

DEVELOPMENT AND EVALUATION OF AN ON-CHIP POTENTIOSTAT FOR BIOMEDICAL APPLICATIONS

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Abstract: Potentiostat-based solutions are widely used as an instrumentation platform for electrochemical and biochemical sensing systems, which are extensively used in areas as diverse as biomedical analysis, food safety and monitoring of environmental pollutants. Biomedical diagnostics is a relatively new application area of these systems, which can allow for in vivo, long-term patient investigation outside of the hospital environment. It is expected that this emerging area will enable physicians to obtain radically new and unique diagnostic information. The development of such an on-chip potentiostat-based sensing system suitable for in vivo biomedical applications is the subject of the present study. The design is realized on a mixed signal silicon breadboard substrate which allows for a low cost and time efficient progression from concept to full integration on CMOS.

1 INTRODUCTION

Various electrochemical-based sensing systems play an essential role in modern life, with increasing demand for their use in biomedical analysis, food safety, bioterrorism agent detection and monitoring of environmental pollutants (Zhang et al., 2007). In general the techniques are performed using an electrochemical cell. This cell typically consists of three electrodes which are placed in an electroactive solution. These electrodes are referred to as the counter, reference and working electrodes. The basis of an electrochemical analysis is the forcing of a voltage across two of these electrodes (between working and reference) and the measurement of the resulting current between them, which is usually provided through the counter electrode (Wang, 2000).

In systems of this type (Ogurtsov et al., 2009) potentiostat-based electronic interfaces serve as the instrumentation transduction platform. The potentiostat circuit is at the core of a whole range of analytical electrochemical techniques including amperometry, voltammetry and impedance based measurements. It is a key component in research in corrosion, batteries, fuel cells, electro synthesis and general electrochemistry.

In the majority of laboratory instrumentation the device is implemented on PCB modules using

discrete electronic components since size or detection limit is not an issue. However, in this work, the size of the device is an issue and the electronic interface must be incorporated in a biomedical device which may be implanted. One possible solution to meet this requirement is the use of IC design techniques to develop an integrated system on a chip. The advantages offered by this solution, besides small size, include the potential for reduction in noise and power and also a decrease of electronic leakage current, which can lead to an improvement of the detection limit.

2 POTENTIOSTAT TOPOLOGY

The function of the potentiostat circuit is two-fold (Doelling, 2000). Firstly it has to force the voltage across two electrodes in an electrochemical cell to a controlled value, i.e. to create a potentiostatic system. To accomplish this task the circuit forces a current through the cell, often through a third electrode. In its most basic form the potentiostat consists of a single operational amplifier referred to as a control amplifier (Ahmadi & Jullien, 2005). In this configuration the current is forced from the amplifier such as to drive the differential inputs to the same value. This topology is at the core of all potentiostats, however many developments have

improved on the basic design (Ayers et al., 2007; Gore et al., 2006; Hasan, 2006).

A second but equally important function of the potentiostat device is to provide for the measurement of the current forced through the cell. A number of approaches can be taken for the current measurement but the use of a transimpedance amplifier is widely accepted as the optimum approach (Gamry Instruments, 2007). Another example forces the cell current through a small resistance and uses a differential amplifier to measure the resulting voltage drop.

The simplified device topology used in this design is illustrated in Figure 1. The control amplifier forces the control voltage, V_{control} , across the reference and working electrode (which is held at virtual ground). In order to hold this equality the current, I_{cell} , is forced through the cell and through the resistor R . The transimpedance amplifier measures this current and generates a voltage, V_{out} , which can conveniently be sampled by an ADC device.

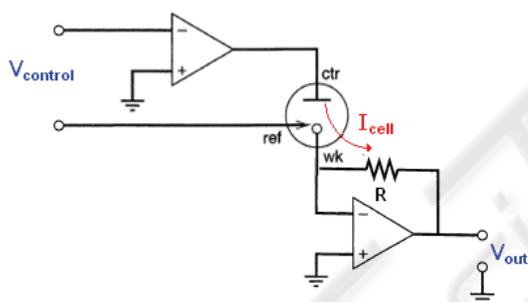


Figure 1: Standard potentiostat topology with inverting control amplifier and transimpedance current measurement.

3 INTEGRATED PROTOTYPING PLATFORM

In general the development of any new mixed signal circuit in the Tyndall fabrication facility, or indeed any facility, would require the layout design and fabrication of many layers (11 for the specified process) and the purchase of a full mask set. To justify a circuit fabrication a batch of 12 to 20 wafers would need to be done. The timescale behind such a fabrication would be in the region of three to four months and the cost could reach €30,000. Even in the best cases with mixed signal design, where the first prototypes are fully functional, they will often not meet the target

specifications and will require additional tweaking to fulfill the requirements. A second iteration is more often than not required to reach the full specification. In many cases three or more iterations may be necessary. The timeframe and cost of these multiple iterations can be prohibitive in many cases. This is particularly true in a research environment.

The integrated circuit used in this work was a prototyping platform based on a silicon breadboard technology. This is an integrated component array which supports a wide range of mixed signal functionality. The motivation of the silicon breadboard was to bring the advantages of gate array technology to mixed signal circuit development. The benefits are particularly relevant to the research environment at Tyndall, where new concepts are being explored and design requirements may change significantly over the course of a project. In these cases initial fabrications are required to obtain a working prototype while a couple more may be needed to meet the technical requirements.

The array, Figure 2, consisted of 1248 logic gates (lower two thirds of die) and an analogue section (upper third of die) consisting of 32 operational amplifiers, 1500 units of poly-poly capacitors, $2\text{M}\Omega$ of resistance in 40 sticks of 6 segments and a range of more specialized components including temperature and humidity sensors. The device is fully customizable by the application of a top layer metal interconnect which requires just a single mask. This gives a cost of just a few thousand Euro and a turn around time of just a few weeks. Undoubtedly the breadboard platform offers a huge advantage in respect of both time and cost.

The breadboard is fabricated using a large geometry (5 micron) on the C5P0 process, as this

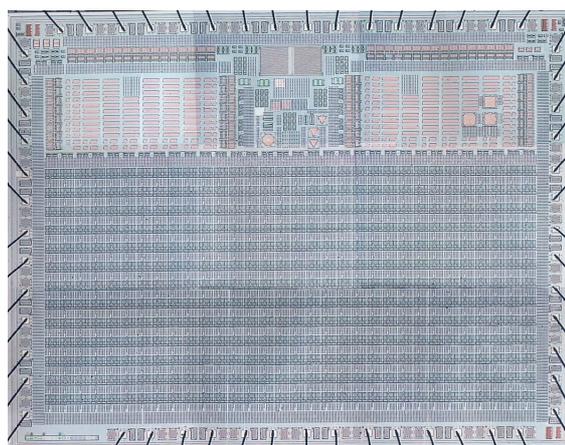


Figure 2: Integrated prototyping platform (8x10mm).

process has been proven and confirmed over a substantial number of lots. The large geometry is considered acceptable as speed is not an issue in sensor applications and the process is more than sufficient to push out the limits of sensitivity. The fabricated die has 56 pads and a size of 8x10 mm. However this is, after all, a development tool so this should not be a major concern. Many of the larger components will be redundant and trimming techniques can be used to reduce the die size.

4 IMPLEMENTATION

The on-chip sensing system interfaces to a three-electrode cell comprising a working electrode, a reference electrode and a counter electrode, as described above. The device was implemented on the silicon breadboard described using four of the amplifiers in the array along with a number of resistive elements. The amplifiers are two-stage devices using a P-input CMOS format. The design provides a slew rate of $1\text{V}/\mu\text{s}$, an open loop voltage gain of 80 dB and a closed loop bandwidth of 10 kHz while maintaining an offset voltage of less than $\pm 2.5\text{mV}$. The resistive elements are created from a combination of poly connect strips and the arrays resistive segments.

A specific requirement is the necessity of an enhanced dynamic range due to the differences in concentrations of target analytes in biological samples and the natural variations amongst patients and samples, which results in a widely varying sensor signal. The potentiostat, Figure 3, provides an exact replication of the applied signal from the digital to analogue converter (DAC) at the reference electrode, due to the feedback via the conducting biological sample solution.

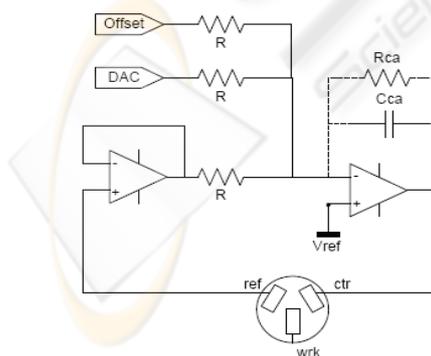


Figure 3: Potentiostat sensor control circuit with input stimulus voltage from DAC and connections to sensor.

The main problem in the design is to ensure system stability under the conditions of a high capacitive load from the working electrode. To ensure a stable device a provision is made to add a bandwidth reducing capacitance (C_{ca} , dotted interconnect) to the feedback path of the control amplifier. Also a bias compensation resistance can be added external to the IC. These components could easily be integrated into the device once their values are optimised.

A system reference voltage can be applied to the control amplifier non-inverting terminal. Equally the amplifier terminal can be grounded and an offset voltage can be applied in adder configuration with the DAC stimulus voltage. The value of the resistance R is not critical so long as the three resistors are well matched; $4.7\text{ k}\Omega$ was selected as it was most convenient for the process. The function of the buffer amplifier at the reference electrode was to eliminate any current flowing through the electrode resulting in a more stable reference for the cell and a more accurate measurement (without offset). The control amplifier can provide a sink or source of 3.5mA for the cell.

The transimpedance amplifier element of the device acquires the cell current from the working electrode and converts it to a corresponding voltage, V_{out} , as illustrated in Figure 4. A significant challenge for the current measurement is to meet the wide range of cell currents encountered in practice. Currents as high as a few mA to as low as a few 10s nA need to be detectable, so the gain range of the amplifier must be large. An integrated gain control block consisting of resistors R_1 and R_2 and a PMOS switch was included. With the switch opens the gain contribution is just the resistance R_1 but when closed the contribution is the parallel combination of R_1 and R_2 . This internal gain function was used in conjunction with an external potentiometer (dotted interconnect) which was first realised as a multiturn variable resistor but later as a 256 tap digital potentiometer for full gain control assuring the required dynamic range.

Another important challenge for the transimpedance amplifier design was to provide uniformity of the frequency response, and to eliminate possible oscillations in the transient process, which can occur from a wide capacitance range of the working electrode connected to the amplifier input. This is a particular concern where the device is controlled by a DAC which can only approximate smooth waveforms with stepped values. Again a provision was taken to connect a bandwidth reducing capacitance across the stage feedback path; that is between the working electrode and V_{out} pin.

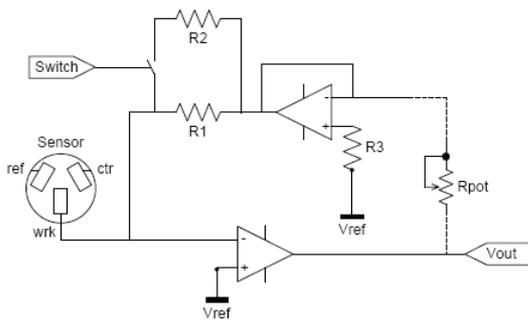


Figure 4: Transimpedance amplifier circuitry for measurement of working electrode current including external digital potentiometer.

5 EVALUATION

In order to evaluate the performance of the developed potentiostat device a cyclic voltammetry analysis was conducted with a gold working electrode in an aqueous 0.5 M sulphuric acid solution (H₂SO₄). For comparison a similar analysis was carried out using a commercial CH Instruments 620B laboratory benchtop instrument. The experiments were conducted in the potential window 0 to 1.5V. The voltammograms recorded for both systems are shown in Figure 5. Using the custom-built potentiostat, the voltammograms display an oxidation peak at 1.3V and a reduction peak at 0.7V. A similar response was seen using the commercial version. The variances observed could be attributed to the use of a different reference electrode for the different systems, an industry standard silver silver-chloride reference was used with the commercial instrument while a plated platinum reference was used for the miniaturised system. Furthermore the developed system had limitations in the DAC resolution of 12 bits while the commercial instrument provides 16 bits waveform synthesiser giving a closer approximation to the ideal analogue signal resulting in a better accuracy. In any case the systematic differences can be isolated from the sample response through calibration. The voltammograms obtained compare well with the literature for gold oxidation and reduction in a aqueous acid solution (Burke & Lee, 1992).

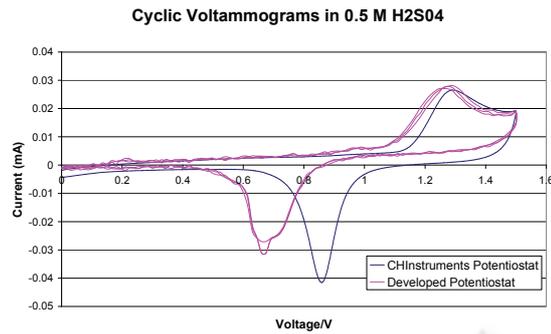


Figure 5: Cyclic Voltammogram for the developed potentiostat and a CHInstruments Potentiostat in 0.5M H₂SO₄.

Further evaluation was carried out to investigate the response of the device when placed in an embedded system. The application of the DAC generated stimulus voltage was a particular concern, since the required analogue signal could only be approximated with a signal stepped between discrete values. The response of the control amplifier and current measurement amplifier to the stepped signal had to be investigated. With sufficient bandwidth reducing capacitances in place (100pF across transimpedance amplifier, and 10pF across control amplifier) the step response was found to be over damped. An expected overshoot was observed in response to a step, Figure 6, but this quickly decayed within a few hundred micro seconds. Thus a stable measurement can be assured so long as a sufficient delay has elapsed between the signal step and current sampling.

As mentioned trimming techniques were used to reduce the size of the die, since many of its

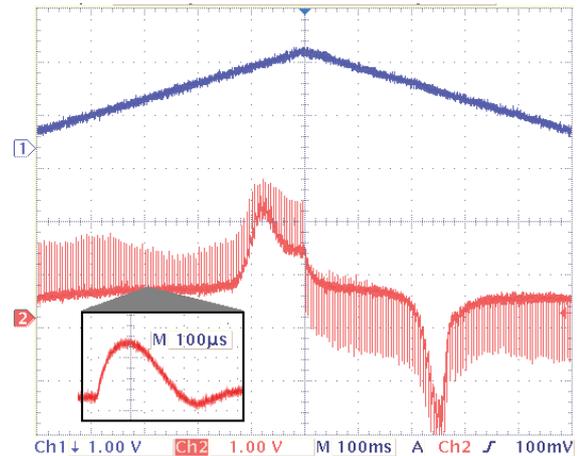


Figure 6: Time domain potentiostat response to a DAC generated cyclic voltammetry signal.

components were redundant in the application. In particular the sensors included in the die could be removed along with most of the logic gates and operational amplifiers. The die was laser cut to a length on 7.5mm giving a final overall size of 8x7.5mm. Some further optimisation of the die size could be obtained with improved routing.

6 CONCLUSIONS & FUTURE WORK

It is clear from the evaluation that the integrated potentiostat developed in this work performed well in comparison with a conventional commercially-available benchtop instrument. Further tests showed that when compared with a similar device assembled with discrete components the integrated version provided improved performance in a number of respects. Obviously there were advantages in terms of size but also the noise immunity and step response was found to be superior for the integrated device. In total the obtained technical characteristics of the device allow us to conclude that the developed chip is suited to the requirements of in-vivo biomedical applications.

The success of the early investigations of this device warrants one or two more iterations to improve on the design. Additional components will be integrated in the next iteration and consideration is being given to the full integration of the potentiometer with the gain control function. Furthermore the DAC could be integrated giving a full system on chip solution. In the longer term the device will be proven and fully evaluated before a full CMOS fabrication is considered. This will dramatically reduce the size of the final product. Using the integrated prototyping platform the road to a full integration will be shortened, and the total cost dramatically reduced.

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