- Brightness sensitivity: a change in certain parameters of the waveform (mainly amplitude) will modify the perceived brightness of the evoked phosphene. A pair of phosphenes is elicited, and the brightness of one of them changes until the patient finds no change.
- Spatial resolution: a pair of phosphenes produced by distant electrodes is evoked consecutively with closer and closer electrodes until the patient cannot differentiate them.
- Phosphene cluster count: a set of 1, 2 or 3 phosphenes from adjacent electrodes is elicited. The patient gives feedback on the number of phosphenes perceived.
- Motion mapping and orientation selectivity: a straight line of electrodes (row, column or diagonal) in the matrix consecutively get activated. The patient indicates the general direction of apparent motion of the phosphene.
- Simple pattern discrimination: a simple pattern (similar to Snellen symbols) and its “mirrored” pattern are consecutively activated in the electrode array. The subject tells if they seem to be different or similar.

5 PHOSPHENE MAPPING AND RE-MAPPING

A key aspect in the design of a phosphene-based visual neuroprosthesis is the ability to evoke patterns of percepts that can be matched to known models from the visual world.

Experiments both with human and non-human subjects have shown that the correspondence between the spatial location of the stimulation point in the cortex and the position of the evoked

phosphene in the visual field can present strong deformations (Normann, 2001). This is especially remarkable for high density arrays of electrodes, in which the correspondence between the stimulation and the perceptual spaces is highly non-linear and non conformal. This fact might be caused by the complex interconnections among the neural cells that respond to stimulation in the area of influence of an electrode. Anyway, a mapping between the location of the activated electrode and the position of its corresponding phosphene in the visual field should be built for every channel of the implant. Correspondingly, an inverse transformation or re-mapping, indicating which electrodes should be activated to get a specific pattern of phosphenes is required in order to evoke recognizable percepts. We describe the solutions implemented for our experimentation platform both for the mapping and re-mapping objectives.

5.1 Phosphene Mapping

Several mapping methods have been used for building a table to determine the spatial coordinates of a phosphene corresponding to the activation of every electrode, as joysticks, dartboards or digital tablets. Our objective in this procedure is not only, as before, to obtain an agile system by avoiding verbal interaction, and by having an automated patient-driven process, but also achieving precision in a process that is very prone to inaccuracy.

Our platform includes a mapping process based on a tactile screen placed just in front of the patient, as exposed in Fig. 8. A consecutive pair of phosphenes is elicited, and the patient touches the tactile screen in the points in where the percepts appear on the visual field. The platform, in training mode, is able to find out the mapping error, as the real location of the evoked phosphenes in the head mounted displays is computer-generated, and can be compared to the position pointed out by the subject.



Figure 8: Example of usage of the automated phosphene mapping system. The platform is being used in training

mode. A sighted volunteer wearing Head Mounted Displays perceives computer-generated phosphenes, and indicates their location on his visual field by touching a tactile screen in front of him.

5.2 Re-mapping Procedure

Once an electrode-to-phosphene map is available, a pattern of phosphenes can be elicited by stimulating the corresponding electrodes. So, whenever a specific distribution of phosphenes is required in the visual field of the patient, a list of electrodes has to be determined. This process is called re-mapping.

The map of phosphenes elicited with intracortical microstimulation appears to be stable for a given patient (Schmidt, 1996). However, there are a limited number of phosphenes available in specific locations of the visual field, which have to be used to evoke any desired pattern.

Our first approach is to project the desired pattern on the center of the visual field, and then, select, for every desired point, the closest phosphene to it. With a reverse look up at the mapping table, its corresponding electrode is found.

Instead of selecting the absolutely closest phosphene in the map to the desired point, we choose the closest phosphene which hasn't already been selected. That way, we can obtain patterns including a maximum number of phosphenes, rather than having more precise locations with less percepts. Although the patterns can present some more deformation, its completeness, along with the training of the patient, is expected to lead to a better recognition, as illustrated in Figs. 9 and 10.

Additionally, this selection procedure enhances the response whenever the distribution of the map is highly uneven. So, in the case we have a region of the visual field covered by a small group of phosphenes, and another region with a high density of percepts, a moving object in the visual field should be composed of the same number of phosphenes. Direct selection of the closest phosphene would lead to a different number of points in a pattern, depending on the location of the object in the visual field (which makes difficult, for example, recognize a moving object as a unit). With our algorithm, an object is always composed of the same number of phosphenes, regardless of its location in the visual field. The shape of the pattern can vary, in an effect similar to looking a moving objective through a frosted glass.

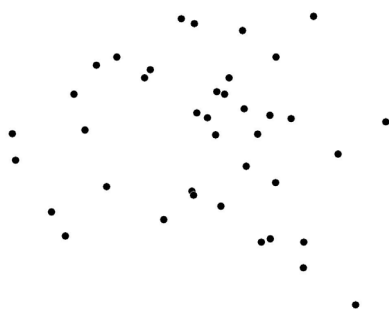


Figure 9: Phosphene pattern that would be elicited after direct selection of the top row and central column of an electrode array. Although the distribution of electrodes forms a “T” shape, the evoked pattern is unrecognizable, so a remapping is required. This set of phosphenes corresponds to a randomly generated mapping (25x25).

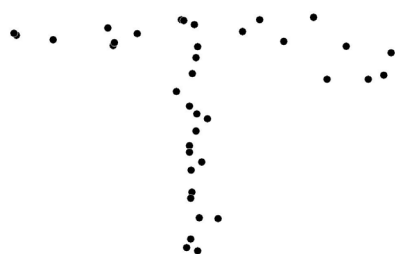


Figure 10: after our remapping algorithm is applied to the previous figure, a different set of electrodes are activated, yielding a better recognizable pattern of phosphenes, closer to the desired “T” shape.

6 ADDITIONAL TOOLS FOR VISUAL NEUROPROSTHETICS

The platform described in this paper is a specific design for the clinical testing stage of a complete visual neuroprosthetic system.

However, corresponding to the whole system architecture depicted in Fig. 2, some other relevant blocks are required for achieving a complete, portable visual prosthesis.

Regarding this point, we give a brief reference of additional platforms and hardware/software tools developed to contribute to the complete prosthetic system. Details of every one of them can be found elsewhere.

Direct stimulation of the visual cortex requires, somehow, replacing the image processing carried out by earlier stages of the visual pathway, such as the spatio-temporal filtering performed by the retina.

For this purpose, a retina-like processing software platform has been developed in Matlab, which allows experimentation with an extensive set of parameters, so that a video or live camera capture can be processed, and the electrode firings (corresponding to the activity of retinal ganglion cells) are obtained. This way, the response of our artificial retina can be compared to the one given by biological retinæ when exposed to the same stimuli.

Further information can be found at (Pelayo, 2004).

A second objective of the CORTIVIS project is to achieve a portable, low power consumption version of the previous retinal pre-processor, so that the patient can wear a camera mounted on eyeglasses frame, and the processor will transmit activation commands to the corresponding channels of the intra-cranial segment of the implant via a wireless link.

A plug-in module for the Retiner program has been built, which is able, to translate the retinal model designed with our software into a configuration file for a programmable logic chip, so that all the retinal processing is carried out by a single, portable integrated circuit. References can be found at (Martínez, 2005).

7 CONCLUSIONS

We present a computer-controlled platform conceived to control a neural interface. The main objective is to provide a friendly and automated way of performing experiments after implantation of an array of microelectrodes into the visual cortex of a patient. The platform serves as interface to handle the complexity inherent to a multi-channel brain-computer link that requires tuning biphasic stimulation pulse trains for every electrode.

Every experimental procedure is automated, and patient-driven, in order to make the tuning and testing process as fast as possible. The platform includes a set of psychophysical tests to determine key features of the electrically evoked percepts.

As previous micro-stimulation experiences confirm, the elicited patterns of phosphenes suffer strong deformations with respect to the distribution of the corresponding electrodes in the array. As the objective is to evoke recognizable patterns, a re-organization (re-mapping) between the stimulation and perceptual spaces is required. Our platform includes a re-mapping algorithm for such a purpose. We also make a brief reference to some additional tools developed by our research group, also

contributing to the development of a complete independent prosthetic system. These tools include a flexible retinal processing model, an automatic synthesizer to program integrated circuits for retinal processing, and a system to include binocular and spatial information in the set of stimuli sent to the brain.

Unfortunately, it is difficult to provide a detailed and standardized comparison against other systems under development. On one hand, these kinds of systems are specifically designed and fitted to control a particular implant, so no compatibility criteria are considered. On the other hand, as neuroengineering is a young field of research, no standards for measuring and comparing the performance of a prosthetic system are available.

Nevertheless, some relevant organizations involved in blindness and low vision research, as the ARVO (ARVO, 2007), or the Smith-Kettlewell Eye Research Institute (SKERI, 2007), are organizing and conducting specific meetings aiming to arrive to a standardized set of tests that will be useful to provide a measurement of the performance of these implants.

ACKNOWLEDGEMENTS

This work has been carried out with the support of the European project CORTIVIS (ref. QLK6-CT-2001-00279), the National Spanish Grants DEPROVI (ref. DPI 2004-07032), IMSERSO-150/06, and by the Junta de Andalucía Project: P06-TIC-02007.

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