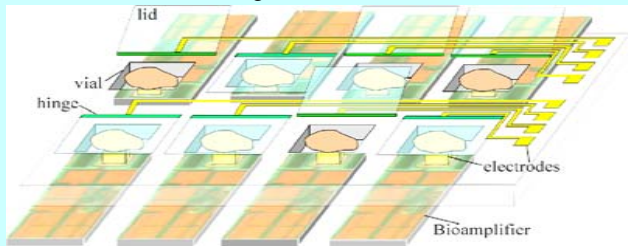


Nicole Nelson^{1,2}, Somashekar Bangalore Prakash^{1,2}, Makeswaran Loganathan^{1,2}, Suvarcha Malhotra^{1,2}

Jack Chaiyupatumpa¹, Jean-Marie Lauenstein¹, Dr. Pamela Abshire¹

¹Electrical and Computer Engineering/ ²Institute for Systems Research

Project Overview



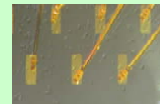
- Bio-labs-on-a-chip for capture and in-situ investigation of cells.
- Micro-electro-mechanical structures form cell-sized cavities (vial) and lids that can be opened and closed. The base of the vial has gold electrodes for recording extracellular electrical signals.
- Devices fabricated on silicon and 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

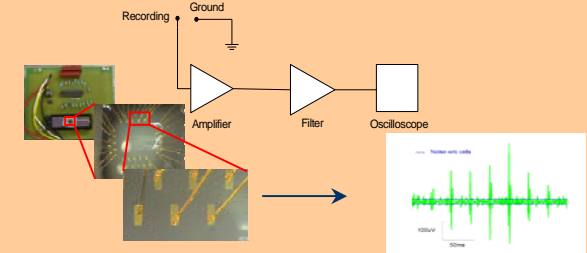
- Integrated Circuits isolated by cell-sized micro vials with lids
- Anticipate reduced environmental noise
- Isolated potentials from single or few cells
- First samples fabricated, but not yet tested with cells



Recordings of Electrical Activity

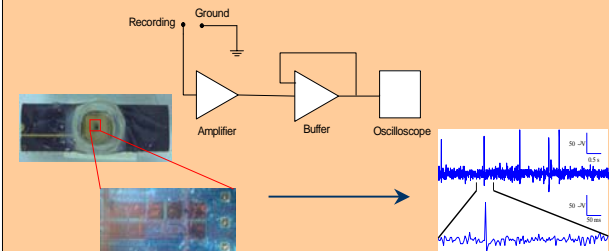
Passive Test Fixture

- Passive test fixture comprises discrete amplifier and band pass filter (8th order; pass band 500-5000 Hz, total gain of 100)
- Silicon die patterned with gold/chromium electrodes and wire bonded into a chip fixture
- Cells are plated onto Cr/Au electrodes on Si substrate.



Active Test Fixture

- Active test fixture comprises of an array of bioamps on a custom VLSI chip in 40 pin DIP chip package with bond wires encapsulated by epoxy and with well to hold culture medium
- Electrodes defined using Al layers in the CMOS process are electrolessly plated with Au
- Silicone RTV used to encapsulate bond wires, to isolate cells from toxic packaging and to form a well to contain the cell medium
- Cells are plated onto Au electrodes on VLSI substrate.



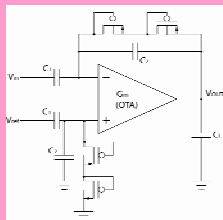
Custom Amplifier Design

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

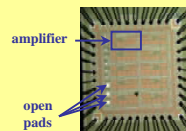
- The interface must amplify weak extracellular signals and isolate the noise in the cell medium from the signals originating from the cells.
- A low voltage, low noise CMOS differential transconductance amplifier designed for a +/-1.5 V supply.
- Has a cut off frequency of 3kHz with low pass characteristics.



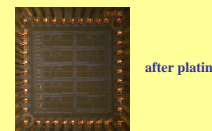
- Fabricated in a commercially available 0.5μm CMOS technology
- Gains of 20, 40, 100, 1000 designed, fabricated, and tested successfully

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.



before plating



after plating



A Silicone Room Temperature Vulcanate isolates cells from toxic packaging and insulates exposed bond wires from cell medium.



A well is formed on the 40 pin DIP chip to contain the cell medium



Fixture developed for testing with cells

Future Work

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

Acknowledgements

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