

A UNIVERSAL MINIATURIZED ELECTROCHEMICAL SENSING PLATFORM
AND ITS APPLICATIONS

BY

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THESIS

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Abstract

We have developed a portable universal miniaturized electrochemical sensing platform, which integrates with a microelectronic sensor strip, that can perform various electrochemical and impedance sensing measurements. This sensing platform works as a miniaturized potentiostat that supports a number of potential waveforms such as cyclic voltammetry (CV) and differential pulse voltammetry (DPV), which are the foundations of modern electrochemical research.

This thesis first explains the theoretical basis and physical implementation of the sensing system, which covers design of hardware, embedded system and sensing algorithm. The circuit hardware principle is based on the three-electrode system widely used in electrochemistry experiments. Then the thesis discloses several real electrochemical applications that can be conducted using the sensing platform, which include measuring nitrate concentration and counting number of white blood cells. This inexpensive, portable device is also suitable for a variety of other applications, ranging from instant food/water quality examination to long-period environmental monitoring.

We tested this lab-on-chip sensing platform under different circumstances and confirmed the results with other commercial analytic testing methods. Even with strip variation and external noise, the sensing platform discussed in this thesis can still produce a fairly accurate result.

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Chapter 1. Introduction

1.1 Electrochemical Sensing and Motivation

Electrochemistry is the branch of chemistry that studies the interaction between electrical energy and chemical change. Electrochemical sensing is the method to transform chemical effects into electrical forms, such as voltage, current or impedance, which can be quantitatively measured and analyzed. The electrochemical methods have been developed for decades, and both established electrochemical technologies (like deep cycle lead acid batteries) and new emerging technologies such as electrochemical reactors and super-capacitors are becoming increasingly commercial [1]. However, we can rarely see any potentiostats around university laboratories or taught in undergraduate courses, which is the fundamental instrument for electrochemistry studies. The low penetration of potentiostats is primarily due to their cost – even the least expensive commercial ones cost thousands of dollars. We recently spent \$3000 just to upgrade the advanced potentiostat (CHI660D, CH Instrument) used in our lab for the additional differential pulse voltammetry (DPV) functionality. Moreover, most existing potentiostats are so bulky that they can only do measurements on fixed stations at laboratories.

However, many electrochemical measurements do not require research-grade accuracy. Some good examples are health-related and environmental applications. An inexpensive, portable miniaturized potentiostat with fewer features but reasonable accuracy would be best suited for such applications. With recent breakthroughs in nano-electrodes and microfluidic channels, electrochemical method is becoming more and more popular in point-of-care testing – the kind of simple testing that can be done at the time and place of patient care [2]. Compared to other classic

analytical methods, the electrochemical method can be easily integrated into a portable electronic device with low cost and programmable features. There is some scientific literature on portable potentiostats with focus on miniaturization [3, 4, 5] and special customized functions [6, 7]. However, these projects either suffer from limited voltage waveforms and thus limited applications, or lack a way to do real-time data analysis.

To overcome the limitation and constraints of existing electrochemical methods, this thesis presents a universal miniaturized electrochemical sensing platform that is able to perform cyclic voltammetry, differential pulse voltammetry and impedance magnitude sensing. The collected data is sent from the system to mobile phone using Bluetooth for real-time analysis through a specially developed phone application.

1.2 Cyclic Voltammetry and Differential Pulse Voltammetry

The voltammetry method is widely used in electroanalytical chemistry. In voltammetry, information about an analyte can be obtained by measuring the current as the potential is varied [8, 9]. Both cyclic voltammetry (CV) and differential pulse voltammetry (DPV) are derivatives of the voltammetry method with an emphasis on studying the electrochemical properties of an analyte in solution [10].

Cyclic voltammetry is a type of potentiodynamic electrochemical measurement. In a cyclic voltammetry experiment, the voltage potential across the working electrode ramps linearly versus time. Different from linear sweep voltammetry, the working electrode's potential changes back and forth between initial and set potential as shown in Figure 1.1(a). This process can be repeated

as many times as desired until features of the analyte become stable. After running for enough cycles, the current at the working electrode is plotted against the voltage potential applied to give the cyclic voltammogram trace. A typical voltammogram is shown in Figure 1.2 [11]. It provides valuable information as the peak current intensity is usually proportional to the concentration of analyte assuming fixed voltage potential sweep rate.

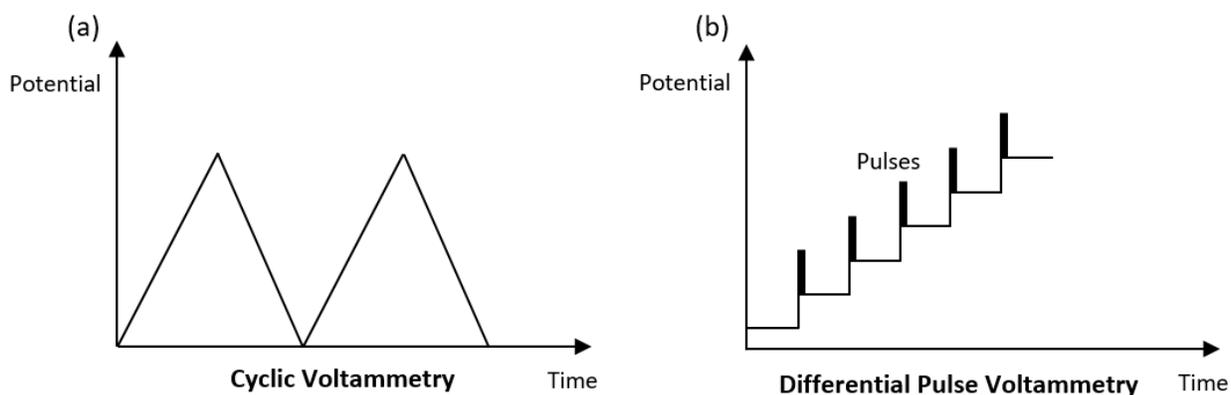


Figure 1.1 (a) Cyclic voltammetry curve voltage potential versus time. (b) Differential pulse voltammetry curve voltage potential versus time.

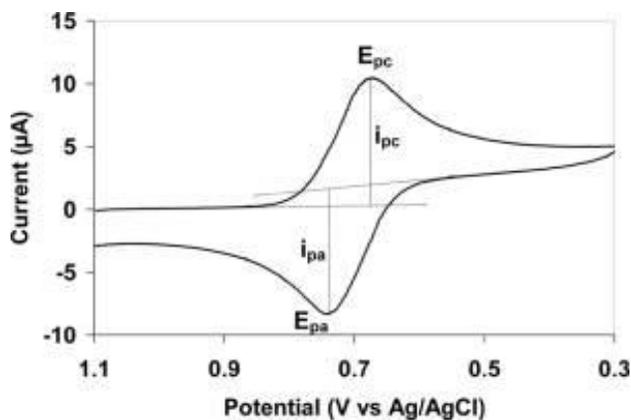


Figure 1.2 Typical cyclic voltammogram current versus voltage potential.

However, cyclic voltammetry is not always effective and accurate, especially when dealing with double layer capacitance. In some electrochemical experiments, the double layer capacitance of

the membrane electrode is far larger than that of wire electrode. Such a large double layer could introduce high interfering charging/discharging current to the actual Faradaic current when the voltammetry method with high scan rate is applied. This results in downgraded sensitivity and poor linear correlation, and thus the CV method is not optimal in this circumstance. A typical application with this kind of problem is white blood cell counting, which will be further discussed in Chapter 4.

On the other hand, differential pulse voltammetry (DPV) is the proper method to effectively reduce non-Faradaic current due to its current-difference mechanism and very slow scan rate [12]. The current difference is taken before and after applying a voltage pulse in order to analyze the Faradaic current caused by the small amplitude of the pulse. Given the short pulse width (50 ms) as the constant diffusion response time, the amount of cell particles can be quantified due to different diffusion response on the membrane electrode. An example of DPV curve is shown in Figure 1.1(b), where small pulses are added on top of the staircase voltage curve.

1.3 Impedance

Impedance measurement is another common electrochemical method for analyte analysis, as plenty of electrochemistry systems can be modeled as the equivalent circuit of resistor and capacitor combinations. Theory like electrochemical impedance spectroscopy (EIS) has been proven efficient in analysis of cell structure, diffusion control and metal coating [13].

Impedance is generally defined as “the total opposition a device or circuit offers to the flow of an alternating current (AC) at a given frequency, and is represented as a complex quantity which is graphically shown on a vector plane” [14].

Quantitatively, the impedance of a two-terminal network can be expressed in equation 1.1 in Cartesian form. The impedance is essentially the summation of the real part, represented by resistance R, and the imaginary part represented by reactance X. It can also be expressed using polar form, such that the impedance is the product of its magnitude and phase.

$$Z = R + jX = |Z| \angle \theta \quad (1.1)$$

A complete list of equations regarding the mathematical relationship between R, X, |Z| and θ is shown in Figure 1.3 [15].

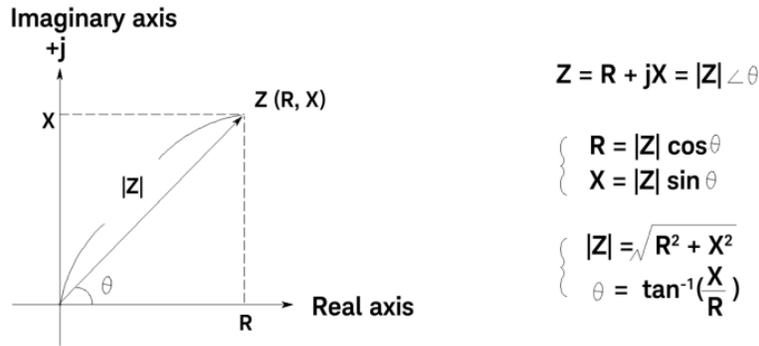


Figure 1.3 Impedance equations.

The impedance measurement of a network is not a simple task, as impedance needs to be determined under alternating current and the algorithm for phase calculation is complicated. We usually utilize an RLC meter when conducting research, but its size and cost limit its use as a point-of-care testing device. There is effort on designing portable impedance sensing devices; for example, our group integrated a commercial IC AD5933 designed by Analog Devices into the portable system [16].

For some impedance sensing applications, it is not necessary to determine the phase θ . Finding the impedance magnitude $|Z|$ would be sufficient. The magnitude of impedance can be measured using the same principle of measuring resistance, which is well established and can be easily integrated into portable devices. This way, we can significantly reduce the complexity and the cost of the sensing platform circuit.

Chapter 2. Three-Electrode System and Hardware Implementation

2.1 Three-Electrode System

A traditional electrochemical system consists of two electrodes, working electrode and reference electrode, and electrochemical reaction occurs on the electrode/electrolyte interface of the working electrode. To study the behavior of analyte at this interface, we need to monitor both voltage potential and current across electrodes. The electrochemistry experiment usually starts by perturbing the system and driving it away from equilibrium, which is done simply by applying a voltage to the working electrode. In order to apply voltage potential, we require some standard electrode whose potential is constant during the process. In a two-electrode system, the reference electrode is the only remaining choice for this job. However, having it act as both the reference and current carrying electrodes will introduce some problems. Even the widely used commercial standard hydrogen electrode (SHE) and silver chloride electrode will depolarize over time due to the passage of current, eventually causing potential drift such that they can no longer work as reference electrodes.

To solve the problem, a third electrode is brought into the system, which is called the counter or auxiliary electrode. The main purpose of the additional electrode is to complete the circuit to carry current and help the reference electrode maintain stable potential.

To summarize, for the three-electrode system, a voltage potential difference is applied across working and reference electrodes, while the current only flows between working and counter electrodes, leaving the reference electrode untouched.

2.2 Three-Electrode System Circuit Realization

The equivalent circuit of the three-electrode cell is shown in Figure 2.1. The capacitor symbol represents the double layer capacitance appearing at the electrode/electrolyte interface. The resistor represents the solution resistance existing in the system that opposes the flow of current. The current generator responds to the excess current generated during analyte chemical reaction at the working electrode.

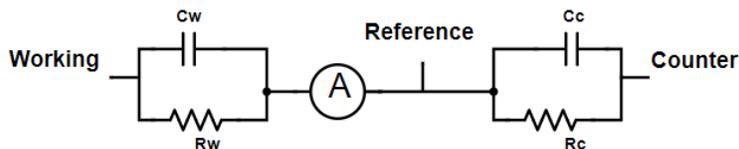


Figure 2.1 Equivalent circuit of the three-electrode cell.

With this background, in order to design a three-electrode electrochemical sensor that manages a cell of this kind, the circuit should have the following properties:

- The potential between working and counter electrodes remains constant.
- The circuit is bipolar such that it can operate regardless of the direction of current generated.
- The output signal of the system can be used to trace back and calculate the actual amount of current generated at the working electrode.
- The sensitivity of the sensing system is at least $1\mu\text{A}$.

An operational amplifier, or op amp, is the best electronic device to handle this kind of precise measurement problem. An op amp is a high-gain voltage amplifier with differential input and single-ended output. An ideal op amp has many properties that are suitable for sensing applications, such as infinite input impedance, zero output impedance, infinite open-loop gain and infinite CMRR. Figure 2.2 shows the minimal circuit implementation of a three-electrode system using op amps, which is also the working principle of a potentiostat [17]. Node CE, RE and WE stand for counter, reference and working electrode, respectively.

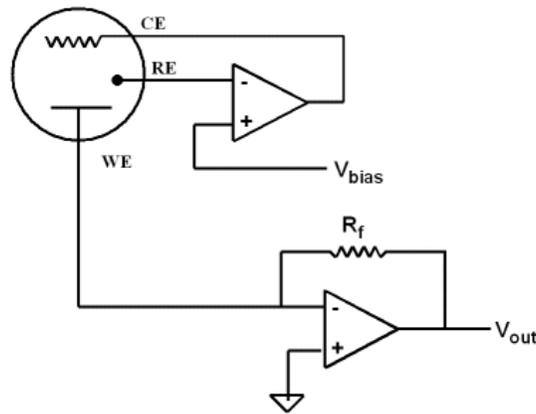


Figure 2.2 Three-electrode system circuit implementation.

The three-electrode system implemented in Figure 2.2 is configured using two op amps. Due to the op amp's feature of infinite input impedance, there will be no current flow in or out of its input terminals. Since the working electrode is connected directly to the inverting input terminal of the lower op amp, according to Kirchhoff's current rule, the current generated at that electrode will entirely flow through the feedback resistor R_f .

Suppose current I_w is generated during electrochemical reaction at the working electrode and flows through resistor R_f . Equation 2.1 depicts the relationship among voltage at the non-inverting terminal and output terminal of the lower op amp, current I and feedback resistor R_f .

$$\Delta V = V_{out} - V_- = I_w * R_f \quad (2.1)$$

Due to virtual ground, op amp inverting and non-inverting terminals share the same voltage potential as long as they fall in the power supply range. Therefore, we can tie the non-inverting terminal of the op amp to a known reference voltage, and then current I_w can be easily calculated from the equation. Note that to avoid negative voltage operation and voltage truncation, the inverting input should hold close to neither ground nor supply voltage. The reason is that, as mentioned earlier, the current could flow at both directions and we should leave some headroom for the peak current.

2.3 Miniaturized Electrode Strip

Miniaturized electrodes are evolving rapidly with the recent development in nanotechnology. The smaller size enables them to have quicker and more accurate sensing by lowering ohmic drops and creating smaller RC time constants. As we shrink the size of the electrode system, the distance between adjacent electrodes gets smaller. Since the equivalent resistance is proportional to the distance, it also gets minimized during miniaturization. This also reduces the response time of voltage steps and thus optimizes sensing speed, as the response time is primarily determined by the RC time constant.

Another advantage of miniaturized electrodes is the potential of integrating them into portable sensing systems. Various sensor strips have been recently designed in our group for electrochemical sensing applications. A good example is the three-electrode sensor strip fabricated for nitrate detection [18]. They all have standard connector size and are therefore compatible with

universal electrochemical sensing platform described here. Miniaturized electrode design and fabrication in real applications will be discussed in detail in Chapter 4.

Chapter 3. Electrochemical Sensing Platform

3.1 Overview

The electrochemical sensing platform is designed for portable usage and real-time data analysis. The system overview is shown in Figure 3.1. It has four major components, which are the microcontroller, power regulator, ADC/DAC, and three-electrode system.

The sequence of events during any electrochemical measurement is as follows: the desired voltage sweeping function such as CV or DPV is first selected. Then the microcontroller sends control signals to the digital-to-analog converter (DAC) through I2C protocol and the corresponding waveform is passed to the three-electrode system to activate chemical reaction. The current generated at the working electrode is converted to a voltage potential and simultaneously recorded by a high resolution analog-to-digital converter (ADC) at the output end. All the captured voltage data is temporarily stored in the microcontroller and sent to the smartphone through Bluetooth at the end of the measurement cycle for peak detection and analysis.

A smartphone-based software platform is developed for receiving sensor data and performing various detection and calculation algorithms. Before the measurement starts, the phone app runs an automated calibration program that sets the baseline of the current. This process can be seen as removing the common mode noise such that the actual generated current can be correctly captured.

Next, some of the important modules in the sensing platform will be discussed in detail so that the user can have better understanding of the working principle of the system.

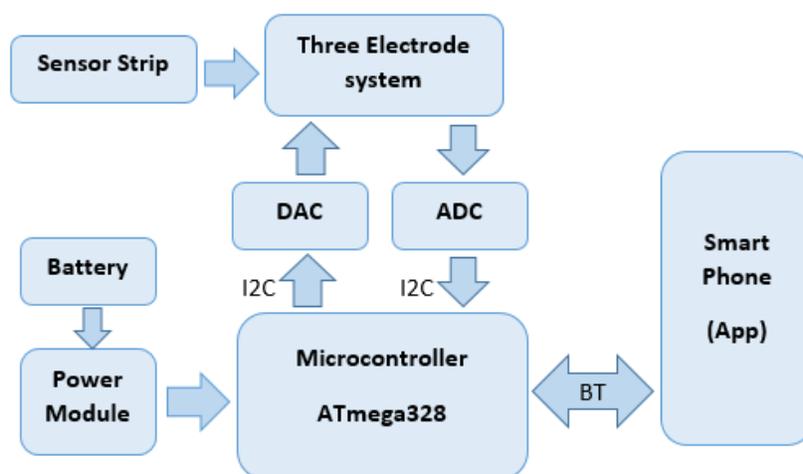


Figure 3.1 Electrochemical sensing platform system overview.

3.2 Power Module

The sensing platform is powered by a standard 9 V alkaline battery, while microcontroller and its peripheral require 3.3 V and other active components like op amps and ADC require 5 V dc voltage. Therefore, some voltage regulators are required to step down the battery voltage and distribute the power to the rest of the system. We also want the output voltage of the regulator to be stable even if battery voltage decreases slightly over time, as even minor voltage drift will result in inaccuracy of current measurement.

As mentioned before, the platform is specially designed for portable usage, and the goal is to have at least 3 hour battery life when in measurement mode. Therefore, we targeted for highest power efficiency during the voltage conversion. The circuit diagram for the power module is shown in Figure 3.2. We started with a buck converter, a type of switching regulator, to step the 9 V battery voltage down to 5.1 V. Comparing to a simple low dropout regulator (LDO), the switching

regulator can achieve power efficiency up to 90 - 95%. However, it suffers from low fidelity of the output signal, so the output voltage will have large ripples due to switching mechanism. This can be solved by adding a second stage to filter out the noise. The common approach is to use a π -shape network or place another linear regulator. We chose the latter as it helps to solve the voltage drift issue due to drop in battery voltage. The voltage outputs from LDOs are set to be 5 V and 3.3 V.

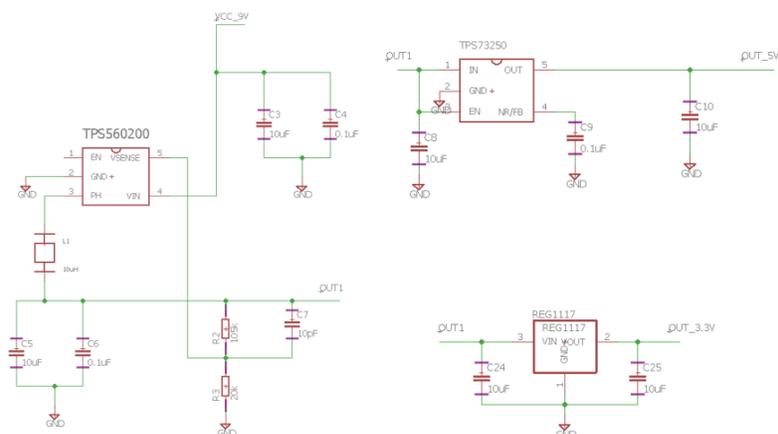


Figure 3.2 Power module circuit diagram.

3.3 ADC/DAC

ADC and DAC serve as the bridge between the microcontroller and three-electrode system. The voltage waveforms are coded inside the microcontroller, and a digital-to-analog converter translates digital information and presents it with an analog form to activate the chemical reaction. Both CV and DPV waveforms are essentially staircase with small square pulses added on. Therefore, a 12-bit DAC is sufficient for this application, as it can provide voltage resolution up to 1.2 mV, which has quantization error far below the specified 5 mV.

On the other hand, the output of the three-electrode system is an analog voltage signal, so it has to be converted back to digital information for the detection algorithm to run. A high resolution 16-bit Delta-Sigma analog-to-digital converter is chosen to capture tiny variations of current generated at working electrode. Since the current is calculated by the voltage difference across the op amp feedback resistor, another thought is to increase the resistance value such that we can use less accurate ADCs. However, big resistance may cause the output signal to go out of supply voltage range and result in truncation, and the larger noise brought by resistor due to the Johnson-Nyquist theorem will downgrade the sensitivity of the system.

The communication protocol between the ADC/DAC and microcontroller is I2C, which is widely used in portable consumer electronics. It minimizes the number of signal lines and therefore reduces the layout complexity. Also the clock stretching property allows slave devices to have additional time to operate under extreme cases.

Figure 3.3 shows some example waveforms at the output node of the DAC. They match the expectation with peak-to-peak voltage noise less than 3 mV.

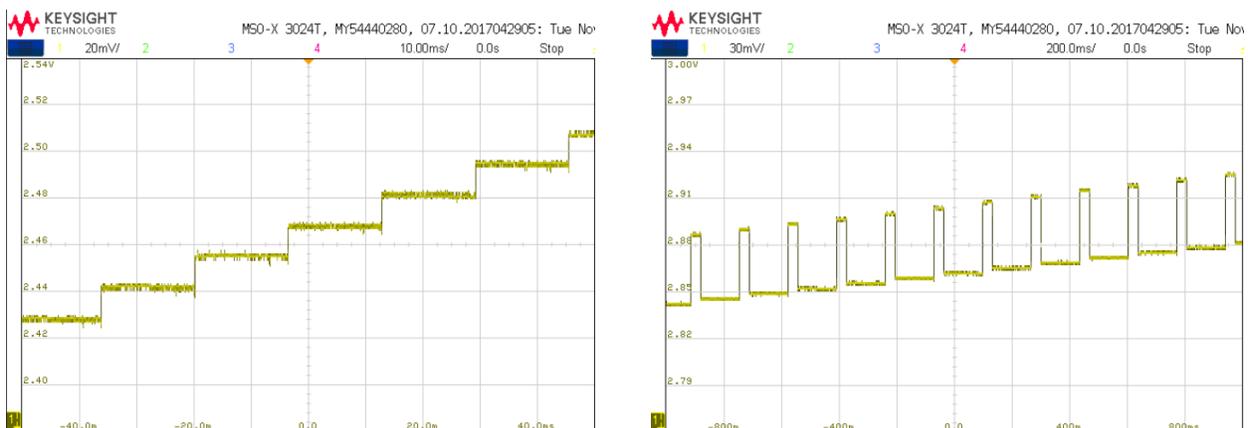


Figure 3.3 DAC output waveform CV (left), DPV (right).

3.4 Three-Electrode System

The circuit diagram for three electrode system is shown in Figure 3.4, and the working principle has been explained in chapter 2. The system consists of two low-noise, precision operational amplifiers, and two 10 kΩ resistors are placed among the working, reference and counter electrodes. They are used to calibrate the circuit components, as every passive components and chips in an IC may have some variations. Moreover, before the experiment those fixed resistors can be used to find the baseline current of the measurement which will eventually be subtracted in the detection algorithm.

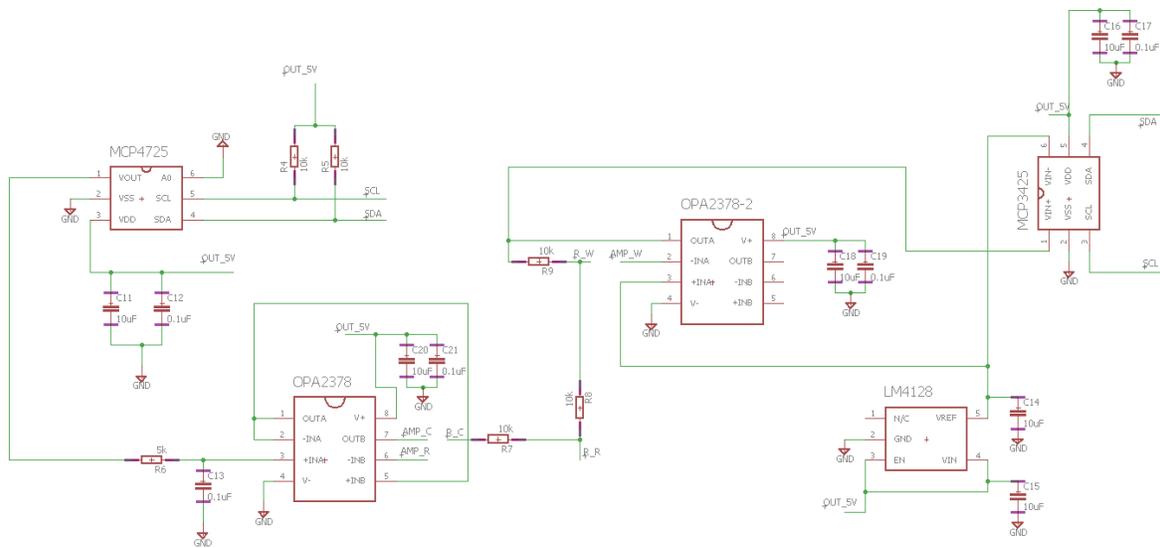


Figure 3.4 Three-electrode circuit diagram.

The value of the feedback resistor is also set to be 10 kΩ, in consideration of the output voltage range, current sensitivity, power consumption and noise. Every 10 μA current generated during chemical reaction will result in voltage difference of 100 mV at the output end. Through experiments on different applications, we conclude this value is optimized for most electrochemical measurements.

3.5 Sensor Strip Connector

Currently there is no standard miniaturized three-electrode connector on the market, as different connector designs are customized for specific applications and they all have diverse sizing and pin layouts. Our group sticks with a TE connectivity AMP connector (shown in Figure 3.5) for electrochemical measurement, such that all the sensing strips designed are compatible with this type of connector.

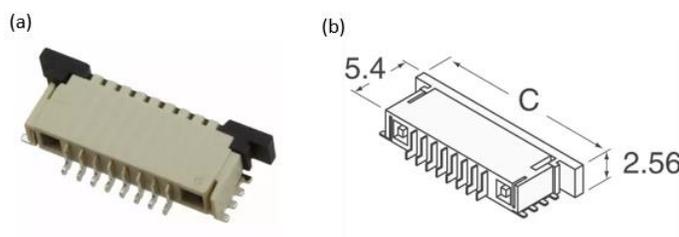


Figure 3.5 (a) Sensing strip connector photograph. (b) Sensing strip connector dimension drawing.

As the connector has eight positions while we only need three for the electrodes, we group and solder the pins together such that it will work with the sensing strip. The eight pins are soldered in a 3-2-3 configuration, i.e., three pins near the edge are connected and two pins in the center are connected. This design leaves a lot of flexibility for the dimension of the sensing strip; the distance and shape of the electrodes can be optimized as long as they have a firm connection with the metal pins. By utilizing this connector, the sensing platform becomes more versatile and is capable of doing various electrochemical measurements by selecting corresponding sensor strips.

3.6 Bluetooth and Mobile Phone

The microcontroller temporarily stores the measured voltage and dumps the entire set of data to the smartphone through Bluetooth at the end of the process. The communication is established through HC-05, which is a serial port Bluetooth module. An integer data array of size 255 is sent from the printed circuit board (PCB) to smartphone during each 'Calibration' or 'Run' process in a serial manner. The baud rate of serial communication is set to 9600 with no carriage return or line feed.

A mobile phone app is developed for receiving data from Bluetooth and performing various detection algorithms. The detection algorithm and formula for current concentration calculation can be customized according to the type of analyte. Chapter 4 discusses different algorithms and equations used in practical applications.

Chapter 4. Applications using Electrochemical Sensing Platform

Previous sections discussed the theoretical basis and hardware/circuit implementation of this universal electrochemical sensing platform. This chapter is focused on describing how the sensing platform can be used to solve real world problems. Applications on white cell counting and Nitrate concentration measurement are used as example, as we have achieved decent sensing results on those projects.

As this thesis emphasizes the role of the electrochemical sensing platform in the sensing application, details on chemical reaction and cell preparation are beyond our scope. If interested, please refer to original publications on those topics.

4.1 White Blood Cell Counting with Paper Electrochemical Sensor

4.1.1 Overview

White blood cells (WBCs) originate in the bone marrow and circulate throughout the bloodstream. The WBC is the main effector cell in the immune system and acts as a cell marker for the early diagnosis of bacterial infection and virally induced infection [19]. Therefore, correctly determining the concentration of WBCs can be beneficial for making therapy decisions and arranging treatment plans.

Traditionally, WBC counting is done by using a hemocytometer under microscope, measuring optical scattering, or applying fluorescence labeling [20]. However, all these methods require bulky instruments and experienced operators, which greatly limit their potential for point-of-care usage.

We therefore designed a paper microfluidic sensor for label-free WBC counting. The physical trapping of WBC was implemented on polyvinylidene fluoride (PVDF) membrane with micro-fabricated interdigitated electrodes, and analytical ion probes were used for electrochemical quantification. Considering the porous property of the membrane electrodes, which provides plenty of charge transfer pathways, differential pulse voltammetry (DPV) was used to quantify diffusion blockage by trapped WBCs. DPV function is well supported by our sensing platform and thus it is the ideal device for such application.

4.1.2 Paper Electrochemical Sensor Fabrication

The paper electrochemical sensor designed for white blood cell counting application contains two parts: the membrane electrode and its mechanical holder.

The membrane-based three-electrode system for electrochemical testing was designed using AutoCAD2011. The designed pattern was cut open on planar acrylic material with a laser cutting tool (Universal Laser Systems X-600) as shadow mask. Metal evaporation deposition (CHA SEC-600 E-Beam Evaporator) was then used to deposit a sequence of 10 nm titanium and 250 nm gold on the PVDF filter membrane. Figure 4.1 shows the completed version.

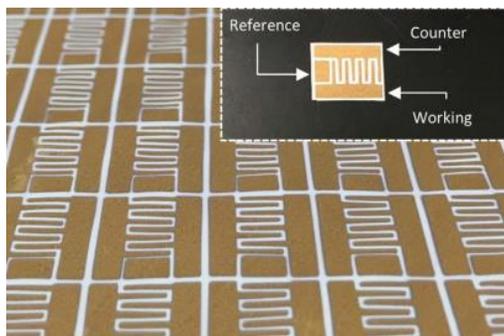


Figure 4.1 Three-electrodes on PVDF membrane paper.

Mechanical design of the portable system was implemented through Solidworks. The designed model was printed using a 3D printer (Ultimaker 2+, PLA material) at the resolution of 60 μm . The membrane electrode is sitting on top of a PDMS block, which was mixed with curing agent at the weight ratio of 10:1 and serves as a hydrophobic supporting substrate. All the PDMS components were finally assembled together with membrane electrode and wires as shown in Figure 4.2.

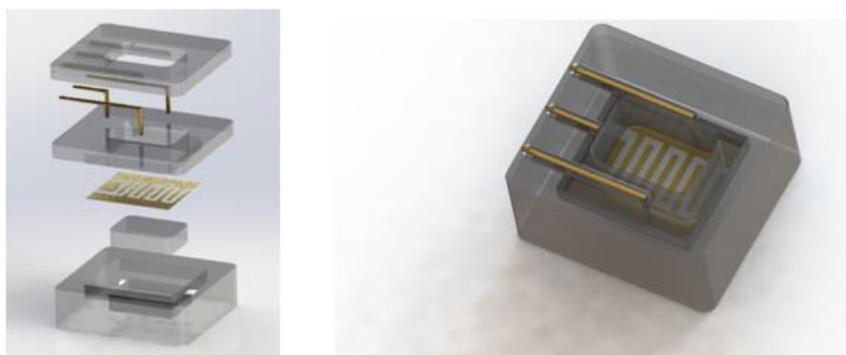


Figure 4.2. Whole package and explosive view of the sensor package

4.1.3 Measurement Process and Results

The sensor package is compatible with the connector described in Chapter 3. The electrochemical measurement can be started as soon as the sensor package is dipped with pre-prepared sample and plugged into the sensing platform. The process starts by calibrating the sensor and determining the baseline of current. The calibration command is sent from the smartphone when the user presses the corresponding button on the app. The microcontroller receives the command through Bluetooth and generates control signals to the rest of the system. After the calibration is completed, the user can begin the measurement by pressing the ‘test’ button. At the end of measurement, all the data

will be sent as an array back to the smartphone for plotting and analysis. The user interface for the mobile phone app is shown in Figure 4.3 (a).

After numerous experiments, we found that this portable electrochemical sensor is capable of doing human WBC counting in the concentration range of $195\text{--}25\text{ k } \mu\text{L}^{-1}$, because the differential pulse voltammetry peak current change in this concentration range can be linearly mapped to WBC concentration. The lower limit for our sensing system is $195\text{ } \mu\text{L}^{-1}$, which is 30 times lower than normal concentration ($\sim 6000\text{ } \mu\text{L}^{-1}$) in blood. The maximal peak current change ($\sim 60\text{ } \mu\text{A}$) is 60 times the current detection resolution ($1\text{ } \mu\text{A}$), which provides a very broad dynamic range for cell concentration measurement.

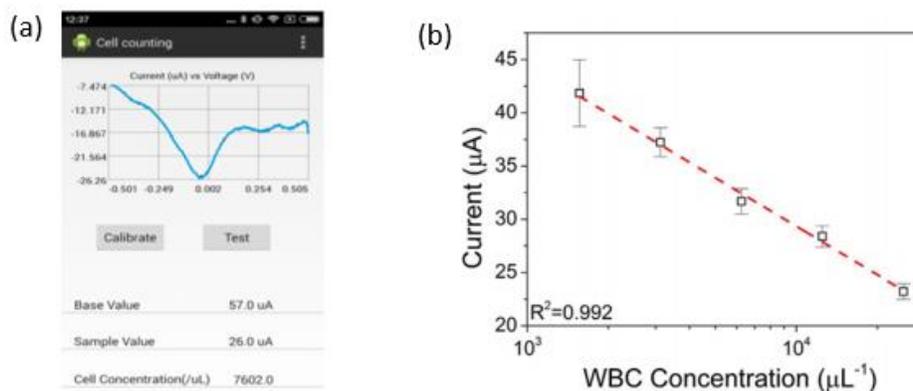


Figure 4.3. (a) Smartphone app user interface. (b) Measurement result concentration versus current.

Normalization by taking the ratio of sample current to background current was performed based on the background current (peak current from electrolyte) to cancel out the variation among different individual membrane electrodes. The normalization method leads to a better fitting in calibration. The coefficient of determination (R^2) for regression fitting was found to be 0.992 throughout the entire concentration range according to Figure 4.3(b). Therefore, the calibration equation to put in the phone app can be expressed as:

$$\text{Concentration} = 10^{116.09 - \text{current}/21.44} \quad (4.1)$$

Comparing to the measurement result using commercial potentiostat, the difference in current magnitude is less than 5%. The error is even lower after we do the fitting of the curve and map concentration with current. In general, the testing data proves that our portable sensing device has good matching with high-end equipment in the WBC application.

4.1.4 Conclusion

In this white blood cell counting application, we demonstrated a novel method of using a universal electrochemical sensing platform to achieve fast label-free WBC counting on micro-fabricated membrane electrode. The sensing principle was based on the linear relationship between electrochemical signal change and the cell concentration under differential pulse voltammetry (DPV) provided by the sensing platform.

From experiments, the dynamic range of this portable system covers three orders of WBC concentration ($10^2 - 10^4 \mu\text{L}^{-1}$), which is sufficient for most common diagnoses. Overall, our mobile WBC counting work shows its potential in future point-of-care applications like inflammation disease diagnosis at home.

4.2 Nitrate Concentration Measurement

4.2.1 Overview

Nitrogen is a vital part of living organisms; however, excess nitrogen could also have adverse health and environmental impacts. Both nitrate and its reduced form, nitrite, may cause environmental pollution and can be toxic to human health. Therefore, effective and accurate nitrate concentration measurement has become an imminent need.

Previous work has been done by our group on using an audio jack based mobile phone sensing device to determine the concentration of nitrate in solution [18]. The device is called ‘MoboSens’ and can be seen as the predecessor of the universal electrochemical sensing platform presented in this thesis. A customized nitrate three-electrode sensing strip was also designed and fabricated for this particular application. The working principles for these two sensing devices are exactly the same. Cyclic voltammetry is applied to the three-electrode system; peak current can be then located around the oxidation and reduction region of nitrate, and the magnitude of current is proportional to the concentration of nitrate in the solution.

4.2.2 Measurement Process and Results

The general measurement process is similar to that of WBC described earlier. First the user will have to dip the customized sensor strip into test solutions and then insert it into the connector on the sensing device. Now the device is ready for measurement as for this application we do not have to measurement background current or calibrate the device. While one significant difference is that we are applying CV instead of DPV in the Nitrate application. The voltage sweeping range is

set to be $-1.6\text{ V} \sim +1.5\text{ V}$ which is optimized for the analyte reaction. After the user starts the measurement on the mobile phone, the voltage across the working and reference electrodes sweeps back and forth in this region for a total of four cycles until the current curve stabilizes. The current data of the final cycle is sent to the mobile phone for peak detection and then converted to the concentration of nitrate.

The measured result and fitting curve are close to what was achieved in the Mobosens paper [18]. Due to the use of a high resolution analog-to-digital converter, data has higher repeatability at fixed concentration, which is considered an improvement in performance.

4.2.3 Comparison and Improvements

As mentioned above, the universal electrochemical sensing platform can be regarded as the enhanced version of Mobosens. They share a lot similarities, such as identical circuit design principle for the three-electrode system, and use common sensor connectors. The new electrochemical sensing platform is not only able to generate more voltage potential waveforms and therefore be used in more applications, it also has better performance in this particular nitrate concentration measurement.

The original Mobosens circuit does not contain a microcontroller, so it requires access to audio jack and a frequency modulator to convert the audio frequency into desired voltage. However, the frequency that audio jack can generate is limited to the audible range, which is around 10 Hz to 20 kHz with a relatively low resolution. Even with modulation, the voltage generated is greatly limited by the nonlinearity and noise brought by the frequency modulation chip CD4046. This results in drift voltage during cyclic voltammetry testing and affects the sensitivity of the system.

Moreover, the audio jack mechanism is different among various smartphone brands, models and even operating systems. New iPhone models do not have audio jacks which largely limits the potential usage of MoboSens. Even for phones with audio jack, often the phone audio jack cannot get activated as the impedance seen by the phone does not match that of the earphone. It is not hard to customize the internal circuit to accommodate one particular phone model, but having it operate on a variety of phones simultaneously could be a big challenge.

In contrast, the universal sensing platform uses Bluetooth, which is a standard communication protocol included in all smartphones. Therefore, it can be used regardless of phone brand and model, and requires no calibration. The voltage waveform is generated directly through the microcontroller and DAC, which eliminates the error brought by modulators and thus provides higher resolution. The 16-bit delta sigma ADC is also much more accurate than the microphone built-in A/D converter, which leads to better sensitivity.

Apart from that, the power module and mobile phone app are getting upgraded, which makes it a better portable sensing platform than MoboSens.

Chapter 5. Conclusion and Future Work

In summary, we demonstrated a portable universal electrochemical sensing platform for point-of-care usage. It contains a circuit board, a mobile application and some customized micro-fabricated three-electrode sensors. It has versatile functionalities and can be used for various electrochemical sensing applications including but not limited to white blood cell counting and nitrate concentration measurement. The hardware platform is found to have accuracy and sensitivity comparable to those of the traditional sensing methodology.

For future work, more sensing techniques, such as electrochemical impedance spectroscopy can be brought into the system. The size of the board can be further reduced through reworking board layout and replacing some ICs with smaller packages. An additional calibration process also needs to be developed to reduce board component variations and thus increase performance.

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