Project Overview

- Bio-labs-on-a-chip for capture and in-situ investigation of cells.
- Micro-electro-mechanical structures form cell-sized cavities (vial) and lids that can be opened and closed. The base of the vial has gold electrodes for recording extracellular electrical signals.
- Devices fabricated on silicon and complementary metal oxide semiconductor (CMOS) substrates. The integrated circuits are fabricated through standard commercial foundries.
- Potential applications in physiology, whole cell studies, collecting cell secretions, medicine, environmental monitoring, and remote biosensing.

Three Stages of “Evolution” for the Electrical Interface

**Previous: passive test fixture**
- Signals travel long distances prior to amplification
- Susceptible to environmental noise

**Currently: active test fixture**
- Signals amplified very close to site of activity
- Expect reduced baseline noise
- Overlapping potentials from many cells
- Successfully tested on bench and with cells

**Near future: instrumented cell clinics**
- Integrated Circuits isolated by cell-sized micro vials with lids
- Anticipate reduced environmental noise
- Isolated potentials from single or few cells
- First samples fabricated, but not yet tested with cells

Custom Amplifier Design

- Extracellular electrical signals from electrically active cells:
  - Small in amplitude (10-500mV),
  - Large unknown DC offset (1-2V possible),
  - Frequency content 100Hz - 8kHz

**Bioamplifier Design**

- The interface must amplify weak extracellular signals and isolate the noise in the cell medium from the signals originating from the cells.
- A low voltage, low noise CMOS differential transconductance amplifier designed for a +/-1.5 V supply.
- Has a cut off frequency of 3kHz with low pass characteristics.
- Fabricated in a commercially available 0.5µm CMOS technology.
- Gains of 20, 40, 100,1000 designed, fabricated, and tested successfully.

Custom Amplifier Packaging

- Al electrodes of the bioamplifier are electrolessly plated with gold.
- Creates a rough layer with a higher surface area.
- Electroless plating is preferred since electroplating requires an electrical connection to the plated surface that will reduce sensitivity and increase noise during measurement.

Future Work

Integrating sensors such as contact imagers and capacitive sensors, to enhance the utility of the Bio-Lab System on a Chip.

Acknowledgments

We thank Dr. William Bentley, Ben Woodard, and Dr. Ed Sybert of the Bio-process Scale-up Facility (BSF), and Dr. Bill Johnson and Dr. Jayaram Gopal of the Laboratory for Physical Science (LPS) and Chesapeake PERL, Inc. for technical assistance and support. Dr. Richard Wieland of Dept of Physics for chip bonding, Dr. Reza Ghodssi and Alireza Modafe of Dept of Electrical and Computer Eng for use of lab equipment, and Dr. Mark Martin of JHU Applied Physics Laboratory for providing test samples. We thank the MOSIS service for providing chip fabrication; these circuits will be used for teaching a bioelectronics course at the University of Maryland. This work was supported by National Science Foundation (NSF) grants 0225489, 0139401 and 0238061, and by the Laboratory for Physical Sciences.