

Vision Project

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Website

<http://rleweb.mit.edu/retina>

1.0 Narrative Description of Progress to Date

The vision project seeks to develop an implantable retinal prosthesis to restore some useful level of vision to blind patients, similar to a cochlear implant for the deaf. Individuals who are born with normal sight but then lose vision slowly from degeneration of their rods and cones are potential candidates. Retinitis pigmentosa and age-related macular degeneration are two important forms of blindness we hope to treat.

Our most recent proof-of-concept experiments have been: 1) human experiments (lasting two to three hours) to assess what blind patients can see when electrical current is delivered to the retina through a 5 x 5 or 10 x 10 microelectrode array, and 2) electrical stimulation and recording from retinal tissue in vitro to study the relation between electrical stimulation and ganglion (i.e., output) cell response.

ACUTE HUMAN SURGICAL TRIALS

We have performed three additional human experiments at the Massachusetts Eye and Ear Infirmary since our last publication about this work in the RLE Progress Report (1999). John Loewenstein was the surgeon. All patients were born with normal vision, and all but the fourth were legally blind with retinitis pigmentosa at the time of surgery.

In these experiments we electrically stimulated the retina via a microfabricated electrode array inserted through an incision in the eye. The patient, awake under local anaesthesia, reported and drew the perceptions that resulted from electrical stimulation. The primary purposes were to 1) obtain activation thresholds with the different sized electrodes, 2) perform two-point discrimination tests, and 3) obtain descriptions of the electrically induced perceptions. The array was removed from the eye after surgery, since we are not yet able to safely implant a chronic prosthesis.

In all three experiments, the stimulator was a controlled current source, and the stimulus waveform was a 1.5 second sequence of biphasic charge-balanced current waveforms at 20 Hz.

Fourth Surgery

This patient, with normal vision (corrected to 20/20) in the operated eye, underwent surgery to have the eye removed due to cancer of the eye socket. Stimulation with a single electrode always resulted in perception of a single spot of "light." In two trials, stimulation through two 400 um diameter electrodes 2mm apart resulted in a reported perception of "two spots," but in other experiments the perceptions did not match the stimulus in such a clear way. In five separate trials she did not recognize the letter "T" when the electrodes were stimulated in a "T" pattern. The threshold for perception was about 50 microamperes for 2 millisecond pulses.

Fifth Surgery

This patient, legally blind with retinitis pigmentosa, had corrected vision of 20/1000 in the operated eye. The patient often reported perception of multiple spots or lines when a single electrode was driven. We obtained a plot of threshold current vs. stimulus pulse duration for pulses from 0.25 millisecond to 16 milliseconds in duration. The threshold current was, for example, 200 microamperes at 4 milliseconds and 800 microamperes at 1 millisecond, substantially higher than for the sighted patient above.

Sixth Surgery

This patient, also legally blind with retinitis pigmentosa, had corrected vision of 20/800 in the operated eye. Stimulation with a single electrode usually resulted in the perception of a single spot of "light." In two-point discrimination tests, the addition of a second stimulated electrode often produced the perception of a larger or brighter object or of motion, rather than a second object as one might have expected. When comparing stimulation with a row of stimulated electrodes with stimulation from a perpendicular column, the patient did not reliably report perception of a pair of perpendicular lines. We obtained a plot of threshold current vs. stimulus pulse duration similar to that reported above, but with thresholds about a factor of two lower, e.g., 100 microamperes at 4 milliseconds and 350 microamperes at 1 millisecond.

All three patients reliably reported perception due to electrical stimulation of the retina and no perception during control tests when no current was applied. No harm to the retina from the surgical procedure or electrical stimulation was evident. No postsurgical change in visual status was detected in the fifth and sixth patient. No patient reliably recognized stimulation in the pattern of a letter, and stimulation with a single electrode often produced the perception of multiple spots in the fifth patient and sometimes in the sixth. The charge density at perceptual threshold is uncomfortably close to recognised safety limits for chronic stimulation, though these limits were established under different experimental circumstances and may not apply accurately to these experiments.

In these acute experiments, with little chance for the patient to adapt to the artificial stimulus, the patients were unable to reliably report very much spatial detail. But the ability of the brain to adapt is phenomenal. Furthermore, other stimulation methods (e.g. subretinal) may have better perceptual results by avoiding stimulation of ganglion cell axons. Implantation of a chronic prosthesis will provide the opportunity to test the ability of the brain to adapt to these abnormal stimuli, and to determine what value such a device might have for a patient. This is our goal.

POWER SAVING TECHNIQUE FOR ELECTRONIC IMPLANT DEVICES

We are developing and have filed a patent disclosure for a circuit idea that is potentially useful for any implant device that delivers electric current to the body through implanted electrodes. Examples include such existing implant devices as the cardiac pacemaker, the cochlear implant and the urinary tract control device marketed by Medtronic as well as devices still in development such as the retinal implant.

A burden in the design and operation of these implants is the delivery of substantial amounts of electric power to tissue. Our technique lowers the amount of power that must be supplied. One advantage of reduced power is improved battery life, a particularly important advantage when the battery is implanted in the body, as in a cardiac pacemaker. Another advantage is reduced heat generation in the body by the implant, an important advantage for a retinal implant, since heat generation in the eye can be harmful. A third advantage is a reduction in the strength of magnetic field that must be generated to supply power to the device in cases where implanted batteries are not used, such as the cochlear implant.

All variations of the invention are based on the observation that metal electrodes in contact with physiological saline have a very large capacitance per unit area. This capacitance must be charged when the electrode is driven. To the best of our knowledge, all existing designs waste the electrical energy that is stored in these electrodes. We propose to reuse it to supply part of the power required in later stimulation of electrodes, instead of burning it in resistances and converting it to heat as in existing devices.

The simplest method of using this stored energy is to partially discharge a charged electrode by temporarily connecting it across a second uncharged electrode that is due to be charged. The discharge of the first electrode would then be completed by shorting its terminals briefly together. The second electrode, now partially charged, would complete its charging cycle by connection to the power supply. This method would supply half the charge and one fourth the energy the second electrode needs by obtaining it from the first electrode, in the case of identical electrodes that are identically charged.

More complex variations on this scheme include multiple steps of connection between the uncharged electrode and the power supply, resulting in greater energy transfer. Another variation is to discharge an electrode by returning some of its energy back to the implanted coil which powers the device, rather than directly to a second electrode.

Another use of the electrode capacitance to save energy is to charge the electrode directly from the unfiltered output of a rectifier, avoiding the losses that voltage regulators and current sources inevitably produce.

Shawn Kelly is developing these ideas in hardware for his doctoral dissertation under Prof. Wyatt's supervision.

IN VITRO RETINAL STIMULATION AND RECORDING SYSTEM

We have completed a new retina stimulation and recording system that improves on our original prototype in a number of ways. The electronics have been put on a multilevel PC board with a separate ground plane to minimize noise pickup. The software has been moved to MSWindows from Linux, to ease maintenance and use. These systems have been completely debugged and work as intended.

We have built a new retina holding fixture that allows us to record with a single microelectrode and stimulate with either a single microelectrode or a microelectrode array. It was fabricated in the MIT machine shop and worked satisfactorily on initial test.

The new system has been used in a set of experiments conducted at the Southern College of Optometry in Memphis by Drs. Ralph Jensen and Ofer Ziv. While their data are preliminary, they show that, regardless of the geometric arrangements of the stimulating electrodes, the threshold for direct stimulation of the ganglion cells (or perhaps their axons) is higher than that for presynaptic cells at stimulus durations below 1 millisecond, but lower at durations above 1 millisecond. The latter result is surprising, since the ganglion cells are closer to the epiretinal electrode than any presynaptic cell. This preliminary finding is in agreement with previous results obtained by Greenberg under different experimental conditions. It offers a convenient way to control the locus of stimulation from a fixed microelectrode.

Scientific Publications

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Presentations

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Shire, D.B., J.L. Wyatt and J.F. Rizzo, "Progress Toward an Inflatable Neural Prosthesis," ARVO Poster Session Abstract, *Investigative Ophthalmology and Visual Science*, vol. 42, no. 4, May 2001, p. s812.

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