Development of a closed-loop neural prosthesis for vestibular disorders


Abstract—Vestibular disorders can cause severe problems including spatial disorientation, imbalance, nausea, visual blurring, and even cognitive deficits. The CLONS project is developing a closed-loop, sensory neural prosthesis to alleviate these symptoms [1]. In this article, we outline the different components necessary to develop this prosthetic. A short version of this work was presented in the NEUREL 2010 [1]. Conceptually, the prostheses restores vestibular information based on inertial sensors rigidly affixed to the user. These sensors provide information about rotational velocity of the head; the prosthetic then transfers the information to the vestibular nerve via electrical stimulation. Here we present a project overview, development details, and summarize our progress in animal models and selected human volunteers.

Index Terms—Neuroprostheses, sensory prosthetic, vestibular disorders, bionics.

I. INTRODUCTION

The vestibular system is composed of sensory organs located in the inner ears. This sensory system detects rotational velocity and linear accelerations of the head. This information, along with lesser contributions from visual and proprioceptive inputs, provides the brain with information about the body’s spatial orientation. Spatial orientation is crucial to facilitate maintenance of balance and also important for many other activities of daily life. Bilateral loss of vestibular organ function (which may occur after infection, ototoxic drug exposure, or trauma to the inner ear) disables the vestibular periphery and results in spatial disorientation, postural instability, self-motion perception deficits, visual blurring (“oscillopsia” due to loss of vestibulo-ocular reflexes), and chronic disequilibrium. Additionally, unilateral loss of function and transient loss of function (e.g. Ménière's Disease) can also present similar symptoms.

There have been decades of both basic and applied research on the vestibular system in both animal models and humans. This project is built on the foundation of basic research that has revealed vestibular stimulation mechanisms that provide a framework for addressing vestibular disorders related to head rotations [2-8]. Specifically, it is possible to externally stimulate vestibular nerves to mimic the natural (healthy) encoding of angular velocity. We proposed to build an implantable device that would provide sensory information directly to vestibular afferent neurons using a similar architecture as the cochlear implants. This device would encode rotational information from artificial sensors and interface with the damaged vestibular system via electrical stimulation of the ampullary nerve. This first generation prosthetic would partially restore the information pathway (at this stage linear acceleration is not transmitted). The prosthetic’s performance could be further improved through a variety of mechanisms including feedback from: the vestibular nerve, outputs of vestibular system reflexes (i.e. VOR, VSR, VCR see [9] for details), or functional metrics. This feedback would enable ‘closed-loop control’, i.e. a control system that adapts its parameters over time to minimize error. Here, we will present an overview of the CLONS 1 project, briefly review current progress and discuss future plans.

II. ARCHITECTURE

Conceptually, the damaged natural components (semi-circular canals) for sensing head rotations will be replaced with artificial devices (e.g. multi-site electrodes, gyroscopes, and electrical stimulation) to partially restore vestibular information flow to the brain. The brain can then incorporate this information with other sensory information to alleviate the adverse symptoms of vestibular injury. Figure 1 illustrates the broad building blocks of the CLONS project focusing on hardware components and control algorithms. Additionally, it contains a disconnected Neurophysiology block that is critical to guide development of the other components and assess prosthetic performance. All of these components are not only connected to a vestibular prosthetic user, but also interconnected with each other. In the next section, we will discuss our research activities for each aspect of this project.

1 CLONS is an acronym for CLOsed-loop Neural prosthetics for vestibular disorders.
III. DEVELOPMENT

We have brought together an eight-partner consortium (seven academic and one industrial) to fulfill the ambitious requirements for this prosthetic. Development can be divided into a variety of categorizations, but here we use:

- Implanted components
- External components
- Control Algorithms
- Modeling
- Neurophysiology

A. Implanted components

Multiple components must be developed and tested to create a robust interface to the vestibular nerve. Specifically, electrode arrays must be developed that offer selective simulation of the three semi-circular canals. These arrays must be biocompatible, durable, and efficacious. Additionally, they must be created in multiple configurations to accommodate three different animal models (guinea pig, squirrel monkey, and rhesus monkey) and for human patients. An example of the guinea pig electrode that has been developed is shown in Fig. 2 using the processing in [10]. The double-sided configuration has proven useful as electrode orientation after surgery is uncertain. Typically, stimulation to one side of the array has been more efficacious than the other. We suspect this effective side is closest to the nerve. The final prosthesis could utilize six of these arrays, with one array per semicircular canal (three canals per ear).

Additionally, it is desirable to avoid percutaneous connections between the electrode arrays and external components to power and record from them. Instead we will use coils to transmit information through the skin to control subcutaneous electronics. These electronics are responsible for both controlling stimulation for the entire array and also recording vestibular responses to stimulation (more details in [11]). The responses are averaged to find the Vestibular Evoked Potential (VEP) and then transmitted to external devices for further analysis. Ideally all implanted circuitry could be positioned inside of the mastoid bone in human subjects for long-term use.

The system design of the implanted stimulation unit is depicted in Fig. 3. The system comprises external and implanted units that are wirelessly connected via an inductive link. The external unit detects the head motion and converts via signal processing the mechanical motions into settings for current stimulation pulses. The settings, organized in frames, are transmitted via the inductive link to the implanted unit. The implanted unit receives these frames and generates the appropriate biphasic current pulses. The pulses are delivered to the individual electrodes to stimulate nerves for the three semicircular canals. The telemetry unit receives power from the inductive link to supply the whole implanted unit, and extracts data embedded in the power stream. The data are then transmitted serially to the stimulator.

The stimulator ASIC [12], as shown in Fig. 3, consists of three identical stimulators functioning in parallel. The stimulators are assigned respectively to the three semicircular canals and work independently to deliver stimulation to the canals. Each stimulator has a stimulation management unit and an output stage consisting of an 8-bit current digital-to-analog converter (DAC) and a switching circuit. The command frames from the telemetry are sent to all three stimulators. The management unit in each stimulator receives the frames. Once the “canal ID” in a frame matches the settings of the stimulator, the management unit loads and decodes the settings from the frame to control the stimulation. The unit sets the current DAC to generate stimulation current with amplitudes between 0 and 1mA and drives the switch circuits to turn on and off the switches at a specific time sequence to generate current pulses with specified pulse width and interval.

Another component that will be either implanted and/or rigidly affixed to the skull is the rotational velocity sensors. Specifically, we are using STMicroelectronics 3-axis gyroscope (LYPR540AH) for the prosthetic’s sensor. This sensor offers some mechanical characteristics that are interesting for the CLONS project such as a measurement range of ±400°/s and ±1600°/s and a -3dB bandwidth of 140 Hz. The device is available in a 4.4 by 7.5 by 1.1 mm package. Thanks to the small size and weight, this gyroscope can be easily integrated in the neuroprosthesis. We have validated it by ‘re-playing’ monkey head movements with a motor. Specifically, we developed a mechatronic platform based on a DC motor (3863A024C, Faulhaber), a motion control (MCDC 3006S Faulhaber),
and a wireless communication unit (V-Link Wireless Voltage Node, MicroStain) (see Fig. 4).

This platform could reproduce different trajectories (e.g., sinusoids and ramps covering the available angular velocities and bandwidth range) and angular velocities from monkeys after vestibular ablation have been used for a preliminary characterization of the gyroscope (see Fig. 5). The results obtained (e.g., RMSE% < 1) are promising and it seems that LYPR540AH can be used as a neuroprosthesis component for the monitoring of the angular velocities of the head in monkeys and humans.

B. External components

Ideally all necessary components for the prosthesis could be rigidly affixed to the skull and remain subcutaneous. This would create multiple advantages, e.g. avoiding the infection risk of percutaneous connections, protecting electronic components, and maintaining exact sensor alignment to the head. In fact, in the final device we envision that all components except the batteries will be internal. However, in this active development stage we are evaluating different control algorithms and computational modeling and each requires different levels of computational power. For the current prototypes we are placing the processing unit externally until we find the optimal control strategy (and necessary computational power).

Moreover, external devices (not part of the prosthesis) will be needed to assess performance. Functional restoration of vestibular information for both animals and humans can be assessed using specific protocols related to peripheral neural responses, vestibulo-ocular function, balance control, and tilt perception. For example, vestibuulo-ocular performance is also assessed in the clinic with humans using visual acuity during 1-D perturbations [13].

A dedicated mechatronic platform for the assessment of function during locomotion has been designed. This device will be integrated with a system for the recording of whole body kinematics and of muscular activities (electromyographic signal). The platform is composed of two treadmills, each powered by independent electrical motors [1]. Each treadmill is provided with an aluminium plane for supporting tester during the motor tasks. Furthermore, treadmills can be moved in the medial lateral direction (300 mm of lateral translation). In order to obtain the required displacement, each treadmill is placed on two cylindrical rails passing laterally through the two treadmills.

The treadmills are moved laterally through two racks each with its driving pinion. The belt slides on the walking plane generating on the tester a lateral perturbation on the foot/feet (e.g. in Fig 6). The platform is provided with a structure where the tester, wearing a harness, is attached by means of a damper-cable-snap-hook system to avoid falls.

A. Control Algorithms

Angular velocity measurements (from gyros) must be transformed to signals which mimic the relationship between firing rate and velocity in healthy semi-circular canals [2]. We use transformation matrices (similar to [14]) but align the signals into semi-circular canal space based on anatomy using a transformation protocol based on [15]. Furthermore, the multi-site electrodes create a wide parameter space where experimental optimization would be infeasible. Instead, we are making functional models of the electrode-nerve interface. These models will allow us to explore the stimulation parameter space in simulations. Similar models are being developed for Vestibular Ocular Reflex (adapted from [16]) and functional metrics.
discussed in the prior section, they can be used to find a first approximation of prosthetic sensitivity to various stimulation parameters.

To facilitate closed-loop vestibular prosthesis control, we are also investigating Vestibular Evoked Potential (VEP). This signal can be measured from the nerve and provide direct feedback about the efficacy of stimulation. Understanding the correlation between VEP features and stimulation parameters (and furthermore VOR) is important to determine the utility of VEP in a vestibular prosthesis. Acquiring noise-free VEP requires relatively complex artifact- and noise-removal techniques, as the recording is proximal in both time and space to electrical stimulation. A first order quantification of the response (including VEP and possibly stimulation artifact) can be identified in unprocessed raw measurements using rectified bin integration (RBI) [17]. Figure 7 shows the Mns “bin” selection Nµs after the biphasic stimulation pulse. The parameters must be properly selected to both avoid artifact (N) and capture the duration of VEP (M).

Preliminary analysis of different stimulation conditions (below and above the vestibular threshold - the level of stimulation necessary to evoke VOR) showed significantly higher RBI (averaged over 200 stimulations) for the above-threshold stimulation (200µA) compared to two below threshold conditions (60µA and 100µA). RBI did not scale with delivered charge or current amplitude (which would suggest contributions from artifact). Instead there was a large change in RBI that corresponds to the vestibular stimulation threshold. However, we are conducting further experiments to confirm these results and better discriminate between VEP and stimulus artifact. If RBI proves to be a descriptive feature of VEP without artifact contamination, we will exploit it for adaptation of prosthetic control.

To enhance the capabilities of the prosthetic, we would like to expand the control models to incorporate body state and modulate control schemes based on multiple information sources. In order to obtain an efficient chronic stimulation, we are optimizing electrical stimulation parameters, quantifying and maintaining electrode-canal interface, and incorporating physiological responses and models.

B. Anatomical Modeling

Our main goal has been to develop a fully 3D model of the vestibular sensors, of their afferents and their multimodal integration in the vestibular nuclei. Dynamical systems and information theory are involved in the principles and in the computational modeling by neuronal networks. Two promising directions for direct application in CLONS project are: 1) contribution to the definition of adapted characteristics of vestibular sensors, 2) determination of the characteristics of a phasic part of the afferent signal. We also plan to develop in the next period a multi-sensory approach based on geometric invariance and Bayesian analysis for studying vestibular use of incomplete information. We believe that these models will provide novel insights into vestibular function and can drive development of better artificial vestibular systems, potentially tested in this project.

C. Neurophysiology

1) Animal Experiments

Here we aim to implant electrodes in mammals and record responses evoked by electrical stimulation. Currently, we are implanting multi-site electrode arrays and investigating the efficacy of these arrays. Search coils were used to record eye movements as an assay of electrode efficacy. Preliminary results in guinea pigs have been promising and will lead to chronic experiments in the near future.

A thin-film electrode (Fig. 2) was implanted near neurons innervating the lateral canal. We were able to evoke eye responses that were primarily horizontal using each of six electrode sites on this electrode. Responses were evoked both using the return (“ground”) paths provided on the electrode (Fig. 8) and via a remote return path. For both return paths, the responses were larger for sites on one side of the electrode (sites 2, 4, and 6) than the other (sites 1, 3, and 5). These recordings confirm an earlier surgical observation that having electrode sites on both sides of the electrode are important to allow optimal results. In practice, the electrode sites on the side that do not generate strong responses might best be used for recording evoked potentials, but this is just a tentative suggestion. When more than one electrode site was stimulated, a response larger than evoked by each individual site was recorded (Fig. 9), which indicates that stimulation of more than one site can be beneficial.

2) Human Experiments

Novel techniques have been developed to place electrodes near the nerve [18]. Recently, we attempted to restore a
baseline “rest” activity in the vestibular pathway without causing too much discomfort to patients, and once in the adapted state, to modulate the restored activity to artificially elicit eye movements. Results in one patient showed that the human adapts to the restoration of a baseline neural activity of the vestibular pathway using steady-state chronic electrical stimulation. Furthermore, the restored activity can be modulated to encode movements of different directions and speed. Thus by pairing a stimulator with a motion sensor, the prosthetic partially mimics the physiology of the healthy vestibular system. This was an important step, as it demonstrates that major prerequisites for the feasibility of a vestibular implant for human use are fulfilled [19, 20].

In the most recent study, we observed that the adaptation to the steady-state chronic electrical stimulation is lost when the electrical stimulation is stopped for 18 hours, and the process of adaptation has to be repeated. If this observation is confirmed, continuous electrical stimulation should be maintained, even when the patient does not need his vestibular implant, at night for example.

IV. DISCUSSION

This short overview has presented some of the highlights of the CLONS project at this stage of its development. Within the next few years, we will deliver a 3-dimensional (3D) vestibular neural prosthesis for chronic animal testing, and we plan to perform the first chronic studies of multi-site stimulation efficacy (of an individual semicircular canal nerve) and the first chronic tests of bipolar stimulation. These chronic studies will be performed using animal models of vestibular loss. Furthermore, tissue from these animals will be processed to investigate the safety of chronic vestibular stimulation. CLONS plans to be the first real 3D vestibular neural prosthesis suitable for human testing and tested in humans during chronic experiments. Chronic animal and/or clinical human trials are planned to assess the effectiveness of the CLONS demonstrator in increasing the quality of life of disabled subjects.

There has been significant progress in the implantable hardware including chronically implanted multi-site electrodes. Additional multi-site electrodes are being fabricated and tested in other species and human electrodes are in the prototype phase. Internal electronics have been fabricated with an acceptable footprint for human implantation. Tests of long-term bio-compatibility are ongoing. A state of the art gyroscope has been acquired and benchmarked with real head movement data. It is currently being packaged for implantation and interfacing with other prosthetic components.

The development of external components has also been
rigorous. A novel treadmill has been developed which can extensively perturb a patient’s balance; thus thoroughly evaluating the capabilities of the prosthetic. Other assessment tests are also being developed for clinical implementation. A protocol and algorithm have been designed to quickly and post-operatively align measures of the artificial sensors with the anatomical location of the SCC. Additionally, we are actively improving the state-of-the-art models of vestibular function to increase stimulation efficacy and evaluate closed-loop control strategies.

Preliminary neurophysiology results are very promising. An acute application of multi-site stimulation suggests multiple advantages – specifically targeting specificity and an apparent superposition of stimulation results. A novel implantation technique has been developed for human patients and after successful acute stimulations with multiple patients; one patient has shown adaptation to chronic stimulation of one canal.

A chronic vestibular prosthesis can create new research paths to investigate clinical and scientific issues including:

1. **Usability:** Does the prosthetic prevent symptoms of vestibular dysfunction in realistic situations during activities of daily life?

2. **Adaptation:** Does the user’s nervous system change after interfacing with the vestibular neural prosthesis? How much does closed-loop control improve overall prosthetic function?

3. **Feedback Utility:** What type(s) of feedback provide the most information to the user in order to provoke an increased and more effective understanding of the environment?

This project’s outcomes will include increased neuroscientific, clinical, and technological knowledge specifically for the addressing vestibular disorders. Furthermore, it can also contribute to guidelines for the development of other bidirectional interfaces and neural prostheses.

**REFERENCES**


