

The Retinal Implant Project

RLE Group

Retinal Implant Research Group

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Introduction to the Retinal Implant Project

The Retinal Implant Project is a joint effort of MIT, the Massachusetts Eye and Ear Infirmary, and the VA Boston Healthcare System, as well as other collaborative branches, to develop a retinal prosthesis to restore some vision to the blind. Diseases targeted include retinitis pigmentosa and age-related macular degeneration, both of which cause loss of the photoreceptors (rods and cones) of the outer retina, but spare the inner retinal ganglion nerve cells which form the optic nerve. As presently envisioned, a patient would wear a camera mounted on a pair of glasses, which transmits image data to an implant attached to the eye. The implant will electrically stimulate the appropriate ganglion cells via an array of microelectrodes.

For many years our group acted as a small research center for the interesting problems facing retinal prostheses. But in December 2002, we changed our direction, expanded our group, and decided to develop our own prototype for chronic implantation. This is a substantial effort, involving fabrication of flexible substrates and electrode arrays, circuit design, biocompatible and hermetic coatings, development of surgical procedures, and vendor development of RF coils and assembly processes. We plan to have a wireless prototype chronically implanted in an experimental animal in 2005.

Development of a First Generation Wireless Implantable Retinal Prosthesis

Sponsors

National Science Foundation Contract BES-020-1681

VA Contract V523P-7057, and other VA support

Catalyst Foundation Fellowship

MOSIS provided IC fabrication

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Over the past several years, we have developed a wireless retinal prosthesis prototype with the functionality, dimensions and mechanical properties required for a human subretinal prosthesis. Figure 1 shows an artistic conception of the prosthesis. Power and data are transferred wirelessly to the implant via radiofrequency (RF) fields from the primary transmitter coils to the

secondary receiver coils. This approach avoids a cable connection between the eye and external hardware. Only the electrode array is placed in the subretinal space beneath the retina. A mockup model of the retinal prosthesis is shown in Figure 2.

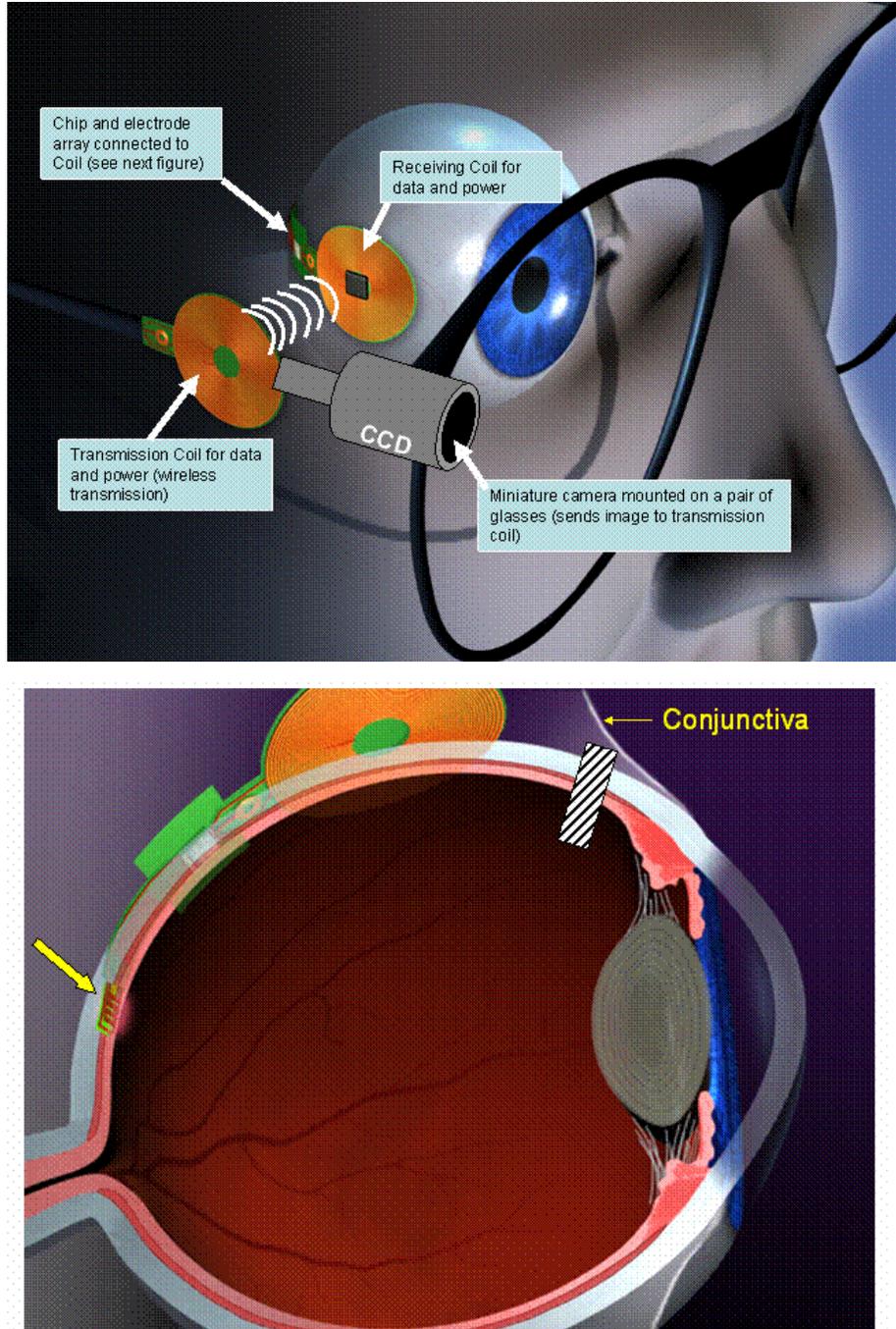


Figure 1. a) Artist's conception of the subretinal implant system. The image obtained by an external camera is translated into an electromagnetic signal wire transmitted wirelessly from the external primary data coil to the implanted secondary data coil attached to the outside wall (sclera) of the eye. Power is transmitted

similarly. Essentially the entire volume of the implant lies outside the eye, with only the electrode array penetrating the sclera. **b)** The electrode array is placed beneath the retina through a scleral flap in the sterile region of the eye behind the conjunctiva.

Mockup of First Generation Implant

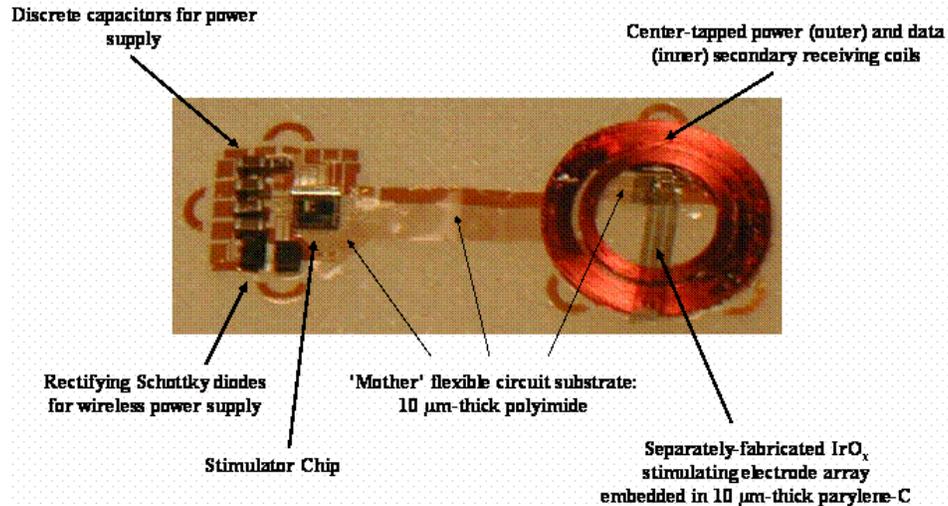


Figure 2. Detailed mockup of the first-generation implant. All parts are mounted on a 10- μm thick flexible substrate, which has conducting wires embedded within. The thin neck is placed beneath the superior rectus muscle during implantation. The implant is sutured to the sclera through the six semicircular tie points shown.

The core of the retinal prosthesis is the 25,000 transistor stimulator chip. This took us about two years to design and has been fabricated (at no expense to the project) by MOSIS. We are delighted that the first chip has passed all tests and functions as expected: it can be used in the initial implant design without modification. The chip was designed for flexibility and can operate at a wide range of externally controlled clock frequencies. It produces variable current pulse durations, amplitudes, inter-pulse intervals and selections of the set of electrodes to be stimulated.

The design and some construction and testing steps for other components of the retinal prosthesis have been carried out in-house: these include fabrication of the microelectrode array, fabrication of an initial version of the flexible substrate, development of a working electronic stimulation controller and test system, development of working power and data transmitters, and the development of a very sensitive soak testing system to check for tiny (picoampere) currents due to saline leakage. Other steps were sourced out to vendors: these include coil winding, flip-chip and wire bonding to the substrate, later versions of the polyimide flexible substrate, iridium oxide deposition on the electrodes, prolonged testing of the electrodes under repeated stimulation, and of course fabrication of the stimulator chip.

During the past five years we have radically redesigned the retinal implant. In previous designs the entire implant was intraocular and the electrode array lay on the inner epiretinal side of the retina. We have now adopted a quite different subretinal design, shown in Figures 1 and 2, where almost the entire bulk of the device is attached to the outside wall of the eye. Our surgical experience in animals suggests that this new design has the following advantages: 1) the risks of surgical trauma and infection are minimized since only the stimulating electrode array penetrates the eye, 2) there is no need to attach the electrode array to the retina with glue or tacks since the

array is sandwiched between the retina and the pigment epithelium, 3) all electronic hardware is located outside the eye so that the heat-generating electronics is not a threat to retina, 4) the relatively spacious ocular orbit (eye socket) allows us to use thicker standard hermetic encapsulation methods for the external electronics, and 5) threshold currents for stimulation of retinal neurons may be lower since the electrode array is closer to outer retinal neurons. It is noteworthy that with small modifications our subretinal prosthesis can also be converted for epiretinal stimulation, if the need arises.

We have recently completed a working “breadboard prosthesis model,” shown in Figure 3, for testing purposes prior to completing the assembly and encapsulation of the first generation implantable prosthesis. The breadboard model receives data and power wirelessly using the same primary and secondary coils, stimulator chip and electrode array as the first generation implant will use. It is built on larger printed circuit boards rather than a miniature flexible substrate but is otherwise electrically identical to the implantable version under development. It allows early testing of the entire wireless electronic system from transmitters to electrode output, as shown in Figure 4.

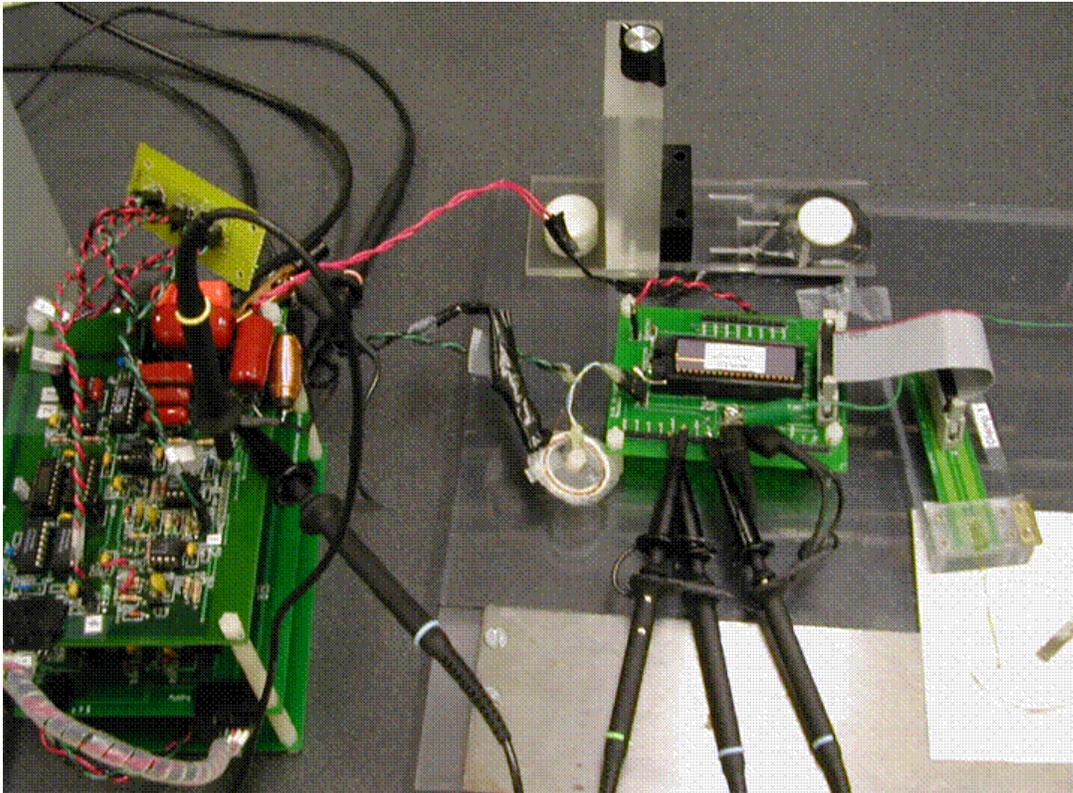


Figure 3. Breadboard prosthesis model on green printed circuit board near center of figure. Power and data transmitters are on stacked set of printed circuit boards at left. Twisted pair of red wires carries current to primary coil beneath the white disc and clear plastic layer near the top center. Twisted pair of red and black wires carries power from secondary coil to chip. Data primary and secondary coils appear as white circle at center of figure. Grey cable harness carries output from current drivers on the chip through a connector to the electrode array in clear dish of saline on white paper at bottom right. Black clips are oscilloscope probes to measure waveforms shown in Fig. 4.

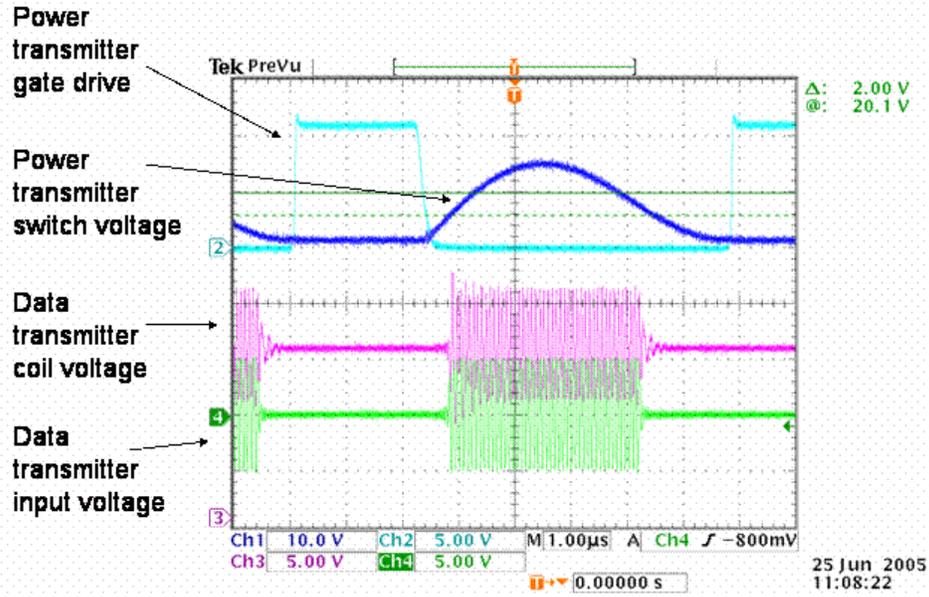


Figure 4. Operation of the power and data transmission systems. **a)** Transmitter side: Power transmitter gate drive (light blue) falls periodically at 125 KHz, causing the transmitter switch voltage (dark blue) to rise periodically at the same frequency. Data transmitter responds to a modulated 13.56 MHz input signal (green) by driving the data primary coil, producing the coil voltage shown in red. **b)** Receiver and implant side: Upper trace (blue) shows voltage output from the data secondary coil (driven by the primary coil signal shown in red at a different time scale in part a.) Middle trace (red) shows the digital signal extracted by the chip from this input. These signals control the current drive to the microelectrodes, resulting in the electrode voltage pattern shown in the bottom trace (green).

The final version of the subretinal prosthesis is now in assembly. We anticipate that two or three months will be needed to resolve assembly details with vendors, electrically and mechanically test the implant on the laboratory bench with wireless input and carry out encapsulation and initial soak testing. We plan to implant the prosthesis in the eye of a Yucatan mini-pig and demonstrate wireless stimulation with cortical signal monitoring in the Fall of 2005.

Stimulator Chip

The design architecture in Figure 5 illustrates the roles of the analog front end, the delay-locked-loop (DLL), the control logic block, and the current driver block. The chip is powered via an inductive link. Current from the power secondary is rectified and filtered using off-chip diodes and capacitors on the implant, with the nominal supply voltage being $\pm 2.5V$. Data (blue trace in Figure 4b) are received through a separate coil placed concentric to the power coil (Fig. 2). Digital data are transmitted as an amplitude shift keyed (ASK) waveform. The carrier frequencies of the power and data are 125 KHz and 13.56 MHz respectively. The analog front-end decouples data from power, while the delay-locked loop (DLL) demodulates and restores the data signal to digital levels (red trace in Figure 4b) and extracts the clock signal from the input waveform. Symbols are encoded as pulse width modulated signals with the rising edge representing a clock pulse, a 50-50% duty cycle encoding a logical 0 and a 30-70% duty cycle encoding a 1. Data and clock are fed to the control logic block. The control block controls the current driver array, which sends biphasic current pulses to the electrode array. Electrode voltage response to the current drive appears in the bottom trace (green) in Figure 4b.

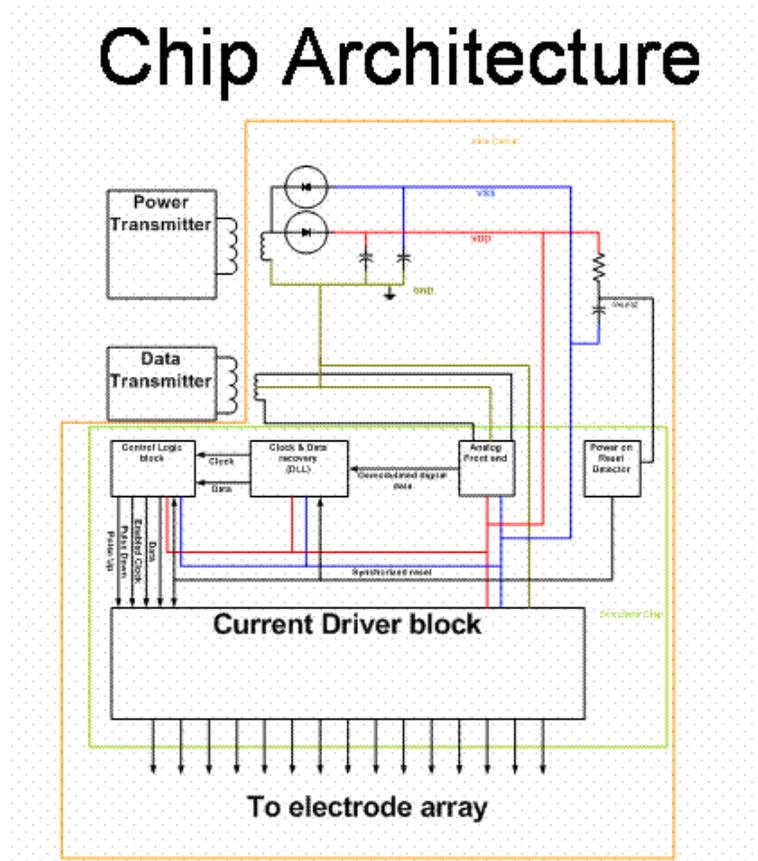


Figure 5. Overall design of the stimulator chip. Function is explained in the text.

The chip is very power-efficient, dissipating only about 1.5mW at low data rates (~100kb/secs) and about 2.5mW at higher data rates (~500kb/secs). We have tested it at a wider range of data rates from 5kb/secs to 610kb/secs. The chip is able to output 800uA per electrode. The pulse width is externally controlled, variable and shared by all electrodes on a given stimulation cycle. The external clock allows maximum control of the implant, enabling power saving when lower clock rates are acceptable.

Microfabrication of Electrode Arrays

The challenge is to create an ultrathin, flexible stimulating electrode array that will pass sufficient current and not deteriorate over years of use. We have fabricated electrode arrays with increasing amounts of charge delivery capacity, since our findings indicate that perceptual thresholds in blind patients require relatively high charge injection. This was accomplished by progressing from initial work with Pt electrodes, to electrochemically activated iridium metal electrodes, to electrodeposited iridium oxide and most recently, to reactively sputtered iridium oxide. This is a pioneering development, since commercial companies developing retinal implants have made the more conservative choice of Pt for their electrodes, despite its charge capacity limitations.

Creation of Flexible Circuits and Implant Assembly and Packaging Technologies

The flexible circuit (Fig. 2) forms the substrate onto which the electronic components of our prosthesis are assembled. Two generations of flexible circuits have been developed by our center and microfabricated with wire-bondable electroplated gold traces 50 microns wide and 3 microns thick on both polyimide and parylene. Strategic alliances were created with fabrication, assembly, and packaging vendors with experience in implantable devices, and a CRADA agreement has been initiated between the VA and Greatbatch-Hittman, Inc. to develop micropackaging technology for future generations of retinal implants.

Wireless Data and Power Transmission System

We have built and tested the power and data transmitters for powering the implant and providing stimulation data for the current sources. Our design was guided by the understanding that high data rates require a high frequency carrier, but power transmission at high frequencies is inefficient. We transmit implant power very efficiently at a low frequency (125 KHz), while the data is transmitted at a high frequency (13.56 MHz).

We use a high-efficiency class E oscillator to transmit power and a simpler but lower efficiency class A amplifier to transmit the lower power data stream. The top two traces in Figure 4a are taken from the power transmitter and the lower two from the data transmitter.

Publications

Journal Articles

Published

1. J.R. Rizzo, S. Goldbaum, M. Shahin, T.J. Denison, J. Wyatt, "In Vivo Electrical Stimulation of Rabbit Retina with a Microfabricated Array: Strategies to maximize responses for prospective assessment of stimulus efficacy and biocompatibility," **Restorative Neurology and Neuroscience** 22: 429-443: (2004).
2. R. Hornig, T. Laube, P. Walter, M. Velikay-Parel, N. Bornfeld, M. Feucht, H. Akguel, G. Rossler, N. Alteheld, D. L. Notarp, J. Wyatt and G. Richard, "A Method and Technical Equipment for an Acute Human Trial to Evaluate Retinal Implant Technology," **Journal of Neural Engineering**, 2 (1), 129-134, (2005).

Meeting Papers

Presented

Wyatt, J.L., J.F. Rizzo, L. Theogarajan, D.B. Shire, S.K. Kelly, M.D. Gingerich, S. Cogan, M. Markova, O. Ziv, "Engineering Development of a Prototype Wireless Subretinal Prosthesis," **ARVO Lecture Abstract, Investigative Ophthalmology and Visual Science**, Ft. Lauderdale, FL, May 1-5, 2005, abstract 1146.

Gingerich, M.D., D.B. Shire, J. Chen, J. Loewenstein, H.A. Shah, J. Sun, J.L. Wyatt, J.F. Rizzo, "Surgical Guides for Electrode Array Implantation into the Subretinal Space," **ARVO Poster Abstract, Investigative Ophthalmology and Visual Science**, Ft. Lauderdale, FL, May 1-5, 2005, abstract 1494.

Shire, D.B., M. Gingerich, J.F. Rizzo, J.L. Wyatt, "Recent Developments in Inflatable Prostheses for Epiretinal Stimulation and/or Recording," **ARVO Poster Abstract, Investigative Ophthalmology and Visual Science**, Ft. Lauderdale, FL, May 1-5, 2005, abstract 1534.

J. L. Wyatt, "Engineering Development of a Subretinal Prosthesis," The Second DOE International Symposium on Artificial Sight, Ft. Lauderdale, FL, 2005.

Published

Kelly, Shawn K. and John Wyatt, "A Power-Efficient Voltage-Based Neural Tissue Stimulator with Energy Recovery," **ISSCC 2004**, San Francisco, CA, 2004.