

ECE 480

Pre-Proposal

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Low-Cost Electrochemical Sensor System for Proteomics

MSU Advanced Microsystems/Controls Research Group

Design Team 2:

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Executive Summary

Early detection of tumor cells among healthy human cells is one of many problems in the medical industry that presents challenges both financially and technically. One possible solution to this problem is using the human body's cellular proteins as detectors. The process of testing for the presence and characterization of protein functions in bi-layer lipid membranes can be accomplished using three individual tests. Each of these tests demands its own set of equipment costing upwards of thousands of dollars. Dr. Mason has tasked Design Team 2 with creating a single efficient unit capable of performing all

three tests. This unit will cost significantly less than the current equipment used for any one of the tests.

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Introduction

The design project our group is presented with is called Electrochemical Instrumentation for Functional Proteomics. We are going to use modern analog components, microcontrollers, and computer data acquisition systems to perform low cost electrochemical instrumentation. Our system will be capable of performing multiple electrochemical techniques including chronoamperometry, cyclic voltammetry, and low frequency impedance spectroscopy to determine the presence or state of proteins. This will accommodate a broad range of signal levels to suit a variety of usage scenarios. Such an instrument would be a great asset to advancing functional proteomics and could lead to improved scientific understanding of biological processes and future generations of drug and treatment options for adverse conditions and diseases. Currently, there is commercial equipment available, but this equipment is quite expensive. Also the current equipment takes significant time to reach an analysis on an electrochemical test. Our group will design a product to improve on current technology while meeting the specifications of our customer.

Background Information

Functional proteomics is the systematic perturbation or functional inactivation of proteins within a given physiological environment to address the potential role of the target protein in a cellular process¹. Changes in the impedance of the protein channel correspond to the opening or closing of the channel in the bi-layer lipid membrane. These changes can occur on the femto scale, which requires extremely precise equipment to measure accurately. Some of the benefits of functional proteomics can be seen in the medical field. Knowing the individual functions of proteins in the human body has great implications for human health in the future. Protein targeted medicines, more effective anti-rejection treatments or even better biological implants² are made possible by knowing specific protein functions. Obviously, functional proteomics is a necessity for creating biological interfaces and electrochemical techniques that will help to advance the medical community.

Low frequency Electrochemical Impedance Spectroscopy (EIS)

“Impedance spectroscopy can be used to investigate the various physical processes occurring at the electrode such as diffusion, charge transfer and double layer capacitance.³” In systems such as cellular bi-lipid layer membranes, the impedance can be modeled as a resistor in parallel with a capacitor. Using EIS, the specific values of each component in the model can be found and used to design circuits to interface with biological systems. This information is determined by sweeping the frequency of a sinusoid input and recording the relative amplitude and phase of the output to create a Bode Plot.

Cyclic Voltammetry

In this test a triangle stimulus is used on the protein solution and the resulting hysteresis curve is then analyzed. This test provides information on the concentration of an electrolyte in solution such as Sodium Chloride in Water. Also, the diffusion rate of ions can be quantified because their movement in the solution creates a current that can be measured.

Chrono-amperometry

An electrochemical measuring technique used for electrochemical analysis or for the determination of the kinetics and mechanism of electrode reactions. A fast-rising potential pulse is enforced on the working electrode of an electrochemical cell and the current flowing through this electrode is measured as a function of time⁴ while the frequency components are also analyzed to give insight to the system.

Chronoamperometry is very useful in numerous applications. Some examples of its versatility are: finding relationships between common pharmaceuticals⁵, helping with the study and creation of electrodes⁶, the study of dental bonding polymers⁷, the study of effects of various brain endorphins⁸, and the creation of body implants.⁹ By no means is this list all inclusive, these examples barely scrape the surface of chronoamperometric potential.

Objectives and Design Specifications

The goal of this project is to create a low cost alternative to commercially available equipment for functional proteomics.

There are several objectives this project must complete. These objectives include the generation of various types and frequencies of voltage signals, the measuring of very small currents ranging from femtoamps to milliamps, and the analysis of the data on a local microprocessor. While performing the above tasks we will need to take the following into consideration:

Cost – The target cost for our final product is under \$100 dollars at mass production.

Size – Ideally the device would be handheld for field use, however initial designs will be tethered to a computer.

Accuracy – Precision current measurement is a must for this project. Great care must be taken in the building and testing of the design.

Power Consumption – In order to meet our final goal of being handheld we need to keep the project low power so it can operate using batteries.

Simple Design (manufacturing purposes) – The intention of this design is to become a manufactured product that is highly repeatable.

Ease of Use (user standpoint) – The finished product should be easy to use and understand.

Feasibility – Ability to complete the selected design choice under designated time constraints.

Satisfaction of Sponsor – Ability to meet sponsors ranked priorities.

Specifications from sponsor ranked by priority:

(1 highest) Feature

- 1 AC readout (10mHz – 1kHz, 10pts/decade)
- 1 DC readout (constant potential and triangle wave modes)
- 1 DC programmable rate and amplitude
- 1 Mode select
- 1 Wide current readout range
- 2 Programmable Vref
- 2 AC programmable amplitude
- 3 Automatic current readout ranging
- 3 Bluetooth connection to a PC (not critical but neat addition)
- 3 DC readout (saw tooth and normal pulse modes)

		DC bias Voltage (volt)	Max voltage	Min voltage	Scale rate(volt/second)	Resolution
DC	triangular/ saw tooth/ constant /voltage pulse wave	1.5-3.5V with 8b resolution, nominal value half of vdd	1V above the DC bias	1V below the DC bias	10m-1v/s	10bits
AC	Sinusoid/ cosinusoid		amplitude		Frequency:	SDFR>70dB
			5mV		1mHz-1KHz, 10 pts/decade	

Table 1: The specifications of the signal generator @5V supply voltage

parameter		Max (volt)	Min (volt)
working electrode current (ampere)	Small range	100n	10f
	Large range	1m	100n

Table 2: The range of the current through the working electrode

FAST Diagram

(Will be included in final proposal)

Conceptual Design Descriptions

There are two approaches we are considering to accomplish this project. The first design will be independent of a computer. The device will be stand alone having the capability for taking measurements, analyzing them locally, and providing the results on a display. The second design will require computer interaction. It will have the capability to take measurements independent of a computer, but the data will be transmitted back to a computer where it will be analyzed and reviewed.

Design 1

This design would be the stand-alone solution for solving this project and would come with many extra features. The extra features would include: high resolution LCD display for graphical interfacing, high computing power for data analysis as well as large storage for holding test results and protein databases. The process that this design will follow will start with the user. The user will select which test they want to perform (chronoamperometry, cyclic voltammetry, or low frequency impedance spectroscopy.) Once selected, the user will be able to adjust the frequency, voltages, scan rates, and mode (triangular/saw tooth/constant voltage/pulse wave). From here the signal generator will produce the selected signal which will then be sent to the potentiostat. Next the signal will enter the given solution. An induced current will then be created from the applied voltage and the impedance of the solution. This current will then travel back to the potentiostat. Now the signal will be conditioned to remove any extraneous noise and it will then be analyzed by the local microprocessor. Finally the results will be displayed to the user.

Design 2

This design will incorporate the computer for analyzing and displaying data. The process that this design will follow starts with the user as well. The user will select which test they want to perform on the device (chronoamperometry, cyclic voltammetry, or low frequency impedance spectroscopy). Once selected, the user will be able to adjust the frequency, voltages, scan rates, and mode also on the device (triangular/saw tooth/constant voltage/pulse wave). From here the signal generator will produce the selected signal which will then be sent to the potentiostat. Next the signal will enter the given solution. An induced current will then be created from the applied voltage and the impedance of the solution. This current will then travel back to the potentiostat. Now the signal will be conditioned to remove any extraneous noise. From here the data will be sent to the computer where it will be analyzed and displayed.

Ranking of Conceptual Designs

(Will be included in final proposal)

Proposed design solutions

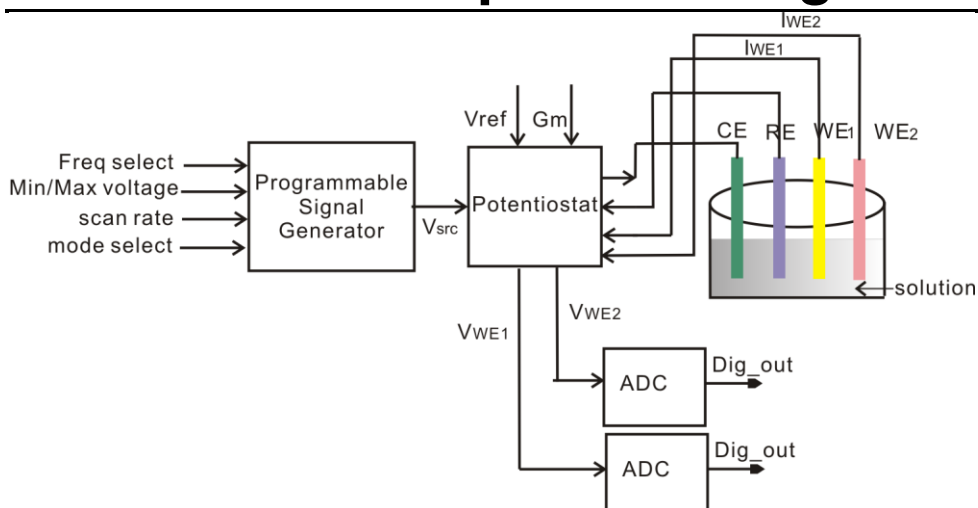


Figure 1: The block diagram of the electrochemical analysis system



Figure 2: The function schematic of the programmable signal generator.

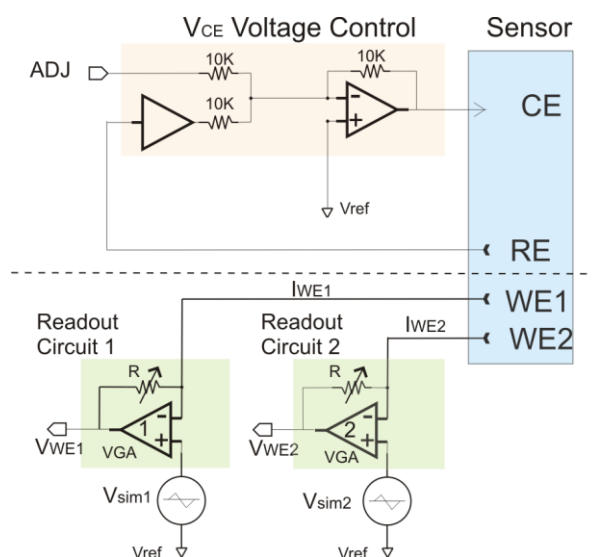


Figure 3: The Architecture of the CMOS bipotentiostat with connected counter electrode (CE), reference electrode (RE), and working electrodes (WE).

Design 1

The process that this design will follow starts with the user. The user will select which test they want to perform (chronoamperometry, cyclic voltammetry, or low frequency impedance spectroscopy) via a three way switch. Once selected, the user will be able to adjust the frequency, voltages, scan rates, and mode (triangular/saw tooth/constant voltage/ pulse wave) using a numeric display. From here the signal generator will produce the selected signal which will then be sent to the potentiostat. The potentiostat can be viewed as the electrochemical interface. The potentiostat consists of a power amplifier, a high input impedance voltage measurement reference, a current measurement input, and a control loop that maintains the required voltage signal. Next the signal will enter the given solution. An induced current will then be created from the applied voltage and the impedance of the solution. This current will then travel back to the potentiostat. The potentiostat will now serve a very important function. It will maintain the required DC conditions on the cell while the frequency response analyzer (FRA) performs the impedance analysis. The signal travels through the FRA where data can be analyzed.¹⁰ After leaving the frequency response analyzer, the signal will be conditioned to remove any extraneous noise. To do this we will use a low pass filter, then we will amplify the signal using a very low noise operational amplifier. It will then be analyzed by the local microprocessor. We will program the processor to operate a program similar to MATLAB or LabVIEW that will compute calculations and display the results. The results will be displayed on a high resolution screen located on the face of the device. The display will be able to show data statistics, Bode Plots and Nyquist Plots.

Design 2

The process that this design will follow starts with the user. The user will select which test they want to perform (chronoamperometry, cyclic voltammetry, or low frequency impedance spectroscopy) via a three way switch. Once selected, the user will be able to adjust the frequency, voltages, scan rates, and mode (triangular/saw tooth/constant voltage/ pulse wave) using a numeric display. From here the signal generator will produce the selected signal which will then be sent to the potentiostat. The potentiostat

can be viewed as the electrochemical interface. The potentiostat consists of a power amplifier, a high input impedance voltage measurement reference, a current measurement input, and a control loop that maintains the required voltage signal. Next the signal will enter the given solution. An induced current will then be created from the applied voltage and the impedance of the solution. This current will then travel back to the potentiostat. The potentiostat will now serve a very important function. It will maintain the required DC conditions on the cell while the frequency response analyzer (FRA) performs the impedance analysis. The signal travels through the FRA where data can be analyzed.¹¹ After leaving the frequency response analyzer, the signal will be conditioned to remove any extraneous noise. To do this we will use a low pass filter, then we will amplify the signal using a very low noise operational amplifier. A PIC will now take the signal and format it so it can be sent to a computer (via cable or Bluetooth). At a computer we will use LabVIEW to analyze and display the measurements. Our display will be capable of Bode Plots and/or Nyquist Plots. The computer will keep a record of all data and graphs.

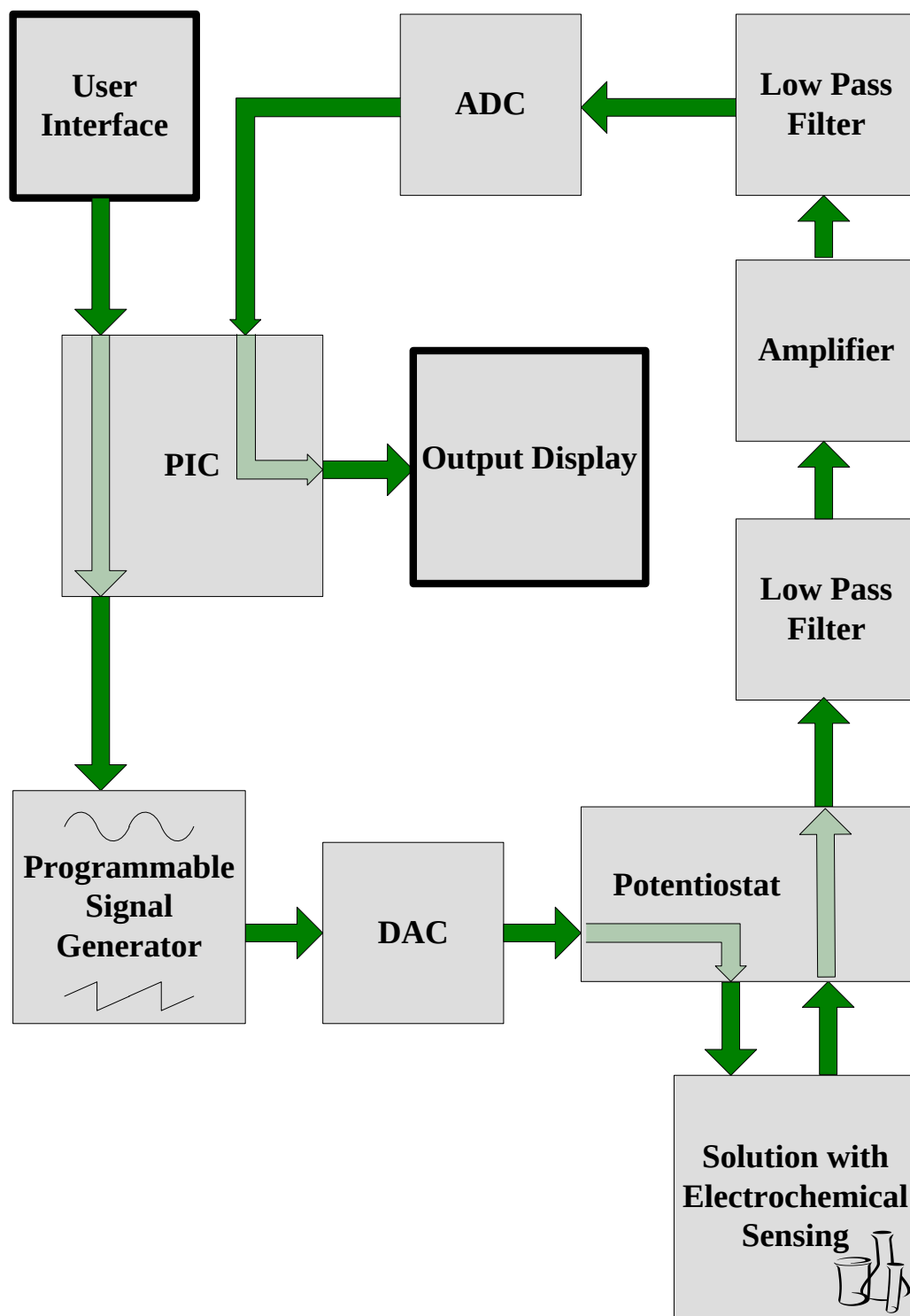


Figure 4: Design 2 Block Diagram

Risk Analysis

Some of the design concerns of constructing a circuit that can achieve these electrochemical techniques are as follows.

Accuracy: When it comes to measuring currents in the femto amp range, most lab equipment will have significant errors in the readings. These errors could be introduced from the tolerance of the components. For measurements in the femto amp range, even the smallest interferences will distort the signal or the measurement. High frequency light from the sun or lights in the lab can induce a current larger than femto amps, which will completely invalidate the results.

Noise: With extremely low currents and low frequencies, noise becomes a big issue. Even the components we add to the circuit board will contain noise that could corrupt our data and yield unwanted results.

Clean Environment: When assembling our design, we have to be extra careful not to add fingerprints or dirt to our circuit. Doing so can result in significant errors in measurements and possibly ruin the circuit altogether. This primarily becomes an issue when dealing with currents in the pico to femto amp range.

Mobility: Moving the device will cause vibrations which produce unwanted noise. The device should be as stationary as possible to prevent skewing the results.

Supplying Power: There will be multiple chips in our design, each with their own power requirements, which makes supplying the correct power to each component mandatory. Supplying too large a signal could burn up a chip.

Battery Life: There are a lot of measurements and data being collected, which might start consuming a large portion of a battery's life. The batteries that we use must be able to store large amounts of charge at a time. For example, when taking a measurement at 1 millihertz, the time it takes to complete one period is 1000 seconds. During this time, the system will be running at full power, acquiring data, which will be strenuous on the battery.

Financial Issues: The commercially available devices in existence that measure currents in the femto amp range are extremely expensive. The cheapest can be purchased for approximately two thousand dollars.

Project Management Plan

(Will be included in Final Proposal)

Budget

Equipment	Part Number	Manufacturer	Quantity	Price
Signal Generator			1	?
Potentiostat			1	?
ADC			1	?
DAC			1	?
Low Pass Filter			2	?
Amplifier			1	?
PIC			1	?
Current Sensors			2	?
Op Amp			multiple	?
ElectroChemical Sensor			2	?
Protoboard			5	?
Wire			-	?

Many of the parts will be free of charge courtesy of the ECE Shop.

Team Member Roles

Luke LaPointe – Web Design

Software Programming

Nick Timpf – Manager

Analog Circuitry

Mark VanCamp – Document Prep.

PCB Design

Brent Woodman – Presentation Prep.

Analog Circuitry

Steve Zuraski – Lab Coordinator

Lab VIEW Programming

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