

## Chapter 1. Custom-Integrated Circuits

### Academic and Research Staff

Professor Jonathan Allen, Professor John L. Wyatt, Jr., Dr. Christopher J. Terman

### Visiting Scientists and Research Affiliates

Joseph F. Rizzo, III, M.D.<sup>1</sup>

### Graduate Students

Andrew E. Grumet, Bradley J. Lichtenstein, Shawn K. Kelly, Joshua D. Moss

### Undergraduate Students

Neelima Yeddanapudi

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## 1.1 Interactive Learning Environment for VLSI Design

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The ILE environment is now being used by subject 6.371 (Introduction to VLSI Systems), thus providing the opportunity for considerable user feedback, which will inevitably lead to further tuning and improvements of the system. Student involvement with the creation of mini-tutorials, covering a wide range of fundamental circuit design issues, is being solicited to understand directly the learning difficulties associated with basic circuit phenomena. Interestingly, the ILE is replacing much larger commercial computer-aided design systems, which have proved to be difficult to install and configure, train, and uti-

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If successful, the second experiment will demonstrate that our concept is feasible in principle, while the first will demonstrate that perceptual quality is sufficiently high to be of practical use to blind patients. The remaining problem of long-term biocompatibility will require major additional effort.

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Dr. Rizzo and Professor Wyatt have obtained final approval to proceed with human trials from MIT's Committee on the Use of Humans as Experimental Subjects. They have obtained approval from the Massachusetts Eye and Ear Infirmary Human Studies Committee, conditional on the chemical tests described above.

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measure the electrical activity of the retina) are carried out once before surgery and five times after implantation.

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### ***In Vivo* Retinal Stimulation in Rabbits**

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designs we also attach two ultrafine wires to allow us to measure current output of the array during preliminary surgical trials.

We are also investigating biocompatible adhesives for safely attaching the microelectrode array to the rabbit retina. We have met several times with a local company to begin testing a material of theirs that we previously assessed and found to have excellent attributes (biocompatible; transparent; can be hardened in the eye by short exposure to UV light, which makes it surgically friendly). We will begin additional tests within two weeks.

The next goal for our animal studies is chronic implantation of a stimulation system in the rabbit eye. The implant must be encapsulated in materials that protect it from the saline intraocular environment. Within the next week, we will encapsulate an intraocular lens/photodiode system using NuSil compounds previously shown by Edell to be effective. Mr. Socha and Mr. Moss have copied a resistive leakage test system for these devices that was developed by Dr. Edell, and it is now ready for use in device testing.

### ***In Vitro* Retinal Stimulation Studies in Rabbit**

Doctoral student Andrew Grumet conducted experiments to characterize retinal responses to microelectrode array stimulation and made methodological refinements. His first round of *in vitro* experiments, performed over the summer, revealed interesting physiologic phenomena as well as the technical limitations of his experimental apparatus. Neural spike activity could be produced with stimulation currents as low as 1 microampere, often in trains lasting up to thirty milliseconds after the termination of the stimulus. The long spike latencies suggested a trans-synaptic mechanism, in which delay-producing chemical synapses separate the directly stimulated cell from the cell under study. But in experiments performed in fall 1998, addition of the synaptic blocker cadmium to the bathing solution failed to eliminate the latent activity. An alternate explanation is that the stimulation currents used, though seemingly small, are nonetheless far above the ganglion cell stimulation threshold for producing single spikes.

Thresholds for producing single spikes, which occur within the first few milliseconds following stimulus application, could not be measured due to stimulus artifacts. With the help of Professor Wyatt, Mr. Grumet performed a detailed electrical characterization of the experimental apparatus, with the goal of identifying and reducing the dominant source(s) of the arti-

fact. The effort identified a number of such sources; the major one being leakage paths on the array between lead wires from adjacent electrodes.

Mr. Grumet is now designing new electrode arrays to minimize such paths. Mr. Shire will fabricate them at Cornell Nanofabrication Facility, and Mr. Grumet will shortly conduct new experiments to probe the lower limits of current required to produce neuronal activity.

### **1.2.2 Problems Encountered or Unexpected Developments**

It is more difficult than we had hoped to make iridium microelectrode arrays with less than 10 percent electrode faults, due to iridium sputtering during deposition. The iridium layer also develops thousands of surface cracks with our present deposition technique. Serious liability and insurance problems at Draper Laboratories had to be resolved before Draper could help us with chemical analysis of possible contaminants. During our biocompatibility study, one rabbit died for reasons unrelated to the implant.

### **1.2.3 Further Progress Expected by June 1999**

We expect to carry out initial versions of the two key proof-of-concept experiments in the next six months including: (1) one or more short-term human surgical trials to determine what the patient can perceive with a 10 x 10 microelectrode array, and (2) trials with rabbits in which we implant a simple laser-driven stimulator and record a cortical signal.

We also expect to achieve short-term encapsulation of a prosthesis in biocompatible materials and verify using the resistance tests the protection it provides against saline leakage. We believe Mr. Grumet will make good quality *in vitro* recordings of rabbit retina response to electrical stimulation using the new microelectrode arrays he designed and that Mr. Shire will fabricate. We expect Mr. Lichtenstein will complete a working graphics-driven stimulation system for use in subsequent human trials. Mr. Grumet will present a poster session at a major conference (ARVO) on his work, and Mr. Kelly will complete his M.S. thesis on the stimulator for human trials. We expect that Mr. Shire will overcome the final difficulties and deliver iridium arrays with very few short circuits, open circuits, or surface metal cracks for use in future human experiments.

### **1.2.4 Meeting Papers**

Grumet, A.E., J.L. Wyatt, and J.F. Rizzo. "Multi-Electrode Recording and Stimulation of the Salamander Retina *in vitro*." Paper presented at the Association for Research in Vision and Ophthalmology Annual Meeting (ARVO), Ft. Lauderdale, Florida, May 1998.

Grumet, A.E. "Short Pulses, Small Electrodes, Low Currents Directly Stimulate Rabbit Retinal Ganglion Cells." Paper presented at the 29<sup>th</sup> Annual Neural Prosthesis Workshop, Bethesda, Maryland, October 28-30, 1998.



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### **1.2.3 Further Progress Expected by June 1999**

We expect to carry out initial versions of the two key proof-of-concept experiments in the next six months including: (1) one or more short-term human surgical trials to determine what the patient can perceive with a 10 x 10 microelectrode array, and (2) trials with rabbits in which we implant a simple laser-driven stimulator and record a cortical signal.

We also expect to achieve short-term encapsulation of a prosthesis in biocompatible materials and verify using the resistance tests the protection it provides against saline leakage. We believe Mr. Grumet will make good quality *in vitro* recordings of rabbit retina response to electrical stimulation using the new microelectrode arrays he designed and that Mr. Shire will fabricate. We expect Mr. Lichtenstein will complete a working graphics-driven stimulation system for use in subsequent human trials. Mr. Grumet will present a poster session at a major conference (ARVO) on his work, and Mr. Kelly will complete his M.S. thesis on the stimulator for human trials. We expect that Mr. Shire will overcome the final difficulties and deliver iridium arrays with very few short circuits, open circuits, or surface metal cracks for use in future human experiments.

### **1.2.4 Meeting Papers**

Grumet, A.E., J.L. Wyatt, and J.F. Rizzo. "Multi-Electrode Recording and Stimulation of the Salamander Retina *in vitro*." Paper presented at the Association for Research in Vision and Ophthalmology Annual Meeting (ARVO), Ft. Lauderdale, Florida, May 1998.

Grumet, A.E. "Short Pulses, Small Electrodes, Low Currents Directly Stimulate Rabbit Retinal Ganglion Cells." Paper presented at the 29<sup>th</sup> Annual Neural Prosthesis Workshop, Bethesda, Maryland, October 28-30, 1998.

