Making Sense of Neuronal Stimulation

Introduction

In modern virtual reality (VR) experiences, the traditional senses of vision and audio are emphasized. However, haptics, or stimulation of the sense of touch, is paramount for immersion. Current approaches to haptics require intensive engineering of haptic gloves, or rely on sonar waves to simulate pressure. These external techniques do not scale to full-body experiences and suffer from limited sensory resolution. This report suggests direct neuronal stimulation as an alternate paradigm for VR haptics by exploring its current application in the medical domain and providing recommendations for stimulus mechanism, creation, and location. We will first explore these concerns in the context of haptic stimulation for sensory feedback in prosthetic limbs. Then, we consider other prosthetics which interface through neuronal stimulation to help design a haptic stimulator. Finally, we'll investigate optogenetics, a light-based biological technique, as an alternative to electrode-based stimulation.

Prosthetics for Paraplegics

The idea of stimulated sensation is premised on a usable stimulus mechanism, which are traditionally implanted electrodes. Current knowledge around intraneural stimulation for haptics is driven by limb prosthetics. However, control had to come before feedback. Integrated prosthetics need to interpret nerve signals to be controlled, which spurred research into interfacing sensors. Microelectrodes became the predominant solution, since they capture electrical signal on the scale of individual cells[13]. From aggregate recordings of skeletal muscle (and neuron) activity, electromyographic (EMG) signal processing enables trained patients to control their prosthetic limbs[14]. More recently, the task of sensory feedback has been considered[7,12], which requires the prosthetics to stimulate interfacing nerves, dictated by its own sensors. Intraneural stimulation was first employed in 1980 by Torebjörk[13] for precisely sensory stimulation. Even then, the study showed sensory percepts could directly be induced by stimulation of individual neurons, which validates the possibility of this whole endeavor.

The second concern is how to create meaningful stimuli. We can consider how the body creates its signals, involving work at the level of designing biomimetic (lit. mimicking biology) receptors that convert mechanical signals into electrical signals. Kim et al.[1] recently created such a mimicked nerve, able to capture haptic information, not only on an individual pressure sensor level, but also scalable to systems that can distinguish Braille based off of motion patterns. They created a soft system that modeled the anatomy of slowly adapting type 1(SA1) neurons, which are the primary sensors responsible for detecting form and roughness. The mechanics are noted to deviate from actual SA1 neurons in terms of pressure responsivity, but not in sensitivity, range, and resolution. The attention to detail is essential, since creating a system that produces signal our bodies can't interpret has little use for haptic VR.

Organic electronics generate a stimulus from a texture, but for VR we need to have a catalog of such stimuli that could be used to make digital surfaces. It's not obvious how we can generate anything complex with a reasonable number of electrodes. A preliminary study[12] shows perceived intensity varies according to stimulus pulse intensity and frequency. There, signals collected over long-term implantation of electrodes informed stimulus design through traditional signal processing methods. However, to develop richer, commercially interesting interfaces, the stimuli must vary its intensity across a large number of stimulated neurons, as different physical textures like sand or wood would. A similar recording calibration phase should be used with deep learning, which sees unprecedented success with reproducing signal in other domains. Kim's mechanical replica is still important because it could capture activation patterns of different materials and textures, electrically codifying touch and contributing the essential "bottom-up" understanding. Such base signal could verify haptic deep learning models, like retina anatomy verifies computer vision, and so we have a method for designing haptic stimuli.

Upper limb prosthetic research details important neural pathways for haptics, which also reveal a choice for interface location in VR application. Actually, the number of required pathways for VR is strictly smaller, since intact individuals can use their proprioceptive (kinesthetic) pathways even in VR, but amputees need such pathways replaced. Currently, amputees perceive their prosthetic limbs from direct stimulation of their peripheral nerves. For example, in a small trial with closed-loop (motor and sensory feedback) control of a hand prosthetic[7], a connection to the ulnar and median nerves (in the forearm) enabled sensory feedback, qualitatively reducing phantom nerve pain. We can add the radial nerves to complete the paths for haptic sensation from the hand to the somatosensory cortex. Since these fibers are the default for limb prosthetics[7], they are well-studied and one good interface location for intact VR users. Since stimulation is expected to induce cortical changes (reducing phantom limb pain), research is needed to see if stimulation would affect an intact individual's somatosensory representation, a potentially undesirable effect. Still, the forearm or anywhere along the length of the arm is a viable location for haptic stimulation.

A Comparison to Other Prostheses

Prosthetics are being developed in other contexts as well. Researchers have demonstrated stimulatory control over perceived taste[3] and texture of food[2]. Others have investigated stimulation of the olfactory bulb to induce smell[4]. These parties tout that their work contributes towards digital codification of perceptions, and some also explicitly aiming to develop immersive experiences. All mentioned experiments all stimulate at the surface level, the start of the respective sensory pathways. The unified framework here suggests we approach the problem of stimulation by tracing neural pathways, which leads to the brain.

As a well studied example, visual prosthetics can inspire how we should benchmark our haptic system. Current visual research focuses on the quality of induced visual artifacts and biocompatibility of these systems, both efficacy indicators. A minimum visual resolution of 625 electrodes in 1 cm^2 of the visual cortex's foveal representation was established by pixelating screens for subjects with regular vision (the actual term was a phosphene simulator, where phosphenes are non-light based visual artifacts)[5]. The experimenters considered this analogous pixel resolution as corresponding to the qualitative perception of stimulated nerves. Though useful, trying to quantify perception seems to infringe on the untouchability of qualia (but this is not so!). Our core problem is qualifying the experience of hearing a person's voice, or the qualia of seeing an apple, numerically. Though it's hard for qualia proper to exist without a "self" as Ramachandran would claim, we can still enforce useful benchmarking standards. The visual ablation[5] does not translate to other senses easily, requiring an intuitive digital representation, while touch is continuous and unfragmentable. Yet from distinguishability tests, our system is successful if say, the stimulus is consistently perceived as "fur" over "wood," even if this recognition is learned. The best benchmark requires amputees to perceive stimulated textures and recognize them, meaning the stimulus was biologically plausible.

Additionally, visual prostheses explore a variety of interface locations in the retina or in the optic nerve[5], which can inspire where we place a haptic system. The main insight gained is that implants closer to the cortex are only used out of necessity, i.e. retinal implants are preferred, but for patients with non-retinal blindness, the eye itself is mostly non-functional. Furthermore, if the optic nerve itself is damaged, the only option is stimulation of the visual cortex[5]. Such cases have lead to the development of cortical stimulation (lit. stimulation of the cerebral cortex) techniques, which requires understanding what roles and dependencies each localized region holds. Fortunately, much of neuroscience focuses on distinguishing exactly these roles. Cortical stimulation can target the regions responsible for each sense. Vision processing (outside of attention) isolates in the occipital lobe, sound processes in the temporal lobe, and touch reflects in its sensory homunculus in the parietal lobe. fMRIs and other recording techniques such as EEGs or PET scans can broadly identify different activation patterns for cognitive tasks, but more precision is needed for targeted stimulation. Otherwise, coarse-level stimulation causes adverse effects such as undesired perceptual artifacts and even pain[5]. The problem of designing stimuli in the cortex is more complex than in the arm.

To determine if cortical procedures could be used, we must explore what exactly activates in the somatosensory cortex. Cortical procedures like ECoG (electrocorticography, recording of cortex's signal) at least enable more precise recordings. One study used ECoG to classify somatosensory activations for different materials' textures in primates (rhesus macaques)[6]. Note that since neuronal representation is distributed, "grandmother" neurons that correspond to distinct sensations do not exist, making recreating particular stimuli harder. To evidence, textural responses were shown to be high dimensional in the macaques, each texture causing idiosyncratic activations in the neuron population[6]. If cortical stimulation were to happen, we'd need a device interfacing with countless neurons across the somatosensory cortex, which is currently both dangerous and technologically infeasible. So though useful in neuroscience, cortical procedures are unlikely to reach consumers.

Since cortical implants are unlikely, we should see if a near-cortical approach would work. In fact, there is already an effective technique in auditory brainstem implants (ABI), which directly interface the cochlear nuclei[8]. This exploits the bottleneck in auditory signal that exists in the brainstem, before it gets transmitted to the thalamus for cerebral processing. Results with ABI are so impressive that some patients can even perform phone calls with the implants, indicating high resolution and accuracy of induced signal. However, ABIs are less clear than regular cochlear implants and have side effects like muscle numbness, due to the relatively large size of the implant and inevitable current spread in electrical stimulation[8,9]. Even flawed, however, these implants set a precedent as a long-term consumer product that employs neuronal stimulation. An analogous bottleneck for touch exists is the dorsal-column medial lemniscus pathway[15]. This is the "near-cortical" alternative for haptics, though there are no current relevant experiments. In such locations, however, the body's haptics are mixed, and current signal production quality is insufficient. As seen, misguided stimulation causes tingling, mislocated perception, and pain. As such even near-cortical stimulation should not be considered with our current knowledge and precision of stimulation.

Optogenetics as an Alternative to Electrode-based Stimulation

We could consider how to improve the precision of stimulation, since it limits how detailed the perceived experience is, given that the representation of texture is distributed. The restriction stems fundamentally from our electrode-based techniques, which also has the drawback of invasiveness, preventing consumer application. A technique called optogenetics can potentially address both precision and invasiveness concerns.

Optogenetics is a technique recently popularizing (i.e. last decade) as an alternative stimulation mechanism to electrodes, indeed improved in many ways. In optogenetics, photoreceptive ion channels are introduced to target neurons via an opsin-carrying virus, which makes them sensitive to light[9]. Light is delivered, originally with a fiber optic tether, and the host neurons can be excited or inhibited in a variety of ways depending on the flavor of the opsin gene. Neighboring neurons do not get excited, so there is no stimulus spread[9]. Precision depends on opsin delivery, a key challenge in optogenetics and research has already indicated carriers can be targeted for specific cell types. As such, optogenetics enables intracortical stimulation[9-11] and is has been safe in non-human trials. Peripheral nerve optic stimulation shows the same behavior as electrode stimulation, with better localization[9]. Indeed, optic techniques achieve single cell spatial and sub-millisecond temporal resolution, better than electrode methods[10]. Recording the activity of stimulated neurons can be done with a hybrid approach that uses transparent electrode recording arrays that do not interfere with the optic stimuli[12]. Most critically, optical stimulation can be 'contactless,' since light can be shined externally[9]. Thus traditional electrode stimulation offers no benefits over newer techniques other than being the incumbent method of choice in the neuroscience community, and an optic mechanism is likely to enable haptic VR.

That is not to say optogenetics has no drawbacks, and it's not ready for consumer use. Different cells are varyingly sensitive to light, and light intensity diminishes by distance and gets absorbed by biomatter, weakening the case for contactless intracortical applications[10].

Additionally, optic techniques lack subcellular control. However, weakened light intensity is a lesser issue in the arm (less biomatter to penetrate). As for control, the precision offered is already better than that of electrical techniques, and awaits improvements from optogenetic research[9]. These drawbacks do not affect the haptic VR use case.

Conclusion

Stimulatory haptics is not yet consumer-ready, but we can identify the most viable location, delivery mechanism, and method of stimulus design. Intracortical and near cortical stimulation have associated risks that won't reach consumers. By scoping to the hand, the forearm becomes the ideal location for its accessibility and known nerves (namely the ulnar, median, and radial nerves) to interface. To improve on stimuli design, we need to how mechanical patterns emerge, both biological and artificial. This will be needed to capture the nuances of physical surfaces. Due to individual nervous system differences, stimuli generation will need user calibration. For the mechanism, a contactless optical technique is ideal for consumer application.

This report has found stimulation to be overall effective in medical application in that stimulation in mapped pathways has predictable, intended effects. Two main topics block VR application. We need more research on the efficacy of contactless optical stimulation in peripheral nerves, since a casual consumer product would be located on an arm and easily detachable. Additionally, since haptic stimulation is used for amputees, we need to explore how we can design meaningful haptic stimuli for intact individuals, the main user base of consumer VR. Currently, external techniques like haptic gloves remain popular, but as neuroscientific understanding matures, the paradigm will shift to neuronal stimulation for its flexible potential.

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