Artificial Retina

Department of Energy

Restoring Sight Through Science

April 18, 2005

The Second DOE International Symposium on Artificial Sight

Symposium Book

Welcome to

The Second DOE International Symposium on Artificial Sight

April 29, 2005
Ft. Lauderdale, Florida

7:00 am	**REGISTRATION, CONTINENTAL BREAKFAST**
8:00	**Greetings and Introduction** **Mark S. Humayun, *Symposium Chair, Doheny Eye Institute and University of Southern California Medical School*** **Elias Greenbaum, *Symposium Co-Chair, Oak Ridge National Laboratory***
8:05	**Michael V. Viola, *Director, Medical Sciences Division, DOE Office of Biological and Environmental Research*** **Dean A. Cole, *Artificial Sight Program Manager, Medical Sciences Division, DOE Office of Biological and Environmental Research***
8:20	**Keynote Speaker** **Yasuo Tano, *Osaka University* — "Artificial Vision: Vision of a Newcomer"**
SESSION 1, HUMAN TESTING **Mark S. Humayun, Chair, *Doheny Eye Institute and University of Southern California Medical School***	
8:40	**Mark S. Humayun, *Doheny Eye Institute and University of Southern California Medical School* — "Clinical Results of a 16 Channel Microelectronic Retinal Stimulator in 6 Blind Patients"**
9:00	**Alan Y. Chow, *Optobionics Corporation* — "Five Year Update of RP Patients Implanted with the Artificial Silicon Retina Microchip"**
9:20	**Eberhart Zrenner, *Tübingen University Eye Hospital* — "Proposal for Harmonization of Functional Tests in Patients with Retinal Prostheses"**
9:30	**Joseph F. Rizzo, *Massachusetts Eye & Ear Infirmary, Harvard University* — "Unexpected Perceptual Results from Electrical Stimulation of Human Retina"**
9:40	**Thomas Zehnder and Ralf Hornig, *IIP Technologies* — "The IIP Retinal Implant"**
9:50	**Panel Discussion. All Speakers**
10:20	**BREAK**
SESSION 2, NEUROBIOLOGY OF THE DEGENERATE RETINA; EFFECTS OF BLINDNESS ON THE BRAIN **Robert E. Marc, Chair, *University of Utah School of Medicine***	
10:40	**Robert E. Marc, *University of Utah School of Medicine* — "Retinal Remodeling: The Dynamics of Retinal Disease"**
11:00	**Ione Fine, *Department of Ophthalmology and Zilkha Neurogenetic Institute, University of Southern California* — "Cortical Plasticity–The Effects of Sensory Deprivation"**
11:20	**Panel Session: R. Marc, S. Sadda, J. Chader, R. Iezzi, I. Fine**
12:00 pm	**LUNCH, POSTER SESSION**

SESSION 3, ELECTRICAL AND THERMAL EFFECTS ON NEURAL TISSUE **Frank Werblin, Chair, *University of California, Berkeley***	
1:20 pm	**Chris Sekirnjak, *Salk Institute for Biological Studies* — "Electrical Stimulation of Mammalian Retinal Ganglion Cells Using Dense Arrays of Small-Diameter Electrodes"**
1:40	**Shelley Fried, *University of California, Berkeley* — "One Pulse—One Spike: A Technique for Precise Temporal Control of Retinal Spiking Elicited by Prosthetic Devices"**
2:00	**John R. Hetling, *University of Illinois, Chicago* — "Dissecting the Retinal Response to Electrical Stimulation"**
2:20	**Gianluca Lazzi, *North Carolina State University* — "Electromagnetic Deposition, Temperature Increase, and Current Spread in the Retina and Surrounding Tissues Due to the Operation of a Dual-Unit Retinal Prosthesis"**
2:40	**Douglas B. McCreery, *Huntington Medical Research Institutes* — "Microstimulation with Chronically Implanted Cortical Microelectrodes"**
3:00	**BREAK**
SESSION 4, ELECTRODE TECHNOLOGY, PACKAGING, MATERIALS, FABRICATION AND BIOTELEMETRY **James D. Weiland, Chair, *Doheny Eye Institute and University of Southern California Medical School***	
3:20	**Philip Troyk, *Illinois Institute of Technology* — "Technological Challenges for Visual Prostheses"**
3:40	**John L. Wyatt, *Massachusetts Institute of Technology* — "Engineering Development of a Chronic Subretinal Prosthesis"**
4:00	**Thomas Stieglitz, *University of Freiburg* — "Development of a Micromachined Epiretinal Vision Prosthesis"**
4:20	**Jun Ohta, *Nara Institute of Science and Technology* — "LSI-Based Stimulus Electrodes for Retinal Prosthesis"**
4:40	**BREAK**
4:50	**Gregory W. Auner, *Wayne State University* — "Development of a Wireless High Frequency Microarray Implant for Retina Stimulation"**
5:10	**Orlando Auciello, *Argonne National Laboratory* — "Science and Technology of Ultrananocrystalline Diamond Films as Hermetic Bioinert Coatings for Artificial Retina Microchip Encapsulation"**
5:30	**Wental Liu, *University of California, Santa Cruz* — "Challenges in Realizing a Chronic High Resolution Artificial Sight Device"**
POSTERS **Elias Greenbaum, Chair, *Oak Ridge National Laboratory***	
6:00	**Posters Session with hors d'oeuvres; Cash bar**
7:30	**Adjourn**

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CLINICAL RESULTS OF A 16 CHANNEL MICROELECTRONIC RETINAL STIMULATOR IN 6 BLIND PATIENTS

M. Humayun[1], R.Freda[1], I. Fine[2], A. Roy[3], H. Ameri[1], G.Fujii[1], R.N.Agrawal[1], R.J.Greenberg[3], J.Little[3], B.Mech[3], J.D. Weiland[1], E.de Juan[1]

[1]Doheny Eye Institute, [2]Zilkha Neurogenetic Institute-University of Southern California, [3]Second Sight Medical Products, Inc.

An FDA approved clinical trial was undertaken to evaluate an epiretinal prosthesis implanted in subjects with bare or no light perception due to retinitis pigmentosa. Subjects were screened using visual psychophysics, electrophysiology, ophthalmic photography, and scanning laser ophthalmoscopy. Six subjects who met study criteria were implanted with a Second Sight intraocular epiretinal prosthesis in the eye with worse vision. Implants consist of an extraocular microelectronic device and an intraocular electrode array, connected by a multiwire cable. The electrode array is a 4x4 grid of platinum electrodes embedded in silicone rubber. Electrodes are wirelessly activated using an external controller. Electrical stimulation was begun between 7 and 15 days post-operative. As of March 2005 6 subjects have been implanted for 8-36 months. Thresholds varied both within and across subjects. S1: 35-1121 uA; S2: 16 – 777 uA; S3: 18 – 412 uA; S4: 20 – 385 uA; S5: 10 – 31 uA; S6: 6 – 41 uA. Five patients demonstrated measurable pupil constriction in response to stimulation with their IRP. Electrical stimuli parameters set to produce optimal visual perception for 2 seconds resulted in an average percent pupil constriction of 23% SD 7.5%. The average time to maximum pupil constriction at these settings was 1557 msec SD 327 msec. Average latency of onset of constriction was 510 msec SD 195 msec after the initiation of the stimulus. Performance using the head mounted video camera suggests that patients are capable of interpreting patterned electrical stimulation. Subjects can localize the position of, or count the number of, high contrast objects with 74-99% accuracy (3 or 4 Alternative Forced Choice (AltFC)), and can discriminate simple shapes such as the orientation of a bar or an “L” (2 or 4AltFC) with 61-80% accuracy. There was no improvement in perceptual acuity when the device was electrically inactive, suggesting that electrical stimulation did not improve the health or function of the retina

*The Science and Engineering of the Intraocular Retinal Prosthesis has been supported by the Office of Biological and Environmental Research, US Department of Energy, the National Science Foundation Engineering Research Center on Biomimetic MicroElectronic Systems (EEC-0310723), the National Eye Institute (1R24EY12893 and EY03040), Research to Prevent Blindness, and Second Sight Medical Products, Inc.

LONG-TERM UPDATE OF THE ARTIFICIAL SILICON RETINA MICROCHIP FOR THE TREATMENT OF RETINITIS PIGMENTOSA

Alan Y. Chow[1], John S. Pollack[2], Kirk H. Packo[2], Ronald A. Schuchard[3]

[1]Optobionics, Naperville, IL; [2]Ophthalmology, Rush Medical Center, Chicago, IL; [3]Ophthalmology, Atlanta VA Rehab R&D, Emory University Eye Center, Atlanta, GA

The long-term durability and biocompatibility of a subretinal Artificial Silicon Retina (ASR) microchip and its capacity to restore visual function in 10 retinitis pigmentosa (RP) patients was studied. A microphotodiode-based ASR microchip that electrically stimulated the inner retina was implanted into the subretinal space 20 degrees from the macula in each of 10 RP patients and followed for 2 to 4 ½ years. Visual function was evaluated by ETDRS letters, grating acuity and automated visual fields. The ASR devices were also stimulated with infrared light to assess implant electrical activity as recorded by ERGs. All patients tolerated the ASR microchip safely. One patient, who underwent subsequent phacoemulsification cataract removal in the implanted eye, developed a superior migration of the implant and subretinal hemorrhage which resolved within 6 weeks. The hemorrhage and implant migration may have been caused by implant vibration due to the ultrasound energy. Implant electrical function was still present at 4 ½ years after implantation although with decreased electrical spike amplitude. Objective and subjective improvements in multiple areas of visual function have persisted for 4 1/2 years in the longest implanted subjects, although 1 of 3 in this group noted some diminution from the best improvement. Some patients implanted for 2 years still demonstrate improving visual function. The greatest improvement has been in optotype and grating acuity, and in contrast perception. The subretinal ASR microchip is well tolerated in RP patients. High-powered ultrasound procedures in implanted eyes should be avoided. Persistent improvements of visual function in the retina both adjacent to and distant from the ASR implant suggest a persistent neurotrophic benefit of the ASR chip in RP patients.

PROPOSAL FOR HARMONISATION OF FUNCTIONAL TESTS IN PATIENTS WITH RETINAL PROSTHESES*

E. Zrenner[1], M. Bach[2], B. Wilhelm[1], C. Kuttenkeuler[1], R. Wilke[1], W. Durst[1], H. Sailer[3], H. Stett[3], H. Sachs[4], V.-P. Gabel[4]

[1]University Eye Hospital, Tübingen, [2]University Eye Hospital, Freiburg,[3]Nature and Medical Science Institute, Reutlingen, [4]University Eye Hospital, Regensburg, all Germany

Purpose: Electronic prostheses for restitution of visual function have been developed for subretinal and epiretinal coupling, as well as for the optic nerve and the visual cortex. There is a need for standardized procedures to assess the functional outcome gained by the image transfer properties of such devices.
Methods: In order to define a minimum set of tests that assess the characteristics of neuroprostheses for visual functions, we propose laboratory tests based strictly on psychophysical threshold assessments additionally to descriptions of field experiments. Tests are presented on a high luminance display screen (max.700 cd/m^2) subtending 25° by 15°. In an increasing series of visual processing demands, psychometric functions are determined by an automated test procedure, taking account of learning and variability.
1. Fixation: Presentation of a bright dot, so that the patient can localize the area where to expect a test target after a tone; measuring time until target is found.

2. Light perception: the patient is being presented 1 or 2 Ganzfeld flashes (with an interval t1) and indicates whether 1 or 2 flashes were seen.
3. Temporal resolution: the interval t1 is varied between the 2 flashes.
4. Location: In addition to a continuous fixation target, a circular stimulus appears at one of 8 different locations with a fixed eccentricity e1.
5. Motion: a random multi-hexagonal black and white pattern of high contrast with an individual hexagon subtending 1° of visual angle is moved in 8 different directions. Frequency-of-seeing characteristics are obtained for various speeds and contrasts.
6. The spatial frequency of a sinusoidal bar pattern is determined the direction of which be correctly recognized by the patient in a four alternative forced choice situation.
7. Further test subunits include spatial resolution and contrast vision by varying size and luminance of targets, optokinetic nystagmus and pupillary light reflexes supplemented by assessing a standardized life quality assessment form.
Summary: We recommend a battery of computerized, standardized tests for patients with visual prostheses to quantify the functional outcome. Common clinical tests insufficiently describe improvements gained by various chip-types, because these test settings are prone to a number of effects not necessarily related to chip-performance.

*Research supported by BMBF 01K008 and Alexander von Humboldt Foundation IV-JAN/1112777 STP

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BIOLOGICAL CONSIDERATIONS FOR A SUB-RETINAL PROSTHETIC IMPLANT

Joseph F. Rizzo, III, M.D.

Massachusetts Eye and Ear Infirmary and the Boston VA Health Care System

Our Boston-based Retinal Implant Project has been developing a sub-retinal prosthesis to restore vision to the blind. The engineering details of this device will be described in this meeting by Professor John Wyatt. Various biological considerations related to the implementation of our device are considered in this presentation. In summary, we have performed extensive evaluations of surgical methods to implant our device and to study the biological reactions that develop following implantation of materials into the sub-retinal space. With respect to the surgery, we are attempting to develop a minimally invasive surgical approach in which we utilize a posterior, ab externo means to implant the prosthesis and insert the stimulating electrode array, ;which is the only part of our prosthesis that will be within the eye. This work, which has been performed on rabbits, pigs and dogs, has yielded a success rate of roughly 70%, which is not yet acceptable for use in humans. We have recently identified a promising means of protecting the retina during the insertion of the electrode array, which is the riskiest part of the surgery. With respect to the biocompatibility of materials in the sub-retinal space, we have demonstrated with chronic implantation studies that a wide range of materials can be implanted without inducing vigorous reactions. More specifically, there was relatively little reaction around 4 of the 6 materials that we implanted, which increases our hope that the one portion of our device that will be intraocular (i.e. the electrode array) may be tolerated within acceptable limits following long-term implantation.

THE IIP RETINAL IMPLANT *

Thomas Zehnder[1], Ralf Hornig[1], Michaela Velikay-Parel[2], Thomas Laube[3], Norbert Bornfeld[3], Matthias Feucht[4], Gisbert Richard[4]

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[2]Universitäts-Augenklinik Graz, Graz, Austria
[3]Universitäts-Augenklinik Essen, Essen, Germany
[4]Universitäts-Augenklinik Hamburg-Eppendorf, Hamburg, Germany

Our group is developing a visual prosthesis for the stimulation of retinal nerve cells with epi-retinal micro-electrodes. The system consists of an implantable Retina Stimulator and several external components. The Retina Stimulator contains an electrode array which is positioned in the area of the macula. The external components comprise a camera and a wireless transmission unit supplying the Retina Stimulator with energy and data. These parts are mounted on a pair of glasses and are connected to a microprocessor carried on a waist belt. The microprocessor provides the image processing and user interface for the system. It also contains a rechargeable battery which supplies the whole system with energy.

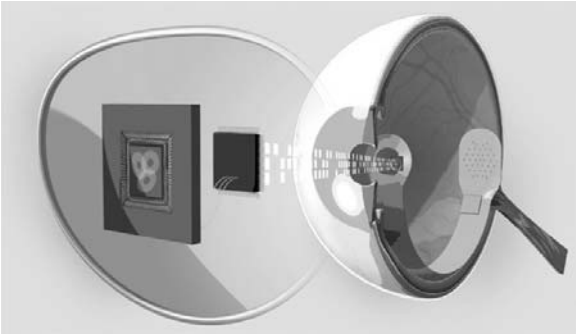

Figure 1 Schematic view of the Retinal Implant system

The safety of electrical stimulation with this Retinal Implant was tested in an acute animal trial with Göttingen Minipigs. We found that 1 mC/cm^2 is a reasonable safety level for retina stimulation with IrOx electrodes. We performed an acute clinical trial with 20 retinitis pigmentosa patients to investigate the functional interface between Retinal Implant and human body. An electrode array was introduced into the eye of the patients and activated using a series of defined current pulses. The visual perceptions of the patients, if any, were recorded. In this patient group we found perception thresholds between 20 and 380 nC per phase for single electrode activation.

*Supported by IIP-Technologies and the European Union.

RETINAL REMODELING: THE DYNAMICS OF RETINAL DISEASE. *

Robert E. Marc, Carl B. Watt, and Bryan W. Jones

Moran Eye Center, University of Utah

Purpose: Phase 3 remodeling is a challenge to integrating bionic devices with the retina in retinitis pigmentosa (RP). We are analyzing the connectivity of rewiring and functional signaling in these retinas. Methods: Human and rodent retinas expressing RP phenotypes were probed by transmission electron microscopy, computational molecular phenotyping (which classifies cells by their small-molecule signatures), and excitation mapping (which reports excitation history using the channel permeant organic cation 1-amino-4-guanidobutane). Results: Microneuromas formed during retinal remodeling are fundamentally corruptive and appear unable to support "visual" signal processing. The phase 1 loss of bipolar cell dendrites persists into phase 3 as an absence of KAr and AMPAr mediated drive. Even so, intrinsic activity occurs which suggests that remodeling uncovers "oscillators" among surviving amacrine cells. Finally, cone survival is the key to preventing remodeling. Human RP retinas possessing no rods and transformed cones show completely normal glutamate receptor function. Conclusion: When deprived of cones, the remnant neural retina will rewire in anomalous patterns and bipolar cells do not restore their dendrites or receptors, even in microneuromas. Conversely, the survival of even transformed cones completely rescues the neural retina.

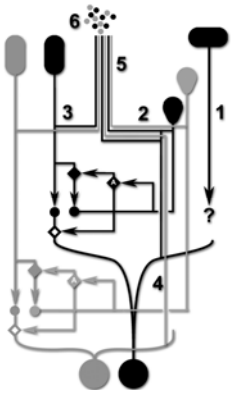

Figure 1. In phase 3, survivor neurons generate new processes. HCs generate axon-like processes (1). ACs form processes (2) that make pre- and postsynaptic contacts. BCs regenerate axons (3), while GCs produce axons and dendrites (4). All can be found in mixed fascicles of neurites (5) terminating in microneuromas (6).

*Research supported by NIH R01 EY02576, EY015128 and Research to Prevent Blindness.

THE EFFECTS OF VISUAL DEPRIVATION*

Ione Fine[1], Alex R Wade[2], Geoffrey M Boynton[3], Brian A Wandell[4] and Donald IA MacLeod[5]

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"Suppose a man born blind, and now adult, and taught by his touch to distinguish between a cube and a sphere … Suppose then … the blind man made to see … Query: whether by his sight, … he could distinguish and tell which is the globe, which is the cube?" Despite the philosophical and psychological interest of Molyneaux's question, cases of adult sight restoration are so rare that even now little is known about perceptual experience after long-term visual deprivation.

We characterized visual processing in a patient (MM) whose cornea was restored by stem cell replacement after suffering severe visual deprivation between the ages of 3 and 43. Deprivation resulted in a behavioral and neural shift in spatial frequency tuning towards low spatial frequencies. MM also showed behavioral and neural impairments in 3D shape perception, object and face recognition. In contrast, MM's performance on color and motion tasks was relatively normal. Consistent with this behavioral data, fMRI activity in MMs MT complex appeared relatively normal.

Long-term interruptions in visual experience, even beyond the traditional critical period, have significant effects on visual processing that differ across visual functions and areas.

*Research supported by the National Instiute of Health, EY014645.

ELECTRICAL STIMULATION OF MAMMALIAN RETINAL GANGLION CELLS USING DENSE ARRAYS OF SMALL-DIAMETER ELECTRODES*

Chris Sekirnjak[1], Pawel Hottowy[2], Alexander Sher[3], Wladeck Dabrowski[2], Alan M. Litke[3] and E. J. Chichilnisky[1]

[1]The Salk Institute for Biological Studies, San Diego, CA, [2]University of California, Santa Cruz, CA, [3]AGH University of Science and Technology, Kraków

Current epiretinal implants contain a small number of electrodes with diameters of a few hundred µm. Smaller electrodes are desirable to increase the spatial resolution of artificial sight. To lay the foundation for the next generation of retinal prostheses, we assessed the stimulation efficacy of micro-fabricated arrays of 61 platinum disk electrodes with diameters 5-20 µm, spaced 60 µm apart. Isolated pieces of rat, guinea pig, and monkey retina were placed on the multi-electrode array ganglion cell side down and stimulated through individual electrodes with bipolar, charge-balanced current pulses. Spike responses from retinal ganglion cells were recorded either from the same or a neighboring electrode. Most pulses evoked only 1-2 spikes with short latencies (0.3-10 ms), and rarely was more than one ganglion cell stimulated. Threshold charge densities for eliciting spikes in ganglion cells were typically below 0.15 mC/cm^2 for pulse durations between 50-200 µs, corresponding to charge thresholds of ~100 pC. Stimulation was achieved continuously for several hours and at frequencies up to 100 Hz. Application of cadmium chloride did not abolish evoked spikes, implying direct activation. Thus, electrical stimulation of mammalian retina with small-diameter electrodes is achievable, providing high temporal and spatial precision with low charge densities.

*****Research supported by the Salk Institute Pioneer Postdoctoral Fellowship, Second Sight LLC, and NEI grant 13150 (EJC), NSF Awards PHY-0245104 and PHY-0417175 (AML), Polish State Committee for Scientific Research, Project 3 T11E 011 27 (WD), NATO Collaborative Linkage Grant (AML & WD)

ONE PULSE – ONE SPIKE: A TECHNIQUE FOR PRECISE TEMPORAL CONTROL OF RETINAL SPIKING ELICITED BY PROSTHETIC DEVICES *

Shelley Fried[1], Hain-Ann Hsueh[2] and Frank Werblin[3]

[1]Vision Science, [2] Biomedical Engineering, [3]Molecular & Cell Biology
University of California, Berkeley

We have developed a stimulus protocol that reliably elicits one ganglion cell spike for each electrical stimulus pulse. On-cell patch clamp recordings were used to measure spiking responses from individual retinal ganglion cells in the flat mount rabbit retina. Small tipped platinum-iridium epiretinal electrodes were used to deliver electrical stimulus pulses.

Long duration electrical pulses (1 msec) elicited a single spike within 0.5 msec of the pulse onset followed by a train of spikes which could persist for more than 50 ms depending on pulse amplitude levels. But only the first directly-driven spike remained intact in the presence of pharmacological blockers of excitatory synaptic input, suggesting that all subsequent spikes are driven by input from presynaptic cells. Short duration pulses (0.1 msec) also elicited the single directly-driven spike without generating later spikes from presynaptic activity suggesting that short pulses activate only ganglion cells. These short duration pulses reliably elicited a single spike per pulse at frequencies up to 200 Hz.

The short duration pulse paradigm can be used to generate spiking patterns of activity in ganglion cells that mimic physiologically-relevant light-evoked responses. Controlled trains of short pulses can mimic the normal modulations of spike frequency associated with changes in intensity or contrast.

*Research supported by DARPA, NIH, Second Sight.

DISSECTING THE RETINAL RESPONSE TO ELECTRICAL STIMULATION *

John R. Hetling[1,2], Monica S. Baig-Silva[1], Casey R. Hathcock[1]

[1]Department of Bioengineering, [2]Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL

Purpose. Understanding the cellular targets of electrical stimulation will be useful in designing microelectrode-based retinal prostheses. The present work adapts traditional retinal electrophysiology techniques to study the response to focal electrical stimuli in rat. **Methods.** Microelectrode arrays (Fig. 1) were placed acutely in the subretinal space. The response of the retina to focal electrical stimulation was recorded at the cornea; this response is termed the eERG (electrically-stimulated electroretinogram). The ERG and the eERG were recorded before and after intravitreal injection of pharmacological agents known to block specific synaptic loci in the retina (ASP, L-AP4, PDA). Subtraction of the pre-injection response from the post-injection response revealed the agent-sensitive components in both wild-type and P23H transgenic rats (a model of autosomal dominant retinitis pigmentosa). **Results.** The eERG is a complex waveform, typically consisting of corneal negative and positive slow waves, and higher frequency oscillations. Pharmacological dissection of the eERG reveals no simple correlation between components of the eERG with those of the single-flash corneal ERG (a-wave, b-wave, oscillatory potentials). The primary target of biphasic stimuli delivered via bipolar subretinal electrodes appears to be the outer nuclear layer. **Conclusion.** The eERG, once fully described, may serve as a non-invasive diagnostic for evaluating the efficacy of retinal stimulation in animal studies.

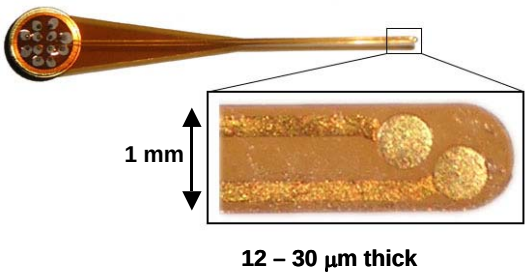

Figure 1. Completed retinal stimulating array (RSA) and cable connector. RSA devices have 12 holes at the connector breakout (left in photo, extra-ocular during use) through which connector pins penetrate; pins make electrical contact with metal traces via conductive epoxy. Each conductive trace extends to the narrow end of the device and terminates in an electrode (right in photo, intra-ocular during use); the RSA device shown uses only two pins to connect with two electrodes. Thickness is 12 microns, width at electrode end is 1 mm, and total length is 5 cm. Any arbitrary electrode design with feature size >10 microns can be readily fabricated in the UIC Microfabrication Applications Lab.

*Research supported by the Whitaker Foundation.

ELECTROMAGNETIC DEPOSITION, TEMPERATURE INCREASE, AND CURRENT SPREAD IN THE RETINA AND SURROUNDING TISSUES DUE TO THE OPERATION OF A DUAL-UNIT RETINAL PROSTHESIS*

Carlos J. Cela, Stefan Schmidt, Sundar Srinivas, Vinit Singh, and Gianluca Lazzi[1]

[1]Department of ECE, NC State University, Raleigh NC 27695

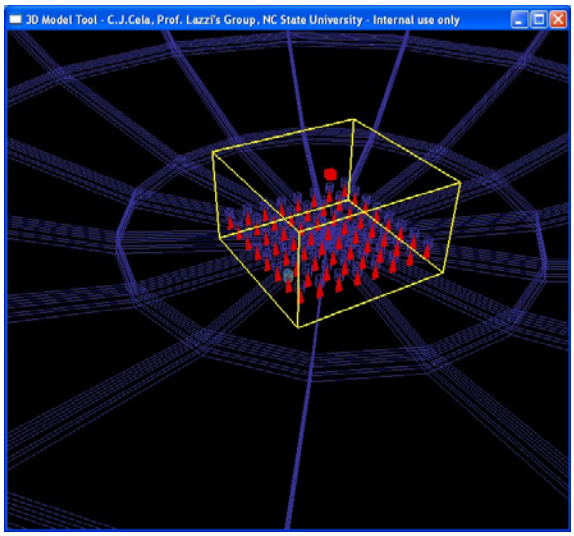

Figure 1. Geometric description of classified retina (transparent), shown with 8x8, 120µm electrode array, for the computation of the current spread in the retina with the multiresolution impedance method. Fundamental resolution is 20 µm.

In this paper we will present recent advances in electromagnetic and thermal modeling of a dual-unit retinal prosthesis. The focus is on computational methods to quantify electrical and thermal deposition in the human tissue with the ultimate goal of minimizing safety concerns and optimizing the overall performance of the system. We will present the latest methods and results for the computation of the temperature increase due to the implanted electronics, electromagnetic absorption due to the external power and data telemetry link, electrical parameters of the radiating and receiving telemetry devices, and current spread in the neural tissue as a function of the geometrical characteristics of the stimulating electrode array. Temperature increase due to the implanted microchip, coils, and stimulating electrode array as a function of power will be shown; location of the electronic components and considerations regarding their individual power dissipation characteristics will be discussed. The effect of electromagnetic radiation due to external telemetry devices (low or high frequency) will also be discussed, with consideration of the Specific Absorption Rates (SARs) needed to meet international electromagnetic safety standards. Finally, we will consider the variations of current spread in the retina and eye due to various electrode array geometries and placement configurations. To this end, we will describe in detail our computational approach based on our own multiresolution impedance method, which will provide the possibility of incorporating in the computational mesh both micro- and macro scale phenomena. Opportunities to include neural cell models in the macro-scale electrical current spread modeling will be discussed, along with the inclusion of other quasi-static effects that represent a challenge for electrical stimulation, such as contact capacitances. In this presentation we will also briefly show how computational methods such as the partial inductance method or the finite-difference time-domain method can provide important parameters for the design of the radiating telemetry devices, ranging from inductance and mutual inductance of coupled coils to SAR computations.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

MICROELECTRODE ARRAYS FOR AN INTRACORTICAL VISUAL PROSTHESIS

Douglas McCreery, Panya Manoonkitiwongsa and Xingdong Liu

Huntington Medical Research Institutes, Pasadena CA

A visual prosthesis based on intracortical microstimulation will entail implantation of a large number of microelectrodes into the primary and/or secondary visual cortex. These cortical areas, with their often complex surface geometry, can best be covered by implanting multiple integrated arrays of moderate size (about 3 mm in diameter) each containing a modest number of individual microelectrodes. At HMRI, array of 16 discrete activated iridium microelectrodes (Fig. 1), each 50 µm in diameter (Fig. 2), have been implanted for more than a year into the cerebral cortex of adult cats. Histologic evaluation of the electrode tips sites has shown some loss of neurons within about 50 µm of unpulsed microelectrodes, but essentially normal neuronal density and normal-appearing neuropil beyond that distance. Seven hours of continuous pulsing of the microelectrodes at 50 Hz and 4 nanocoulombs per phase resulted in marked depression of the electrical excitability of nearby neurons. Prolonged (e.g 10 days) of stimulation with these same parameters resulted in some loss of neurons near the pulsed tips. However, these parameters are well in excess of what is required to excite nearby neurons. These continuing studies illustrate the importance of carefully tailoring the parameters of intracortical microstimulation to the particular application.

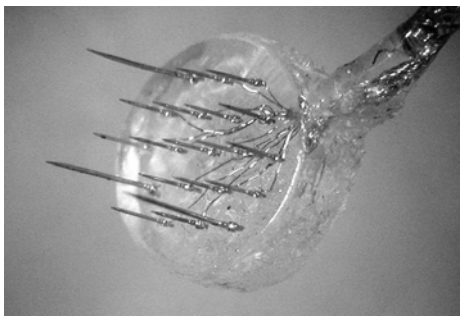

Figure 1

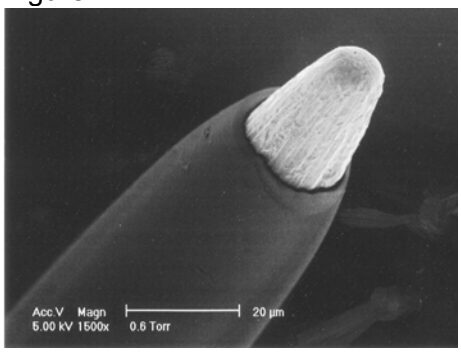

Figure 2

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Supported in part by a Bioengineering Research Partnership grant from the National Institutes of Health (RO1-NS40690-01A1)

TECHNOLOGICAL CHALLENGES FOR VISUAL PROSTHESES*

Philip R. Troyk
Illinois Institute of Technology

Research towards a neural prosthesis for restoration of vision in humans has a history dating back to the pioneering work of Giles Brindley in the late 1960's. Although this initial investigation, and subsequent work focused on stimulation of the primary visual cortex, more recently many groups have emerged that are considering electrical stimulation at the retina. Estimations of the minimal number of stimulation electrodes that might provide some usable sensory function are crude at best. However most groups, whether working at the cortex or the retina, have used the figure of ~1000 as a target number of stimulation sites. Although retinal stimulation seems attractive from the standpoint of spatial mapping and neural coding, the engineering challenges, for design of implantable electrodes and hardware, faced by designers of retinal prostheses are formidable. In contrast, the cortex, by virtue of its relatively larger size, presents a more manageable situation from the standpoint of implantable hardware design. However, the distorted mapping and convoluted geometry of the cortex does not allow for a straightforward relationship between placement of electrodes and visual percepts. Therefore, the cortex presents a considerable challenge in understanding what stimulation strategies might be used to communicate with the cortex. For both cortical and retina systems, a stable electronic/neural interface must be established, i.e. an electrode interface that allows for chronic injection of electrical charge without deterioration of the electrodes or surrounding neural tissue; The "ideal" microstimulation electrode remains elusive. Packaging of electronic circuitry and routing of lead wires to the electrodes remains unsolved for both the retinal and cortical approaches, although some proposed designs are now being evaluated. And, processing of images, captured by an electronic imaging device, and the conversion of the image information into neural stimulation pulses that allow for interpretation of the artificial input to the human visual system have not yet been demonstrated in a manner that mimics natural vision. The premise that with enough phosphenes an image will be perceived, remains conceptual. During the past year, we have considered all three of these issues relative to the feasibility of an intracortical visual prosthesis system.

*Research supported by the National Institutes of Health, NIBIB

DEVELOPMENT OF A MICROMACHINED EPIRETINAL VISION PROSTHESIS*

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The potential of microsystem technology was used to design and develop an epiretinal vision prosthesis within the EPI-RET consortium in Germany. Fundamental work was done to design a substrate with integrated electrodes and to develop an assembling and packaging technology that preserves material and system properties to obtain good surface and structural biocompatibility. Design studies led to a polyimide-based electrode carrier that allows an adaptation to the eye globe with little stress on the retina after tack fixation. The implant was designed with an inductive link for energy supply and data transmission that was located within an artificial intraocular lens (IOL). An integrated ribbon cable leads to the electrode array where an application specific integrated circuit (ASIC) has to select electrodes and to deliver current pulses. Hybrid assembling techniques were applied to ensure high flexibility during microelectronic development cycles and system changes. Parylene C was deposited as encapsulation layer over the implant except the electrode array. The receiver and current source part were additionally encapsulated in silicone rubber. So far, chronic animal experiments proved the functionality of an implant test system for one year. Cortical activation of a 25 channel implant was proven in cats with an inductively powered system.

*Research supported 1995-2003 by the German Federal Ministry for Education and Research when the author was with the Fraunhofer Institute for Biomedical Engineering (St.Ingbert / Germany).

LSI-BASED STIMULUS ELECTRODES FOR RETINAL PROSTHESIS*

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[2] Vision Institute, Nidek Co., Ltd.
[3] Department of Visual Science, Osaka University Medical School
[4] Department of Ophthalmology, Osaka University Medical School

We have developed an LSI-based stimulus electrode array for suprachoroidal transretinal stimulation and subretinal stimulation. The array consists of several microchips based on Si-LSIs, each about 500 μm square (Fig. 1). Each microchip has nine Pt/Au stacked bump electrodes compatible with standard LSI structures (Fig. 1(b)). The microchips connect to each other via two wires, not including the power supply lines, and are set on a flexible polyimide substrate. Notable features of our device are as follows. First, it is thin and bendable, as shown in Fig. 1(c), enabling close contact with ocular tissues when implanted. Second, introducing an LSI into the microchip makes it possible to integrate smart functions such as, for example, a photosensor able to_generate biphasic pulses in subretinal stimulation. This provides the device with high performance and versatility. In addition, the LSI reduces the input/output pads needed in the device: only the two signal lines of stimulation and control are required apart from the power supply. The control line operates the entire set of microchips and each microchip includes enough circuitry to decode the control signal. Third, the device can be connected with other devices; such a daisy chain could combine a large number of electrodes, potentially over 1000.

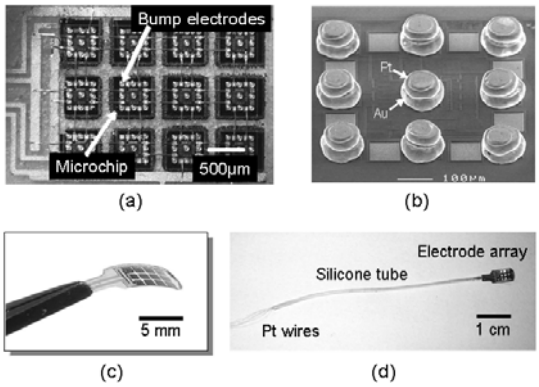

Figure 2 LSI-based stimulus electrode array. (a) the assembled electorde array, (b) Pt/Au stacked bump electrodes on one LSI microchip, (c) the bendable electrode array, and (d) the electode array with Pt wires covered with silicone tubing.

*Research supported by the New Energy Development Organization (NEDO) of Japan, and Health and Labor Sciences Research Grants, Japan.

DEVELOPMENT OF A WIRELESS HIGH FREQUENCY MICROARRAY IMPLANT FOR RETINA STIMULATION *

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We have developed an electrical stimulator and diagnostic research microarray with wireless power and communications to facilitate spatial stimulation of retina tissue. A third generation 32x32 prototype of this retinal neural implant array has been developed. Integrated into the microarray is a functionally graded Ti/IrO2 microbump electrode system for interface with neural tissue with decreased impedance for stimulation. The microarray is designed for basic research to determine retina tissue stimulation thresholds and spatial effects. The array is connected to a telemetry chip, which uses magnetic induction for wireless power with a digital overlay for communication. In our design, changes in the induced current in the telemetry coil are used to send information to the reading coil. Since the reading and telemetry coil are magnetically coupled, the current change can be sensed for bidirectional communication. Combined this chip set provides a 1024 array that can stimulate neural tissue spatially, can sense neural signals spatially, and has wireless power and communication in a package of less than 2 mm size. Further, the implant is encapsulated in a composite of wide bandgap semiconductor and an overcoat of Heparin for biocompatibility. The design and experimental characterization of this implantable chip set will be presented.

* Research Supported by NSF Grant #s 0086020, and 98770720, Michigan Life Science Coridor (MLSC) Grant # 294, the WSU smart Sensors and Integrated Microsystems (SSIM) Program, and the Ligon Research Fund

ULTRANANOCRYSTALLINE DIAMOND AS A HERMETIC, BIO-INERT COATING FOR IMPLANTABLE MEDICAL DEVICES *

Xingchen Xiao[1], J. Wang[1] , J. A. Carlisle[1], and O. Auciello[1]
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[3]Doheny Eye Institute, University of Southern California, Los Angeles, CA

Biomplantable functional devices in the human body must not trigger immune reactions or poison the implant environment, i.e. they must be both bio-inert and bio-compatible. In particular, silicon-based microchips, such as those under development for artificial retinal implant, must be protected by a bioinert/biocompatible layer, since silicon and silicon dioxide are both slightly soluble in water, and, for devices that must interact with the biological environment via electrical signals, are subject to hydrolysis and other deleterious electrochemical reactions. Therefore, the work described here focuses on developing hermetic, mechanically robust, bio-inert/biocompatible ultrananocrystalline diamond (UNCD) coatings that can be deposited at ≤ 400 ºC for encapsulation of CMOS-based microchips [Fig. 1(a)]. We will discuss the synthesis, microstructural and electrochemical characterization of UNCD coatings grown on high-conductivity Si test substrates in a microwave plasma enhanced chemical vapor deposition (MPECVD) system using an Ar-rich $CH_4/Ar/H_2$chemistry. As an example of application of UNCD hermetic coatings, a series of UNCD-coated high-conductivity Si samples were prepared by growing UNCD films with different hydrogen content in the plasma (in the range 2- 20 %), and at different substrate temperatures (in the range 400-800 ˚C). The samples were used to conduct leakage current tests in PBS (phosphate buffered solution) to test the hermetic/bio-inert properties of UNCD coatings for protection of a Si-based microchip being developed as part of an artificial retina. The data revealed that UNCD grown using 1% hydrogen in the plasma and ~ 400 ˚C substrate temperature exhibit the lowest leakage current (~ 4 x 10^{-7} A/cm^2 at –5 V) when tested in the PBS solution [Fig. 1(b)]. Possible mechanisms responsible for the effect of hydrogen incorporation in increasing the electrochemical inertness of UNCD coatings will be discussed. In addition, *in vivo* tests of bioinertness of UNCD coatings were conducted via implantation of

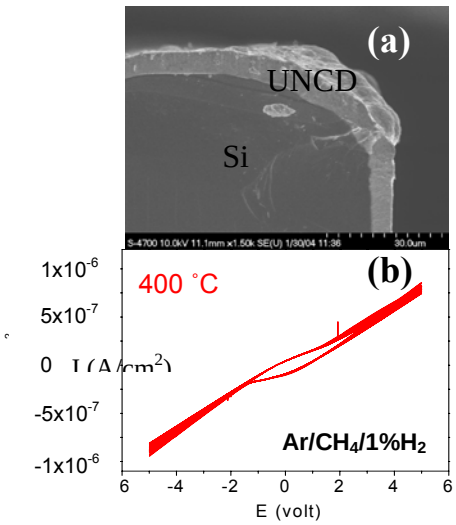

Figure 1. (a) SEM picture of UNCD coating on Si chip showing the hermetic, dense, encapsulation nature of UNCD bioinnert films; (b) Leakage current vs. voltage curve from electrochemical measaurements in PBS solution for high-coinductivity Si coated with UNCD fim grown with 1% hydrogen in the CH_4/Ar plasma.

UNCD-coated Si samples into rabbit eyes. Some *in vivo* and *in vitro* test results showed that UNCD coatings have good biocompatibility and biostability with the physiological environment, while others exhibited some degradation. Further studies are necessary to optimize the UNCD coatings in order to improve their reliability as a hermetic/electrochemically inert coating for bioimplantable devices.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

CHALLENGES IN REALIZING A CHRONIC HIGH RESOLUTION ARTIFICAL SIGHT DEVICE*

Wentai Liu[1], Mohanasankar Sivaprakasam[1], Guoxing Wang[1], Mingcui Zhou[1], James D. Weiland[2] and Mark S. Humayun[2]

[1]University of California at Santa Cruz, [2]University of Southern California

A high resolution artificial sight device is necessary for providing prosthetic vision in blind patients affected by Retinitis Pigmentosa (RP) and Age-related Macular Degeneration (AMD) while restoring visual function to a level that would allow reading, unaided mobility and facial recognition. The key electronic components that will enable such a high resolution prosthetic device (more than 500 pixels) are wireless power telemetry, wireless data telemetry and stimulator. Many challenges exist in the way of realizing these components. High efficiency power transmission, bi-directional communication between the implant and the external units, efficient stimulation of the retina are some of them. In addition to the functionality, the electronics have to be realized in a miniaturized and integrated form to enable a fully implantable chronic device. This talk will identify these challenges and describe the engineering barriers to be overcome. Some solutions will be proposed to address these challenges; results of the proposed solutions in the form of prototype implementation of integrated circuits and their measurement results will be presented.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

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HISTOLOGICAL STUDY OF THE RETINA AFTER IMPLANTATION OF EPIRETINAL PROSTHESIS WITH SPRING-MOUNTED ELECTRODES*

Hossein Ameri[1], Dilek Guven[1], Ricardo Freda[1], Murat Okandan[2], Kurt Wessendorf[2], Guanting Qiu[1], James Weiland[1], Mark Humayun[1]

[1]Doheny Retina Institute, Doheny Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, CA, [2]Sandia National Laboratory, Albuquerque, NM

Purpose: To study the mechanical effect of epiretinal prosthesis with spring-mounted electrodes in dogs.
Methods: The device is a silicon, square 5x5-mm array with 81 electrodes and an attached silicone cable. Electrodes are attached to the array by micro-machined springs and can move perpendicular to the array surface, a maximum of 100µ. Four devices were implanted in dogs: two were implanted acutely during a terminal surgery; two dogs underwent surgery for chronic implantation. All cases underwent standard pars plana vitrectomy with peeling of posterior hyaloid membrane. One of the sclerotomies was extended and the device was introduced into the vitreous cavity and fixed to the retina with a Grieshaber retinal tack.
Results: During the acute experiments, some of the electrodes broke and it appeared nearly impossible to introduce the device into the eye without damaging the electrodes. Moreover, insertion in one animal caused some peripheral retinal damage. Observations of the first two acute experiments led to development of a special sleeve-shaped metal tool for easier insertion of the array into the eye. The insertion tool was used in both dogs that underwent chronic implantation; in both cases all electrodes were intact after implantation. On postoperative day 2, ocular trauma in one dog caused intraocular hemorrhage and dislocation of the implant. In the other dog the eye was enucleated after 2 weeks. Optical Coherence Tomography (OCT) prior to enucleation showed some electrodes were not in close contact with the retina. Histology demonstrated retinal folds and indentation of the retina by some electrodes.
Conclusions: This study demonstrated the feasibility of implanting a retinal prosthesis with spring-mounted electrodes, using a special insertion tool. Retinal indentation indicates close contact of some electrodes with the retina. Work is underway to modify the array to ensure all electrodes remain in close contact with the retina.

*Research supported by Department of Energy, Research to Prevent Blindness, Fletcher Jones Foundation, NEI Grant EY03040.

ULTRANANOCRYSTALLINE DIAMOND AS A HERMETIC, BIO-INERT COATING FOR IMPLANTABLE MEDICAL DEVICES *

Xingchen Xiao[1], J. Wang[1] , J. A. Carlisle[1], and O. Auciello[1]
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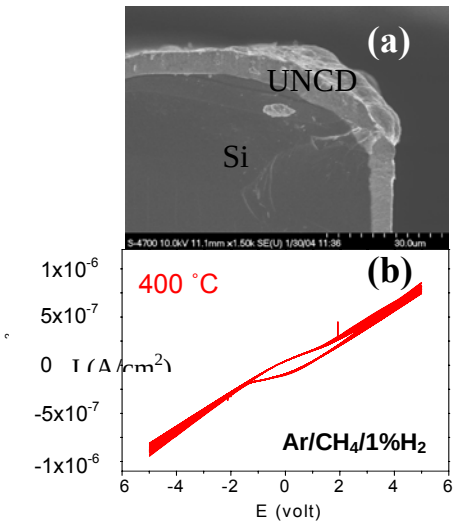
Biomplantable functional devices in the human body must not trigger immune reactions or poison the implant environment, i.e. they must be both bio-inert and bio-compatible. In particular, silicon-based microchips, such as those under development for artificial retinal implant, must be protected by a bioinert/biocompatible layer, since silicon and silicon dioxide are both slightly soluble in water, and, for devices that must interact with the biological environment via electrical signals, are subject to hydrolysis and other deleterious electrochemical reactions. Therefore, the work described here focuses on developing hermetic, mechanically robust, bio-inert/biocompatible ultrananocrystalline diamond (UNCD) coatings that can be deposited at ≤ 400 ºC for encapsulation of CMOS-based microchips [Fig. 1(a)]. We will discuss the synthesis, microstructural and electrochemical characterization of UNCD coatings grown on high-conductivity Si test substrates in a microwave plasma enhanced chemical vapor deposition (MPECVD) system using an Ar-rich $CH_4/Ar/H_2$chemistry. As an example of application of UNCD hermetic coatings, a series of UNCD-coated high-conductivity Si samples were prepared by growing UNCD films with different hydrogen content in the plasma (in the range 2- 20 %), and at different substrate temperatures (in the range 400-800 ˚C). The samples were used to conduct leakage current tests in PBS (phosphate buffered solution) to test the hermetic/bio-inert properties of UNCD coatings for protection of a Si-based microchip being developed as part of an artificial retina. The data revealed that UNCD grown using 1% hydrogen in the plasma and ~ 400 ˚C substrate temperature exhibit the lowest leakage current (~ 4 x 10^{-7} A/cm^2 at –5 V) when tested in the PBS solution [Fig. 1(b)]. Possible mechanisms responsible for the effect of hydrogen incorporation in increasing the electrochemical inertness of UNCD coatings will be discussed. In addition, *in vivo* tests of bioinertness of UNCD coatings were conducted via implantation of UNCD-coated Si samples into rabbit eyes. Some *in vivo* and *in vitro* test results showed that UNCD coatings have good biocompatibility and biostability with the physiological environment,



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*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

DEVELOPMENT OF A BIOENCAPSULATION AND NEURALOGICAL INTERFACE FOR RETINAL IMPLANTS*

G. W. Auner[1], J.P. McAllister[1,2], C.A. Jaboro[1], S. Ng[1], A. Wang[1], and K.M. Abramczyk[1]

[1]SSIM/Chemical Engineering/Electrical and Comp Engineering, [2]Dept of Neurosurgery, Wayne State University, Detroit, MI.

The biocompatibility and bio functionality of a neural implant can determine the viability and effectiveness of a neural stimulating array. In order to enhance the tolerance of chronically implanted devices, new encapsulation methodology are required. In addition, enhancement of the electrode interface with neural tissue can greatly improve device tolerance and performance. Our work involves the development of differential surface modification of the bio encapsulation to inhibit bioreactivity in general but to selectively increase bioreactivity in the regions of the electrodes. This is done by chemically modifying the device encapsulation and laser and biological processing of the electrode regions. Heparin and hyaluronan, two naturally existing biocompatible polymers were covalently attached to the fluorinated surface by photo-immobilization, and the hydrophobicity of the surface was dramatically reduced after such immobilization. This novel immobilization protocol eliminates the destructive activation on the fluorinated surfaces. Further, the processing of the electrodes to form microbumps and the precursor growth of neurons on the electrode surface are presented. The biocompatibility and biostability of such modified surfaces are investigated in continuing studies both *in vitro* and *in vivo* on animals.

* Research Supported by NSF Grant #s 0086020, and 98770720, Michigan Life Science Corridor (MLSC) Grant # 294, and the WSU smart Sensors and Integrated Microsystems (SSIM) Program.

POLYMER-BASED MICROELECTRODE ARRAY TECHNOLOGY FOR AN EPIRETINAL PROSTHESIS *

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Flexible microelectrode array technology development continues at Lawrence Livermore National Laboratory (LLNL) as part of a larger multi-laboratory and institutional collaboration creating implantable epiretinal prostheses. These devices are intended to help restore vision to those suffering from retinitis pigmentosa and macular degeneration as Dr. Mark Humayun's team (Doheny Eye Institute) has demonstrated electrical stimulation of epiretinal neurons results in visual perception.

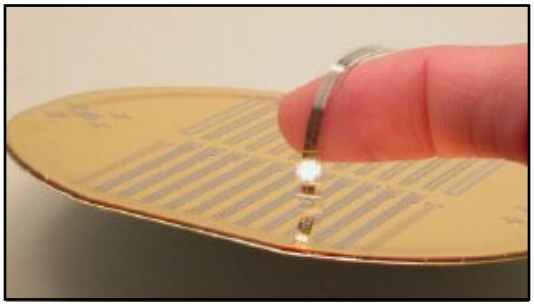

Figure 1. Batch microfabrication processes are being developed to produce flexible polymer-based microelectrode arrays for an integrated epiretinal prosthesis.

Integrated microfabrication technology coupled with integrated circuit and wireless technologies provide means to viable prostheses. LLNL's primary focus is implantable, compliant microelectrode arrays. Electrode arrays are fabricated by depositing conductive metal traces on a polydimethylsiloxane (PDMS). See Figure 1. PDMS is desirable for long-term implantation as it is biocompatible, exhibits low water permeability and high oxygen permeability. These electrodes are highly flexible and conform uniformly to the retinal surface. In initial mechanical evaluations USC surgeons found devices used in a six-month chronic implant easy to handle without damaging the retina or the device during the procedure. Subsequent coherence tomography measurements indicate the array remained conformal without adverse effects to the retina. Efforts continue to increase robustness of platinum metallization and electrode density. Processes for selective PDMS removal by reactive ion etching and laser ablation are being optimized.

*Research supported by the DOE Medical Sciences Division, Office of Biological and Environmental Research, and was conducted under the auspices of the U.S. Department of Energy by Livermore National Laboratory, contract number W-7405-ENG-48.

CHANCES AND CHALLENGES FOR OPTIMAL RETINA ENCODER (RE*) TUNING

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Assuming the availability of a multi-electrode neural interface at the retinal output in blind subjects with retinal degenerative disorders, we studied the conditions for successful joint information processing of both retinal prosthesis and brain. We propose a novel, learning Retina Encoder (RE*) to simulate the complex mapping operation of parts of the retina, to simulate miniature eye movements, and to provide individual, perception-based tuning of RE*.

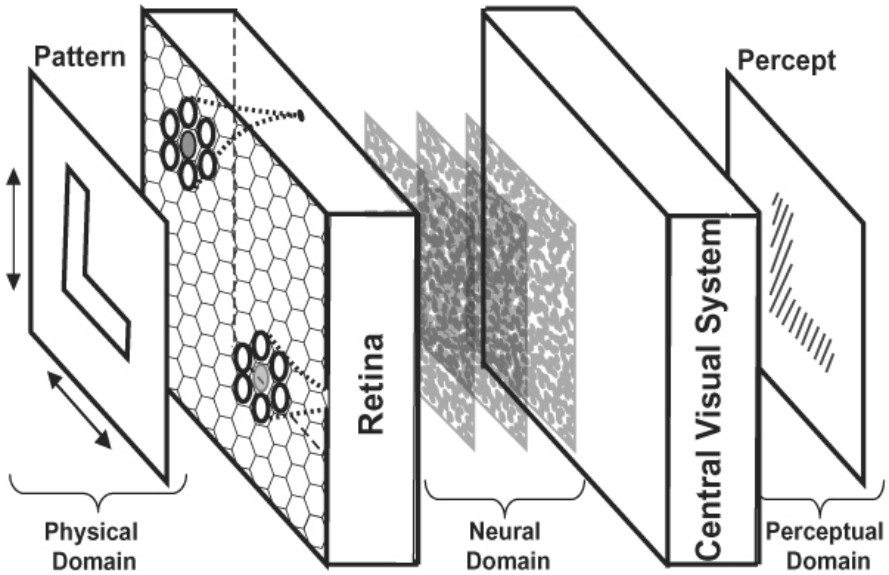

Figure 1 Schema of the human visual system as sequence of two mapping operations. Input pattern P1 can be moved by simulated miniature eye movements during fixation (see arrows).

The human visual system (Fig. 1) is modeled by a retina module (RM) composed of spatio-temporal (ST) filters and a central visual system module (VM). RM maps optical patterns P1 in the physical domain onto retinal output vectors R1(t) in a neural domain, whereas VM has the challenge to map R1(t) in a neural domain onto a visual percept P2 in the perceptual domain. Since the retinal output data stream is highly ambiguous, we assume that VM generates visual percepts only if the retina implant-generated simulation of R1(t): a) is properly encoded, b) contains sufficient information, and c) can be disambiguated. For this purpose, the novel RE***** considers both ambiguity removal and simulated miniature eye movements (SM) in addition to dialog-based tuning capabilities.
Our psychophysical RE* simulation experiments in subjects with normal vision showed that: (1) dialog-based RE* tuning initially yielded only part of the pixels of a given output pattern P2 corresponding to those of input pattern P1, whereas the remaining pixels were still blank due to ambiguity. (2) Subsequent tuning following elicitation of a SM yielded a significant improvement or even completion of P2. (3) The number of required dialog iterations to reach a nearly perfect P2 depended on the corresponding ST filter classes and was in the range of 200-1000 iterations. (4) Upon completion of the tuning phase with a small set of P1 patterns, any P1 could be decoded by RE* (using at least one SM as a small shift of P1) into P2 equal to P1 with good quality.

FAST OPTICAL IMAGING OF LIGHT-FLASH EVOKED NEURAL ACTIVATION IN AMPHIBIAN RETINAS *

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Imaging of the fast intrinsic optical responses closely associated with neural activation promises important technical advantages over traditional single and multi-channel electrophysiological techniques for dynamic measurements of visual processing and for validating electrical stimulation paradigms. Optical measures of retinal function can be non-invasive, with high spatial resolution and 3-dimensional imaging capability. Using single point optical coherence reflectometry, we have previously measured dynamic near infrared (NIR) scattered light changes from frog retina activated by a visible light-flash. However, the application of OCT for fast neural imaging was limited by a low signal-to-noise ratio (SNR) and high background intensity. Hundreds of averages were typically required for recording useful optical responses. Here, we demonstrate improved SNR in a simple imaging configuration, through optimized illumination and improved optical design. Our results with frog and salamander retinas indicate that the SNR of optical measurements using a NIR light emitting diode (LED) at ~950 nm is at least 3 times better than earlier measurements with a shorter wavelength (~800 nm) superluminescent laser diode (SLD). This may reflect a reduction in speckle noise as well as improved physiological response due to reduced photo-bleaching of visual pigment. Using a photodiode detector, we routinely measured dynamic optical responses in single passes, at the level of one part in 10^4 of background light. Recently, we have demonstrated the feasibility of imaging dynamic optical responses in isolated retinas, using a 14 bit commercial CCD. This camera provides spatial resolution of > 1 megapixel, and is capable of recording in excess of 125 frames per second at reduced spatial resolution. In rapid image sequences we observed evidence of multiple response components with both negative- and positive-going signals with different timecourses. These responses show complex but consistent spatial organization from frame to frame. Because of the close juxtaposition of responses of opposite polarity, high resolution imaging disclosed larger fractional responses in individual pixels, in some cases exceeding two parts in 10^3. Our experimental results and theoretical analysis suggest that the optical responses may result from dynamic volume changes corresponding to ion and water flow across the cell membrane, associated with neural activation.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

RETINAL PROSTHESIS MICROELECTRODES: THE ROLE OF MATERIALS SCIENCE RESEARCH IN ELECTRODE PERFORMANCE UNDER REAL-WORLD OPERATING CONDITIONS*

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Photosensitive multipixel microelectrode arrays that are implanted on the retina can stimulate viable retinal neuronal cells and restore partial vision in patients suffering from degenerative macular disease and retinitis pigmentosa. Neural electrodes of novel design and core composition are being evaluated using advanced instrumentation, and compared with benchmark platinum electrodes. Criteria for electrode performance include the safe and effective depolarization of retinal neurons at charge densities of 0.1-1.0 mC/cm^2 with relatively low resistance to current flow. Safe stimulation in physiological solution implies long-term, stable electrode function without electrode degradation or local accumulation of byproducts of electrochemical reactions. Stimulation pulse patterns that fit these criteria are balanced, biphasic and can have an intraphase delay (1). Under the right conditions, surface electrochemistry that occurs during the cathodic phase is reversed during the anodic phase. We have measured gaseous hydrogen production during biphasic stimulation of Pt and carbon fiber microelectrodes in synthetic vitreous humor under physiological conditions. Sensitive hydrogen sensing techniques record thresholds of electrolysis as a function of charge density (current amplitude, dwell time, and electrode geometry). Images (SEM) of the electrodes taken before and after long-term stimulation show the relationship between electrode core composition and stability of electrode structure with chronic stimulation.

1. Lilly, J.C. “Injury and Excitation by Electric Currents: The Balanced Pulse-Pair Waveform” in *Electrical Stimulation of the Brain*, edited by D.E. Shear, published by the Hogg Foundation for Mental Health (1961).

*Research supported by the Medical Sciences Division, Office of Biological and Environmental Research, US Department of Energy.

INCREASED SURVVALAND DECREASED LENSE EPETHELIUM CELL APOPTOSIS INDUCED BY PEROXYNITRITE

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ABSTRACT

PURPOSE. To observe if puerarin increased survival and decreased lens epithelium cell (LEC) apoptosis induced by peroxynitrite ($ONOO^-$) **.**

METHODS. Diabetic cataract animal model was established by intra-peritoneal (ip) injection of streptozotocin (STZ, 45mg/kg, n=72). These animals were divided into two groups - puerarin treated group and purerarin untreated group. Control group (n=36) received normal saline ip. Morphologic changes of lens were observed with slit lamp analysis. Animals were sacrificed at days 20, 40, 60 after streptozotocin injection for further analysis. Amount and percentage of apoptotic LEC were determined by flow cytometry. Nitrotyrosine (NT, the foot print of $ONOO^-$) was examined by immonohistochemistry. Apoptosis-related genes were analyzed by gene array.

RESULTS. Compared to control group, mild opacity of lens was observed in purerarin treated group, while severe opacity of the lens could be seen in the animals treated with STZ alone. Mild apoptosis of the LEC was observed in control group on days 20, 40, 60. In puerarin group, mild apoptosis of LEC was observed at day 20, significantly increased on day 40 while at day 60 apoptosis of the LEC was markedly decreased. Time dependent increase in apoptosis of the LEC was observed in STZ group. The pattern of NT expression was similar to the pattern of apoptosis in all groups. Similarly, iNOS expression followed the same pattern as detected by Gene array. Apoptosis-related genes including BCL-2, NF-κB, SOD were up-regulated while TNFR1-FADD-caspase signal transduction pathway were down-regulated in puerarin group. Opposite results were seen in STZ group.

CONCLUSIONS. Puerarin increased survival and decreased LEC apoptosis induced by $ONOO^-$.

MINIATURE MULTI-CHANNEL HIGH-SENSITIVITY IMPLANTABLE MEMS PRESSURE SENSOR AND CMOS READOUT SYSTEM

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Implantable high-sensitivity micro-machined pressure sensor array has been developed to measure the pressure changes in vivo. Our first generation 3-channel microelectromechanical systems (MEMS) based sensor array has a pressure sensitivity of 0.01 mmHg and maximum pressure of 300 mmHg. Newly-designed second generation 10-channel array, in which each sensor element has a thickness of 605 nm, provides at least two-order higher sensitivity and is able to detect a deflection in nanometers. We have also successfully designed and fabricated an ultra-sensitive 10-channel 0.5 μm Complementary Metal-Oxide-Semiconductor Transistor (CMOS) integrated circuit (IC) signal readout chip. The CMOS readout chip coverts the electrical resistance change in MEMS sensor to a voltage signal with less than 0.8 mW power consumption per channel. Preliminary experimental results suggest that our innovative signal readout and power management circuit have high sensitivity and stability. This readout chip has 93.6 dB gain, 2.3 MHz band-width, and very low draft (<10 μV/hour). This technological break-through in signal transduction has removed the primary hurdle in system miniaturization of sensor readout system. Wireless data link and RF power charging capabilities can be added to existing design that would provide safe and easy access to motion and pressure changes inside body from outside readout unit.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

NOVEL NANOCAST METHOD OF CREATING IMPLANTABLE HIGH ASPECT RATIO ELECTRODES ON THIN FLEXIBLE SUBSTRATE WITH NANOPARTICLES

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**** Second Sight Medical Products, Inc., Sylmar, CA 91342**

A novel approach is described to fabricate a high-aspect ratio, patternable, and implantable electrode array with metal nanoparticles and micro-fabrication process. In our initial tests, we were able to create 2D and 3D patternable structures with a height to width ratio greater than 10:1. Nanocast electrode pads could be as tall as about 1000 micrometers with conductive leads 25 micrometers thick, while the width ranges from 10 to 250 micrometers. The unique fabrication process of this nanocast method is able to fuse the entire stimulation circuit including stimulating electrode, connection trace, and contact pad into one integrated continuous structure in which the different sections of structure might have different height, width, and shape. The fabricated electrode is highly robust and very flexible. Using micro-fabrication processes, three-dimensionally patternable structures can be fabricated in a very reproducible fashion and are of high quality which is suitable for mass production. More importantly, the entire fabricated structure can be packed at room temperature into bio-compatible flexible substrates, such as Poly-dimethylsiloxane (PDMS), parylene and polyimide, and other temperature-sensitive or vacuum-sensitive materials. These nanocast electrodes not only have the same electrical resistivities as their bulk materials, but also have low impendence and outstanding electrochemical properties.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

MOLECULAR PHOTOVOLTAICS AND THE PHOTOACTIVATION OF MAMMALIAN CELLS

Tanya Kuritz[1], Ida Lee[2], Elizabeth T. Owens[1], Mark Humayun[3], and Elias Greenbaum[1]

[1]Chemical Sciences Division `Oak Ridge National Laboratory	[2]Department of Electrical Engineering, The University of Tennessee	[3]Doheny Eye Institute and Dept. Opthalmology, USC School of Medicine

Photosynthetic reaction centers are integral plant membrane protein complexes and molecular photovoltaic structures. We report here that addition of PSI-proteoliposomes to retinoblastoma cells imparts photosensitivity to these mammalian cells as demonstrated by light-induced movement of calcium ions. Control experiments with liposomes lacking PSI demonstrated no photosensitivity. The data demonstrate that Photosystem I, a nanoscale molecular photovoltaic structure extracted from plants, can impart a photoresponse to mammalian cells in vitro. Figure 1 is a conceptual illustration of the method used to impart photosensitivity to the retinoblastoma cells. We have previously shown that the photovoltaic properties of isolated PSI reaction centers are preserved after extraction from photosynthetic membranes. The open circuit electrostatic potential of a single PSI reaction center is about 1 V. The closed-circuit potential, measured under conditions of hydrogen photoevolution, is at least 0.6 V based on the known energetic requirements to evolve molecular hydrogen from water at pH 7 and room temperature. Photoactive mammalian and neural cells are new photobiological systems that are of fundamental interest and may have potential application in the area of artificial sight.

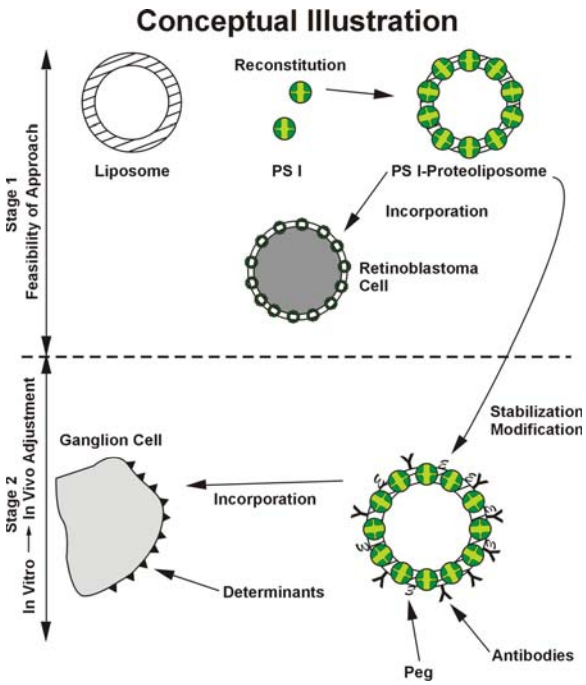

Fig. 3 Conceptual illustration of the method for incoporating PSI reaction centers in mammalian cell membranes

*Research supported by the Medical Sciences Division, Office of Biological and Environmental Research, US Department of Energy.

ELECTROPHYSIOLOGICAL RESULTS OF SUBRETINAL CHIP IN RABBIT RETINITIS PIGMENTOSA

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Eye Center, People's Hospital, Peking University

Abstract

Objective: In recent years artificial electrical stimulation of the retina is hypothesized to improve visual function of retinitis pigmentosa, even in the retina area distant from the implant. A clinic trial is going on. A small piece of micro-photodiode arrays (chip) can improve the visual function? It can improve the Full-Field VEP and ERG?

Methods: A round form-photodiode arrays of 3mm diameter with ca. 90 microelectrodes were implanted into subretinal or choroidal space of 6 pigmentosa rabbit eyes and 3 normal rabbit eyes. All of right eyes are chip implanted eye and left eyes as control. Focal-ERG (2 weeks after surgery) and Focal-VEP (4 weeks after surgery), Ganz-field ERG and Ganz-field flash-VEP (5 weeks after surgery) were measured.

Results: For focal ERG the amplitude of the b-waves increased in 4 RP eyes and 1 normal eye, worse in 1 RP eye, no change in 1 RP eye and 2 normal eyes, For focal-VEP the main amplitude increased in2 RP eyes and 1 normal eye, no change in 4 RP eyes and 2 normal eye, For Ganz-field Flash VEP the main amplitude increased 2 RP eyes and, decreased in 3 RP eyes. No change in Ganz-field ERG for all RP eyes and normal Eyes between chip-implanted eyes and eyes without chip.

Conclusion: We could not find any significant increased amplitude of Ganz-field VEP and Ganz-field ERG after subretinal or choroidal micro-photodiode arrays implantation neither in RP rabbit eyes nor in normal rabbit eyes, but an improvement of amplitude by focal ERG and focal VEP. was obtained in some RP eyes and normal eyes.

CHALLENGES IN REALIZING A CHRONIC HIGH RESOLUTION ARTIFICAL SIGHT DEVICE*

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A high resolution artificial sight device is necessary for providing prosthetic vision in blind patients affected by Retinitis Pigmentosa (RP) and Age-related Macular Degeneration (AMD) while restoring visual function to a level that would allow reading, unaided mobility and facial recognition. The key electronic components that will enable such a high resolution prosthetic device (more than 500 pixels) are wireless power telemetry, wireless data telemetry and stimulator. Many challenges exist in the way of realizing these components. High efficiency power transmission, bi-directional communication between the implant and the external units, efficient stimulation of the retina are some of them. In addition to the functionality, the electronics have to be realized in a miniaturized and integrated form to enable a fully implantable chronic device. This talk will identify these challenges and describe the engineering barriers to be overcome. Some solutions will be proposed to address these challenges; results of the proposed solutions in the form of prototype implementation of integrated circuits and their measurement results will be presented.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

A tissue change after suprachoroidal-transretinal stimulation with high electrical current in rabbits

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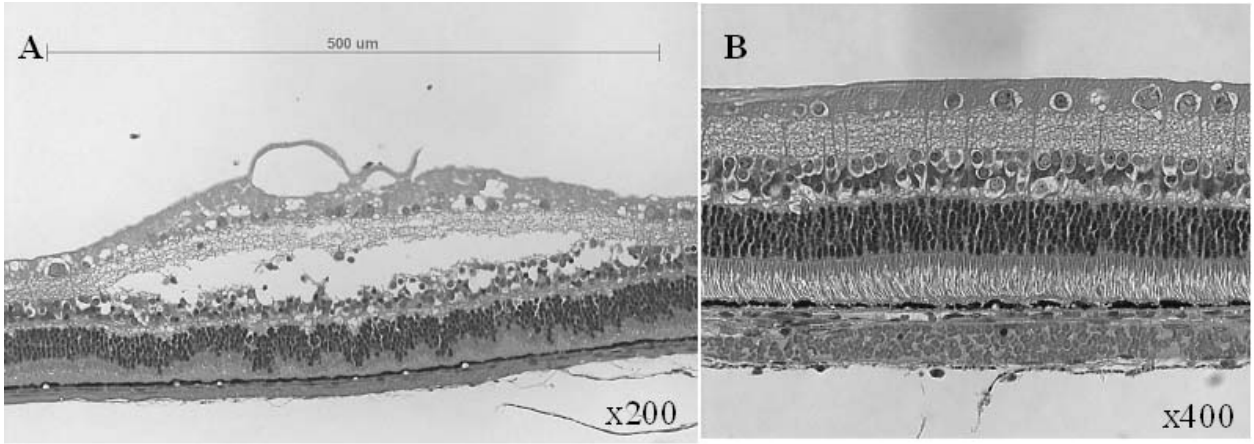
Purpose: To investigate the safety range of current by suprachoroidal-transretinal stimulation (STS) using a high-current continuous stimulation.

Method: Sclerotomy was performed at the area just beneath the visual streak of rabbits and the platinum electrode (Φ=100μm or 200μm) embedded in silicone plate was attached on the fenestrated sclera. Return electrode was placed in the vitreous cavity. Retina was stimulated by biphasic pulses (anodic first, duration; 0.5 msec, frequency; 20 Hz) with a current ranged from 1 to 3 mA continuously for an hour. The rabbit eyes were enucleated immediately after the stimulation, fixated with glutar-aldehide, embedded in paraffin and stained with hematoxylin-eosin.

Result: For Φ=100μm electrode, no histological change was observed with a current of 1 mA, but retinal change was observed with a current of 1.5 mA.
For Φ=200μm electrode, no histological change was observed with a current of 1.5 mA but with a current of 2.0 mA, retinal change was observed. The residual scleral thickness was 50-100μm.

Conclusion: The results of acute experiment suggested that a relatively large amount of current was able to be injected with STS method without tissue damages. In the next step, an experiment with chronic stimulation is needed to verify the safety of STS method.



A: The retina was damaged by one-hour continuous biphasic-pulse stimulation with a current of 2mA *(Φ=200μm electrode).*

B: The retina was not damaged by stimulation with a current of 1.5mA *(Φ=200μm electrode).*

*Supported by Health Science Research Grants from the Ministry of Health, Labor and Welfare, Japan

DESIGN OF AN OPTICALLY-CONTROLLED HIGH-RESOLUTION ELECTRONIC RETINAL PROSTHESIS *

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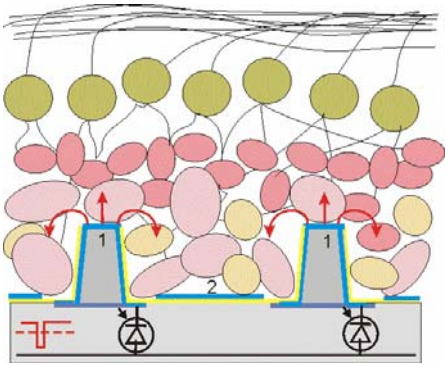
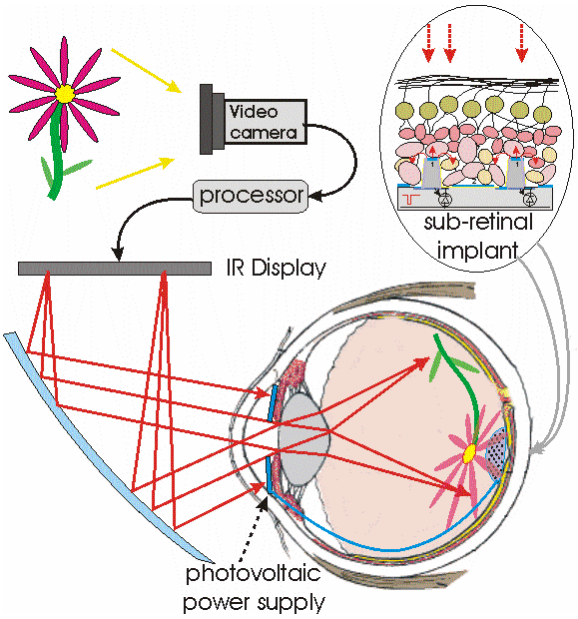
It has been demonstrated that electrical stimulation of the retina can produce visual percepts in blind patients suffering from retinal degeneration. However, current retinal implants provide very low resolution (just a few electrodes), whereas thousands of pixels would be required for functional restoration of sight.



We present a design of an optoelectronic retinal prosthetic system with a stimulating pixel density of up to 2,500 pix/mm^2 (pixel size of 20 µm, corresponding geometrically to a maximum visual acuity of 20/80). To operate at such high pixel densities, very close proximity (on the order of 10 µm) of electrodes to target cells is required. This intimate proximity between electrodes and cells is achieved by causing the retina to migrate into porous subretinal electrode arrays. Two basic geometries of sub-retinal implants are presented: perforated membranes and protruding electrode arrays.



To provide for natural eye scanning of the scene, rather than scanning with a head-mounted camera, the system operates similar to "virtual reality" devices. An image from a video camera is processed and then projected by a goggle-mounted infrared LED-LCD display onto the retina, activating an array of powered photodiodes in the retinal implant. The goggles are transparent to visible light, thus allowing for the simultaneous use of remaining natural vision along with prosthetic stimulation. Optical delivery of visual information to the implant allows for real-time image processing adjustable to retinal architecture, as well as flexible control of image processing algorithms and stimulation parameters.

*Research supported by the Air Force Office of Scientific Research.

TISSUE DAMAGE BY CHRONIC ELECTRICAL STIMULATION *

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Electronic retinal prostheses are under development and testing, while the safety limits for electrical stimulation of the retina are not yet well established. We studied the threshold of cellular damage as a function of pulse duration and electrode size on chicken retina in-vitro and chorioallantoic membrane (CAM) of chicken embryo in-vivo using propidium iodide staining. Minimal current density inducing cellular damage was detected with one pulse and with multiple pulses (7,500 pulses applied at 25 Hz for 5 min) ranging in duration from 6 μs to 6 ms per phase, and electrode (pipette) diameters from 0.1 to 1 mm. With pipettes larger than 0.35 mm in diameter the threshold current density was found to be practically independent of the pipette size and scale reciprocal to a square root of pulse duration ($t^{-0.5}$). On CAM the threshold current density for single pulse varied between 0.21 A/cm^2 at 6ms to 5.8 A/cm^2 at 6μs, and for multiple pulses, between 0.012 A/cm^2 at 6ms to 0.42 A/cm2 at 6μs. On retina the threshold for multiple pulses varied between 0.055 A/cm^2 at 6ms to 1.3 A/cm^2 at 6μs. With small pipettes (below 0.2mm) the threshold current density was rising reciprocal to the square of the pipette diameter, i.e. acting as a point source so that the damage threshold was determined by the total current. Interestingly, the strength-duration dependence on small electrodes (0.1 mm) was less steep, approximately $t^{-0.25}$.

*Research supported by the Air Force Office of Scientific Research.

A MODEL OF THE ELECTRICALLY EXCITED OPTIC NERVE: INFLUENCE OF ELECTRODE ARRANGEMENT ON NERVE EXCITABILITY*

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Institute for Laser Medicine & Biophotonics, Shanghai Jiao-Tong University

This was part of work that contributes to the first multidisciplinary research project on Retina Prosthesis in China: the C-Sight (Chinese Project for Sight), funded by the Science and Technology Commission of Shanghai Municipality (STCSM). The C-Sight is to develop a visual prosthesis for blindness. The prosthesis will function by electrically stimulating healthy optic never through a penetrating multi-electrode-arrays. The design of such a prosthesis includes both geometry of electrode array (shape, size, electrode arrangement on the array) and electric stimulation parameters (current pulse amplitude, waveform). Among these parameters, the electrode geometries such as the relative placement of electrode have great influence on the nerve excitability, the resolution of electrodes, and the information coupling efficiency.

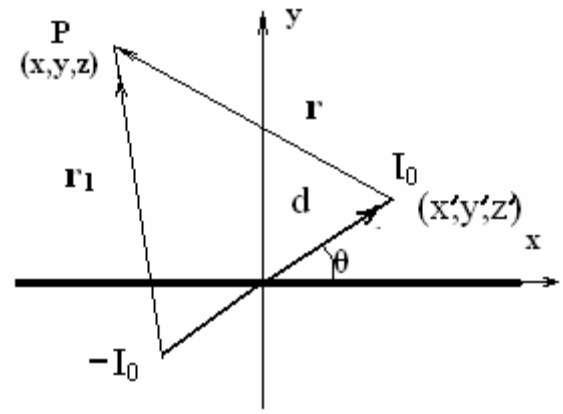

Figure 4 A schematic diagram show the relative placement of two electrode and optic nerve.

In our study, we first develop expressions for electric sources of electrode. In computational modeling of electrical stimulation , The electrodes are driven singly versus a distant return and the source is often modeled as a point source. But in reality, one can never have a single isolated monopole current source because of the need to conserve charge . A dipole of arbitrary orientation is illustrated in Figure 1, the electric field of dipole is the addition of the source and sink field:

$$\Phi_d = -\frac{I_0}{4\pi\sigma r} + \frac{I_0}{4\pi\sigma r_1}$$

where σ is the tissue conductivity, We can compute the field in any point in term of d ,the distance between the *source* and *sink*) and θ, the angle of dipole relative to the x axis, where the optic nerve was along. The nerve is along the x axis. The electrode current dipole. Secondly, we select FCM optic nerve model as our membrane models. The FCM model is a more complex model based on work by Fohlmeister *et al*. In this model, there are the five conductances, which all are modeled as active nonlinear ion channels. Under the dipole field, we predict the threshold response of FCM model by varying the parameter d and θ .The threshold response is the minimum stimulation current to initiate an action potential .

By numerical computation and computer simulation, we conclude that the longer distance between the electrode, the higher exciting stimulation threshold is, and when the dipole electrode is perpendicular to the nerve, the higher stimulating current is needed to initiate an action potentials than other direction cases.

*Research supported by the Science and Technology Commission of Shanghai Municipality

C-SIGHT: A NOVEL APPROACH FOR RETINAL PROSTHESIS *

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The C-Sight (Chinese Project for Sight) is the first multidisciplinary research project on retina prosthesis in China funded by the Science and Technology Commission of Shanghai Municipality (STCSM). The goal of the C-Sight Project is to develop an implantable microelectronic medical device that will restore useful vision to blind patients.

In our project, we are the first to propose the penetrating multi-electrode-arrays with specific configurations into the optical nerve as a neural interface to couple the encoded electro-stimuli into the axons of the ganglion cells for vision recovery. Optic nerve is chosen as a neural interface or stimulating site in our prosthesis design because the optic nerve can be accessed via a minimally invasive procedure and is relatively spared by the most prevalent degenerative eye diseases, and it serves as a compact conduit for all of the information in the visual scene.

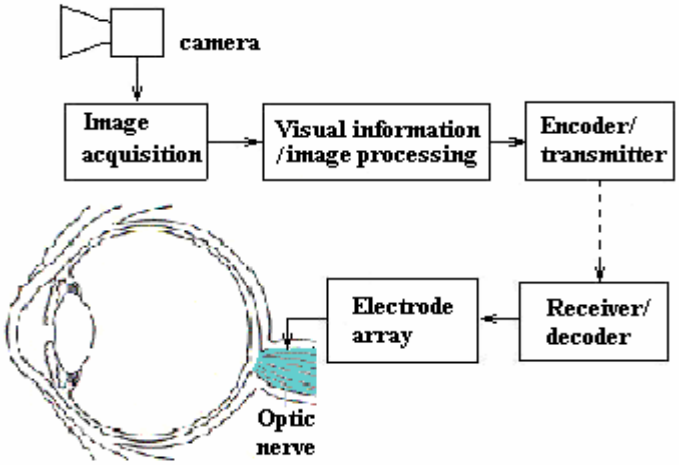

Figure 5 An retina implant with a encoder outside the eye and an stimulating electrode array penetrating into optic nerve.

Another important feature of our prosthesis is that the function of photoreceptors of retina is replaced by a solar powered self-contained implantable device.

The overall structure of our prosthesis is shown in Fig.1. It contains a "retinal encoder" encoding the processed visual information as trains of electrical impulses with a specific spatiotemporal stimulation pattern. The encoded information is conveyed by the penetrating multi-electrode-array directly into the optic nerve where action potentials are generated and are conveyed to the brain's visual cortex.

Our system described herein illustrates a more practical approach towards phosphene vision in the initial stages. With our further understanding into the retinal encoding process, the C-Sight implant will be continuously refined and optimized.

*Research supported by the Science and Technology Commission of Shanghai Municipality

ACUTE HUMAN TRIAL FOR EPIRETINAL PROSTHESIS: WHAT DO THE PATIENTS SEE?

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[5]IIP-Technologies GmbH, Bonn, Germany

The purpose of this multicenter study was to characterize visual perceptions elicited by acute electrical stimulation of the human retina using a newly developed epiretinal implant in subjects suffering from photoreceptor degeneration. A total of 20 patients with visual acuities ranging from 1/50 to no light perception were included. Stimulation procedure was done during a pars plana vitrectomy with a maximum duration of 45 minutes. A microcontact film with IrOx-electrodes connected to a current generator was positioned epiretinally. In standardized interviews after the stimulation procedure 19 of 20 patients reported one or more visual perceptions in close time correlation to single stimulation events. Predominantly pleasant perceptions of objects ranging in size from a head of a match to a football as seen from one meter distance were reported. The majority of objects were described as round, oblong or angular. The predominant colors were white, yellow and blue. The relatively small size of the perceived objects implies that the epiretinal implant might evoke more complex images by an optimal spatiotemporal stimulation pattern of electrical impulses. However, the considerable variety of visual perceptions suggests that in addition a significant learning process will be required to reach optimal performance with chronically implanted devices.

FLEXIBLE PARYLENE-BASED TECHNOLOGIES FOR INTRAOCULAR RETINAL PROSTHESES*

Damien C. Rodger[1,2], Wen Li[1], Dilek Guven[3], Hossein Ameri[3], James D. Weiland[3], Mark S. Humayun[3] and Yu-Chong Tai[1]

[1]California Institute of Technology, [2]Keck School of Medicine of the University of Southern California, [3]Doheny Retina Institute, Doheny Eye Institute, Keck School of Medicine of the University of Southern California

Our overall goal is to fabricate a retinal multielectrode prosthesis system using parylene C as the primary substrate. Many attributes of parylene C make it ideal for intraocular implant applications, including its strength and flexibility, its pinhole-free highly-conformal chemical-vapor deposition at room temperature, its transparency, its low water permeability, and its ease of manipulation using standard microfabrication techniques. In order to study the intraocular biocompatibility of the material, unmodified parylene C was implanted in the vitreous cavity of two rabbits for six months, and histological analysis of their retinas was performed post-mortem. Analysis of the retinas of the implanted right eyes of both rabbits showed no detectable difference from the left eyes which served as controls. We have also fabricated and tested prototypes of the three components of a parylene-based intraocular system, including a 16x16 platinum multielectrode array, a chip-level integrated interconnect (CL-I^2) high lead count package for direct integration of the application specific integrated circuit (ASIC) and discrete capacitors, and a multiple-metal-layer radio-frequency (RF) inductively-coupled coil. In addition, a parylene test structure with an attached ASIC that simulates the complete intraocular system has been fabricated, and surgical implantation in an enucleated pig eye has generated positive results.

*Research supported by the National Science Foundation Engineering Research Center on Biomimetic MicroElectronic Systems (EEC-0310723) and by a fellowship from the Whitaker Foundation.

PROSTHETIC VISION SIMULATION WITH NORMALLY SIGHTED AND VISUALLY IMPAIRED PEOPLE*

Matthias Walter[1], Gislin Dagnelie[2], and Lindsey Yang[2]
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Our experiments use video camera images that are convolved by a computer in real time to represent phosphene vision. (Figure 2) The program allows us to set a broad variety of parameters as number of phosphenes per row and column, contrast, grey level etc. In these experiments we use a board consisting of 8x8 squares. Most of them are black some are white. The test subjects are asked to count the white squares and later in the experiment to cover them with black checkers.

Figure1: Test subject using black checkers to cover the white squares on the 8x8 "checker" board.

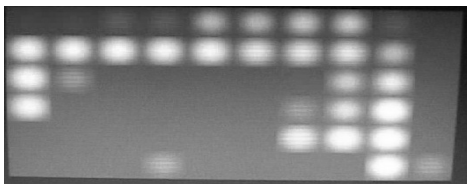

Figure2: Image of the view of a board as a test subject perceives it.

Our aim is to determine how much environmental information people are able to obtain using the crude pictures today's electrode arrays would deliver. We also try to develop methods of learning on how to get the most out of the images presented.

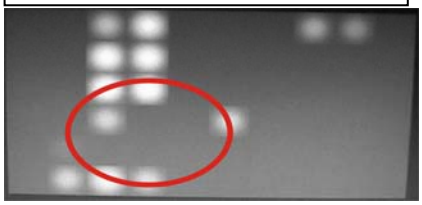

Figure3: Image the test subject sees when he is trying to place a checker on a white square. In the red circle the checker and the finger of the hand are "visible".

The results show that each subject developed a different method and also lowered his time usage for the set task as well as his error rate. This is clearly visible in the test results. (Figure 4 and 5)

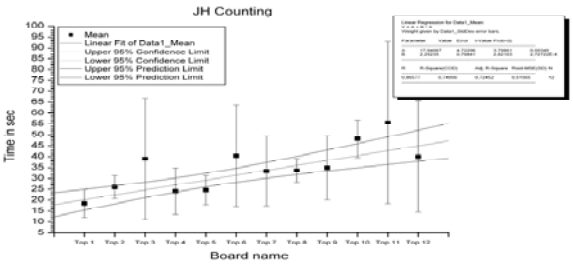

Figure4: Plot of the time used for counting in the beginning of the experiment. A linear fit was made because it is to be expected that the time used for counting the squares is linear depending on the number of squares. The standard deviation (error bars) was very high.

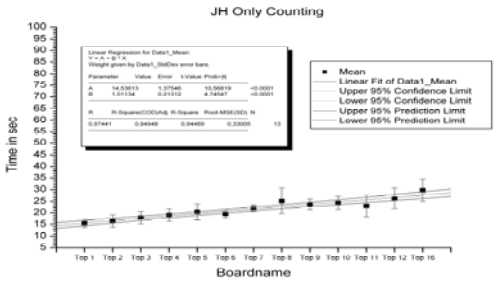

Figure5: Plot of the time later in the experiment. It can be seen that now the time used has become shorter and the times in themselves were much more consistent (small error bars).

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INTEGRATED ELECTRONICS AND MICROMECHANICAL STRUCTURES FOR RETINAL IMPLANT APPLICATION*

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In conjunction with our CRADA partners in the Artificial Retina Program, we are developing an integrated (MEMS/electronics) electrode array. Our approach uses micromechanical springs to couple the electrode array (on the order of 5mm) to the curved and potentially irregular surface of the retina, while using on-chip electronics (same silicon substrate as the electrodes) to address the dense array of electrodes with far fewer number of interconnect wires than would be required if all electrodes were directly connected to current sources.

The unique spring electrode design allows the individual electrodes to move in relation to the overall implant, providing positive contact between the electrodes and the retinal tissue over the whole implant surface. This approach also lends itself to a tiled assembly of smaller sub-arrays, which leads to smaller projected displacements at each electrode site. The tiled elements are held together in a shaped polymer frame that also serves as the interconnect cable and fixation platform.

The critical functionality that is enabled by the on-array electronics is the demultiplexing and routing of data and currents between the electrode array and the drive electronics. Without this functionality, all electrodes would have to be driven directly, leading to a very thick and unmanagable interconnect cable, especially as the retinal implant proceeds beyond several hundred electrodes.

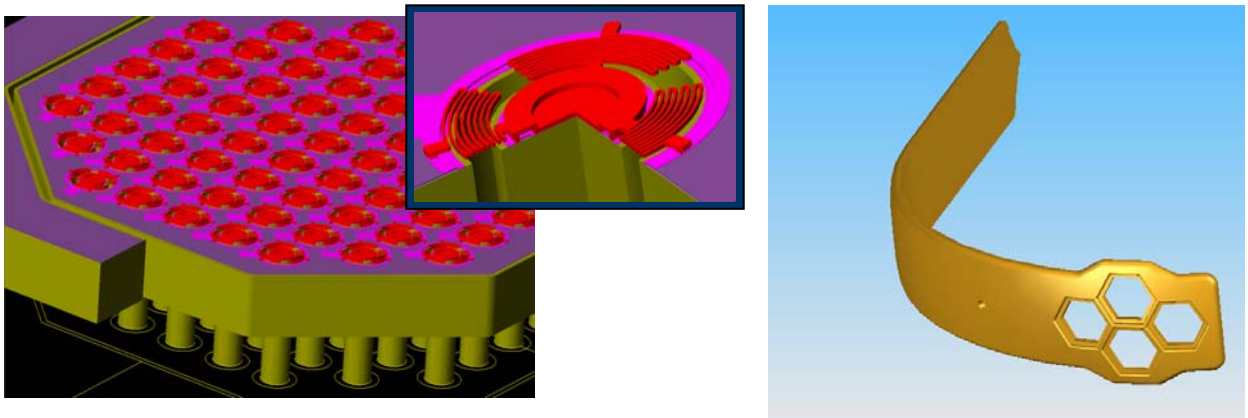

Figure 6 3D models of the hexagonal electrode array (insert showing a cut-away of the individual electrode with the springs) and the polymer frame for holding the tiled array.

*Research supported by the Office of Biological and Environmental Research, US Department of Energy.

ENGINEERING DEVELOPMENT OF A SUBRETINAL PROSTHESIS

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The Boston Retinal Implant Group has switched its focus from an epiretinal to a subretinal design over the past three years because of a number of potential avantages to the subretinal approach: the mechanical and thermal advantages gained by removing the bulk of the implant from the interior of the eye, the minimally invasive surgery required to insert the electrode array beneath the retina, the ability to avoid attachment of the array to the retina using tacks or glues, and the possibility of removing an implant without trauma.

Our design transmits power at 125 KHz and data at 13.56 Megahertz to secondary coils attached to the temporal region of the sclera. Power and data transmitters have been designed and tested. A 30,000 transistor fully custom microchip has been fabricated in the AMI 0.5 micron process. It is designed to receive RF data up to 1.35 Mbits per second, decode it using a delay-locked loop, and use it to control on-chip current sources to power the subretinal electrodes. The present design has only 15 electrodes, but the chip is designed to expand easily to drive many more.

The chip is connected through a flip-chip bonding procedure to a flexible polyimide substrate that is sutured directly to the sclera. The flexible substrate is connected to either the electrode array or else to a test array to monitor electrical output during testing. We plan to complete a 1-week implantation in Yucatan mini-pig this year, in which we will apply stimuli and monitor cortical response.

TOWARDS AN IMPLANTABLE MICRO pH ELECTRODE ARRAY FOR RETINAL IMPLANTS

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Electrical stimulation of neural tissue requires charge injection into the biological environment. This is achieved through both Faradaic and non-Faradaic reactions at the interface of electrode/tissue surface. Some Faradaic reactions have the potential to dramatically alter pH levels. Changes in pH can have a significant effect on the electrode/electrolyte interface. A shift in pH at the electrode/electrolyte interface will change the electrode's corrosion potential and cause electrode materials to dissolve. Large pH changes also affect cell function by altering the structure and activity of proteins, ionic conductance of the neural membrane, neuronal excitability and even cause tissue damage. This paper reports on recent developments in pH sensors for the neural prostheses, especially retinal prosthetic devices. The effects of stimulus induced pH changes for a variety of stimulation parameters in a retinal implant have been investigated. Electrodes were stimulated using monophasic and biphasic pulses at different intensities and frequencies. pH levels were recorded using a pH microelectrode and verified using a pH color indicator (phenol red). Preliminary results using a planar micro pH electrode array for possible in-vitro and in-vivo pH measurements are also discussed.

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Notes

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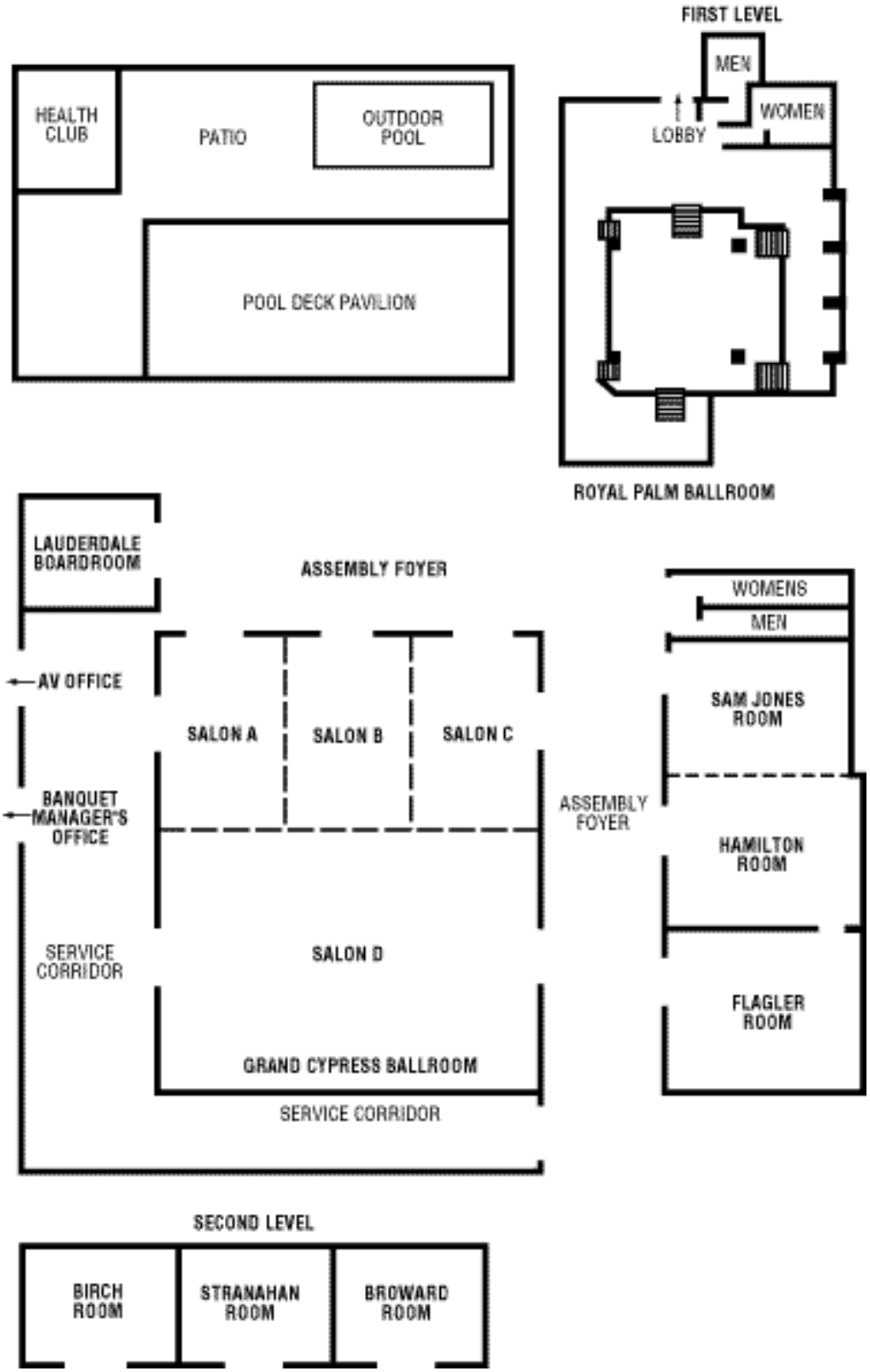
Hotel Layout



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