# CORTICAL STIMULATION FOR THE EVOCATION OF VISUAL PERCEPTION

Daniel Wagenaar, CNS 247, March 5, 2004

**Restoring vision in the blind by direct cortical stimulation has been a dream since the discovery of electricity in the 18th century. In the centuries since these optimistic beginnings, researchers have made important progress in several aspects of the problem, although in many ways the ultimate goal still seems as distant as ever. In this paper I will review the current state of the art of human cortical stimulation, and discuss some of the outstanding problems.**

## Introduction

Severe blindness affects a large number of people. In the US alone, 1.3 million people are legally blind, including 55,000 children. Accordingly, restoring vision for these patients has been a powerful dream throughout medical history. Attempts to evoke visual sensations in blind patients through cortical stimulation date back to the 18th century, when the discovery of electricity inspired an astounding range of medical experiments, hoping to harnass the magic of this new force (LeRoy, 1755). No miraculous cures were found however, and more realistic explorations of the effects of electrical stimulation on visual perception had to wait until the 20th century. Even now, no prostheses are available that provide a useful degree of visual functionality through cortical stimulation, but our understanding of the technological challenges has much improved, and it doesn't seem outrageously optimistic to expect that major breakthroughs will be made in the next decade.

### Goals

Before setting off on a discussion of the various experimental results that have been obtained in the last 50 years, let us consider what goals a visual prosthesis might aim to achieve.

**Reading** One of the first goals that many research papers mention, is reading. Indeed, restoring the ability to read normally would be of immediate and obvious benefit to patients. One should keep in mind though, that Braille reading is a powerful alternative, especially for people who are blind since a young age. With modern advances in OCR technology, converting almost any printed text to Braille is relatively straightforward.

**Mobility** A second benefit of a visual prosthesis could be an improvement in spatial awareness, leading to improved mobility. Even a relatively modest sensor array might prove useful in detecting looming stimuli, providing greater safety and thus greater confidence in many environments including (pedestrian) traffic.

**Face recognition** A final important benefit might be gained in the social environment. While devices in the immediate future may not have sufficient resolution to accurately reveal facial expressions, the number of pixels that allows face detection and even recognition is surprisingly low (see below), and may be within reach.

It is worth considering that there are at least two alternative approaches to restoring vision by electrical stimulation: retinal implants (Humayun et al., 2003; Rizzo et al., 2003), and stimulation of the optic nerve (Delbeke et al., 2003; Veraart et al., 2003). However, in this paper, I will focus exclusively on cortical stimulation. For broader reviews, see Greenberg (2000) or Maynard (2001). Uhlig et al. (2001) (in German) provide a historical overview.

## Early enthousiasm

The first full-scale experiment in which an array of electrodes was implanted in a human patient was performed by G. S. Brindley and colleagues in Cambridge in the 1960s (Brindley and Lewin, 1968). After feasibility studies in baboons, they implanted a grid of 80 electrodes over the occipital cortex of a 52 year old woman, whose vision had gradually deterioted as a result of glaucoma, until she became totally blind following a retinal detachment. The prosthesis was placed subdurally, but did not penetrate into the cortex. Stimuli were delivered to the electrodes via an array of radio receivers, implanted below the skin but outside of the skull, and covering most of the right cerebral hemisphere. This arrangement obviated the need for skin-penetrating wires and thus reduced the risk of infection tremendously. Communication with the stimulator was achieved using a transmitter array embedded in a rubber skull cap placed directly over the receivers.

The surgery was very successful, and subsequent experiments yielded a wealth of information, described in a very thoughtful[1] 1968 paper (op. cit.).

### Phosphene psychophysics

About half of the 80 implanted electrodes could be used to evoke phosphenes — visual percepts — by current injection[2]. Most phosphenes took the form of very small bright dots, though more peripheral phosphenes were more extended, and cloud-like in shape. Some stimuli resulted in two or even three dots. The geometry of evoked percepts followed the known geometry of the represention of visual stimuli in normal adults. This mapping was not respected by additional phosphenes that were sometimes evoked by very strong stimuli.

Phosphenes evoked from different electrodes were always distinguishable, even between adjacent electrodes. For most pairs, there was no interference between stimuli, even if the distance between electrodes was only 2.4 mm. In a small subset, however, paired stimulation resulted in a line-shaped phosphene stretching between the positions of the point-shaped phosphenes that the members of the pair would evoke individually. Overall, simple patterns of phosphenes could be predictably constructed by simultaneous stimulation of several electrodes, and the authors suggest that letters would be readable with 50 electrodes per letter, assuming ‘favourable placement’.

[1] However, the authors do not report whether the implant was eventually removed, nor why the patient agreed with this very invasive procedure.

[2] The authors report pulse strength in terms of the voltage generated rather than the current injected, making comparison with other studies difficult.

The authors proceed to study the effect of pulse trains, rapid flicker stimulation (no flicker-fusion frequency could be found, surprisingly), non-visual sensations (very strong stimuli resulted in headaches of various sorts) and the effects of eye movements (resulting in phosphene movements seemingly consistent with those of retinal after-images).

### Other early work

In the 1970s, Dobelle and colleagues implanted an array of 64 electrodes in a 35 year old man blinded by a gunwound which lesioned his optical nerve. This array consisted of platinum disks, spaced at 3 mm, placed subdurally as for Brindley's array. They established that phosphene maps followed cortical geometry very well, both in V1 and in V2 (Dobelle et al., 1979). However, they also found that the amount of current needed for subdural stimulation is about 1–2 mA (Girvin et al., 1979), which would cause major heating if applied continuously and at high electrode density. Equally problematic, they found that phosphenes were often extended, and that for many electrodes it was impossible to evoke phosphenes singly — multiple distinct dots were perceived or none at all.

Brindley and Lewin close their 1968 paper with great optimism:

> Our findings strongly suggest that it will be possible, by improving our prototype, to make a prosthesis that will permit blind patients not only to avoid obstacles when walking, but to read print or handwritng, perhaps at speeds comparable with those habitual among sighted people.

This optimism proved to be misplaced. Because of the large currents required and the limited resolution implied by large electrodes, eventually a consensus was reached that superficial stimulation was fundamentally unsuitable for a functional prosthesis. A long hiatus without new human experiments followed.

## Intracortical stimulation

Nearly 20 years later, the first intracortical electrode array was implanted in a blind human volunteer[3]. The array consisted of 38 individually positionable micro-electrodes, with exposed tip area 200 $\mu m^2$, comparable in size to a neuron. In the three decades since the work of Brindley, ethical guidelines had been tightened considerably, and Schmidt et al. (1996) elaborate on how they ensured that volunteer, a 42 year old woman, blind since age 20, understood that this experiment would not give her any direct benefits.

Initially, phosphene mapping was frustrating, because the subject could not reliably distinguish phosphenes caused by stimulation from spontaneous visual activity. This problem was eventually resolved by presenting stimuli in series of ten shorter trains, 200 ms long, at 1 s intervals. (Each train consisted of biphasic current pulses delivered at 200 Hz.) This allowed the subject to perceive phosphenes as dots that blinked in a characteristic way, which made detection quite reliable. As expected, the current required to evoke phosphenes was much smaller than for superficial electrodes,

[3] This type of array had previously been tested in a normally-sighted patient who required surgery on the occipital cortex for other reasons.

with threshold currents around 20 $\mu$A for 200 $\mu$s pulse width[4]. Only two of 36 electrically intact electrodes failed to evoke phosphenes at currents up to 80 $\mu$A.

As in the earlier experiments, phosphene mapping corresponded roughly with electrode placement. Phosphene sizes varied between electrodes, from pin-point size to about 1°. Phosphene size was modulated by pulse amplitude, but not in a systematic way. Narrowly supra-threshold stimuli always evoked single phosphenes, but for a few electrodes, stronger pulses caused a pair of phosphenes to be seen, close together, but not necessarily of the same size. Strong pulses usually elicited white, grey or yellowish percepts, while near-threshold pulses often evoked colored phosphenes. Color perception was consistent for any given electrode. In contrast to Brindley's findings, Schmidt *et al* find that phosphenes are not sustained for more than 1 s by continuous trains of stimuli, but they report that breaking the stimulus into 200 ms blocks with 25 ms between blocks extends this duration.

Interactions between stimuli could make it much harder to use an implant to present images, so Schmidt *et al* study interactions between phosphenes evoked by simultaneously stimulated electrodes. Pairs of electrodes with 250 $\mu$m spacing interacted synergistically, with a pulse on one electrode reducing the threshold current for the other electrode up to 37%. Such interactions were not observed between more distant electrodes. However, when stimulating several electrodes simultaneously, bright phosphenes sometimes obscured weaker ones. The subject could alleviate this problem by fine-tuning the currents delivered to individual electrodes. It was found that simultaneous stimulation removed much of the individual idiosyncrasies of the phosphenes involved — all phosphenes became roughly equidistant, and similar in shape — but they did not lose their location. This was an unexpected bonus, as the subject stated that this interaction would make 'more complex patterns or images easier to interpret than if each phosphene had its own unique depth, size, colour, shape and texture.'

At the end of their paper, Schmidt *et al* are more guarded than Brindley and Lewin in their optimism, but still look forward to a bright future with new and better experiments:

> [These results] are very encouraging in terms of the feasibility of a visual prosthesis. . . . [T]he implantation of several hundred microelectrodes will be essential for determining a blind subject's ability to recognize complex images and evaluate information transfer rates. With this information, it should be possible to determine the feasibility of a visual prosthesis based on [intracortical stimulation].

## A new period of caution

Just when useful prostheses seemed around the corner, a tragedy occurred. A volunteer at NIH died of infection after pulling at the external side of his implant[5]. Further experiments were put on hold, as the ethics of invasive experiments on humans who do not gain direct medical benefit from those experiments were re-evaluated[6].

[4]Longer pulses, which corresponded to lower threshold currents, were later found more pleasant to the subject, who described the resulting phosphenes as 'more substantial'.

[5]R. Andersen, personal communication. I was unable to find more details about this incident in the literature.

[6]However, Dobelle continued experiments, after moving to Portugal, and now performs implantation surgery commercially. Although he has not been publishing in the scientific literature, in 2002, he reported having so far implanted 7 blind patients (http://www.dobelle.com/downloads/article.pdf) with arrays of around 60 electrodes. He is currently working towards larger arrays, and 'promises a 512-electrode system that will be cost-comparable to a guide dog' (op. cit.).

## A step back: review of requirements

In the mean time, psychophysical experiments continued. One such experiment found that for retina-stablized presentation of short words, 50–100 pixels per letter were needed (Bagnoud et al., 2001). The authors suggest that this result should apply to intracortical stimulation, but it is actually doubtful that retinal stabilization is comparable to direct cortical stimulation, because of the temporal dynamics of the retinal ganglion and LGN which strongly disfavor static images. Another experiment tested face discrimination in a forced-choice setting, using arrays of various sizes of dots with various spacings and various levels of 'dead pixels' (Thompson et al., 2003). They conclude that 10x10 arrays, with high contrast and most pixels intact, or 16x16 arrays with less optimal conditions, are useful for recognizing faces. This study also exclusively used static images (although without retinal stabilization), which probably leads to a considerable underestimate of performance.

## Focus on technology

Simultaneously, efforts to improve the technology have continued. Arrays with ever increasing numbers and densities of electrodes have been developed. For example, Richard Normann's 'Utah' array (Normann et al., 1999) contains 100 electrodes at a density of 6.25 $mm^{-2}$. These electrodes penetrate 1.5 mm into the cortex, so as to reach into layer 4. In this case, high density came at the price of losing the ability of positioning electrodes individually. Inserting high-density arrays into cortex was initially difficult, because the electrodes, although very thin, tended to deform the cortex rather than penetrating it. Normann and his group solved this problem by devising a method to rapidly inject the array using an air piston.

The Utah array has been used to map the visual cortex of cats at high resolution (Normann et al., 2001). It was found that the representation of simple features was quite complex, from which the authors conclude that significant pre-processing will be needed before camera data streams can be used for evoking image percepts. Stimulation with these arrays have been limited to simple tests in auditory cortex (Normann et al., 1999), presumably because phosphene psychophysics is hard to perform with non-lingual subjects[7].

Cortical stimulation is not limited to electrical stimuli: an exciting new approach to microstimulation delivers *chemical* stimuli by integrating microfluidics on a silicon chip. Current prototypes deliver neurotransmitters through an array of sprinklers in an all-or-none fashion (Cheung et al., 2003), but researchers at Georgia Tech are working on a design that allows individual addressing of each channel (neuro.gatech.edu). Whether such devices can deliver bandwidths high enough for transmission of moving images remains to be seen.

A more detailed review of current technology, including three-dimensional arrays for reaching into several cortical layers, and new wireless devices to allow intact-skin prosthesis was recently published by Wise et al. (2004).

[7] It is remarkable how much more research has been focused on multi-electrode recordings than on multi-electrode stimulation, despite the fact that the technology is no more complicated (Wagenaar and Potter, 2004). Much of this has to do with the fact that it is easier to study the complex physiological effects of simple sensory stimuli than to reverse-engineer which particular complex electrophysiological stimulus led to an observed simple behavioral effect, but clearly this trend must be broken before cortical prostheses can become a reality.

## Outlook to the future

There is a consensus that further experiments on humans are unwarranted until devices offer a promise of benefit to the recipient. This will probably require several hundred functional pixels, so perhaps 1000 electrodes allowing for a plausible failure rate. Multi-electrode array recording technology is now reaching this number (Litke et al., 2003), but 3D arrays have not, nor has stimulation technology. The ability to stimulate each of 1000 electrodes at rates up to 100 Hz will be critical. Until this level of sophistication is reached, researchers will have to devise clever animal experiments. So far, phosphene psychophysics has not yielded to this approach.

One critical agendum for the next experiment on a human volunteer will be to study the effects of temporally structured stimuli, for two reasons. First, the ultimate goal of these prostheses is to restore vision for real-world use, and the world is not static. Second, our visual system is optimized for moving stimuli, and performs much more poorly on static images.

In stark contrast to this goal of providing rich spatiotemporally structured animated images, the experiments performed thus far have been limited to extremely simple stimuli. Mostly, stimuli consisted of current pulses (or trains) on single electrodes. Even stimuli involving small numbers of electrodes have been rare. This is unfortunate, since even the pre-computer-age technology of Brindley was capable of multi-site stimulation. The interaction of several phosphene-inducing pulses is of the greatest interest, since ultimately these prostheses are intended for imaging, not just for showing bright dots.

To demonstrate the importance of exploiting the temporal dimension of the visual system, consider the two images below. They were acquired with a digital camera, and down-sampled to 7x9 pixels. Afterwards, they were upsampled again to remove pixel-edge artifacts which are otherwise very salient features that distract from image recognition. Even so, these images are not readily recognizable. Moving images at this resolution are quite a different story: the movies from which these stills were taken, contain enough information to extract not just the category, but even the identities of the subjects of the images (www.its.caltech.edu/∼wagenaar/cns247).

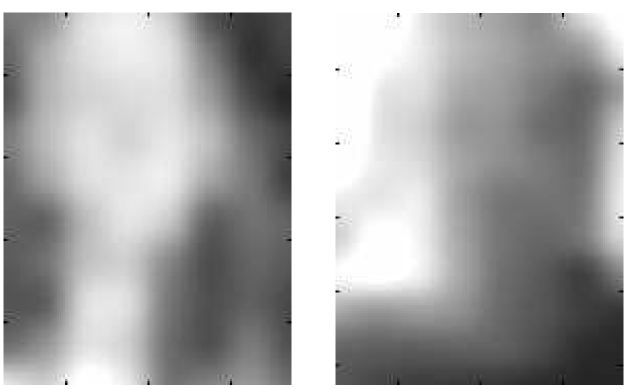

**Figure 1.** Two examples of 7x9-pixel images, blurred by a Gaussian filter with a radius of 0.35 pixel.

This simple experiment suggests that with appropriate stimulation, even a relatively small array of perhaps 100 pixels might be useful. If new technology continues to be improved at the rate seen in the last decade, it seems likely that Dobelle's promise of arrays of several hundred electrodes with sufficient durability for long term implantation may be realized soon. Until then, more research is needed into the psychophysics of image recognition, so that software can be developed to optimally use the small bandwidth that electrode arrays will inevitably have when compared to the intact visual system. Ultimately, to be useful in everyday life, all of this technology will have to be miniaturized to the point where it becomes wearable. Fortunately, consumer electronics is driving the production of ever small cameras and computers, so that at least this aspect will not be a major obstacle.

Prostheses good enough to convince those who have never had vision, and thus have long learned to cope without, may not become available for quite a while yet. On the other hand, within the next ten years or so, researchers may well be able to develop devices that will enthuse people who lost their vision as adults.

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