

Glucose Meter Reference Design

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INTRODUCTION

This application note describes the basic glucose meter design using Microchip's PIC® 8-bit PIC16LF178X XLP device.

A glucose meter is a medical device used to determine the concentration of glucose in the solution. The glucose concentration is measured in units of milligram per decilitre (mg/dl) or millimole per litre (mmol/L), depending on the different regions.

The glucose meter is a key element of the Home Blood Glucose Monitoring (HBGM) device used by people with diabetes mellitus. The measurements can be taken multiple times in a single day.

PRINCIPLE OF GLUCOSE MEASUREMENT

The glucose meter determines the concentration of glucose in the solution. This application note focuses on the design of a glucose meter, including the necessary hardware design and software development.

Most glucose meters are based on electrochemical technology. They use electrochemical test strips to perform the measurement. A small drop of the solution to be tested is placed on a disposable test strip that the glucose meter uses for the glucose measurement. The two most common methods used in electrochemical measurement of glucose are the Colorimetric method and the Amperometric method.

Colorimetric Method

In this method, the typical sensors such as LEDs or photo sensors form the analog interface. These sensors are followed by a Transimpedance Amplifier (TIA) for the glucose concentration measurement in the solution. The Color Reflectance principle is used in this method to sense the color intensity in the reaction layer of the test strip by the photometry. The glucose meter generates a numerical value, that is a measurement of the glucose concentration present in the solution.

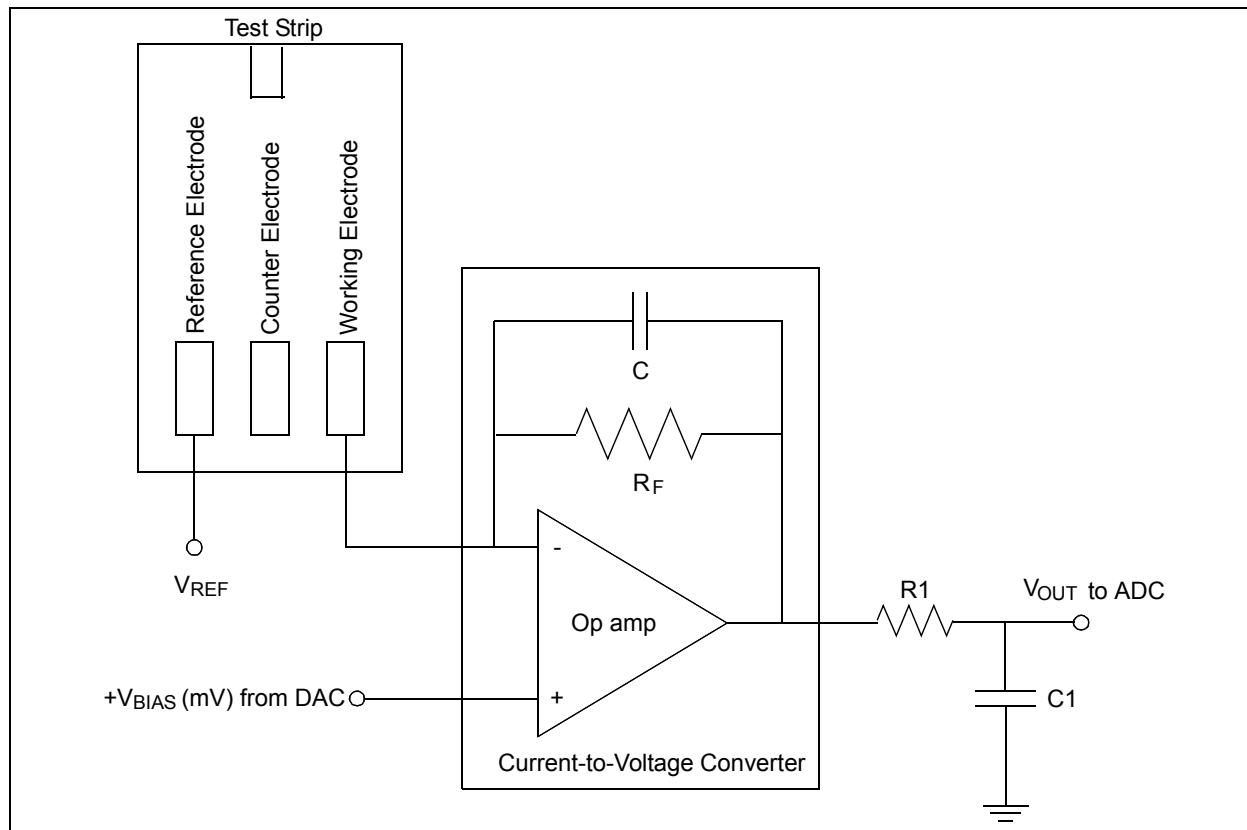
Amperometric Method

In this method, the electrochemical test strip contains a capillary that is used to draw in the solution placed at one end of the test strip. The test strip also contains an enzyme electrode containing a reagent such as Glucose Oxidase. Glucose undergoes a chemical reaction in the presence of enzymes and electrons are produced during the chemical reaction. These electrons (i.e., the charge passing through the electrode) are measured and this is proportional to the concentration of glucose in the solution. An ambient temperature measurement is also made in order to compensate for the effect of temperature on the rate of the reaction.

TEST STRIP WORKING PRINCIPLE IN AMPEROMETRIC METHOD

The majority of glucose meters are electrochemical and use the Amperometric method. [Figure 1](#) illustrates the glucose meter test strip working principle.

FIGURE 1: GLUCOSE METER TEST WORKING STRIP PRINCIPLE



The test strip forms the main biochemical sensor where the sample of solution is placed. The test strip has the following electrodes:

- **Working electrode:** Electrons are produced here during the chemical reaction. This electrode is connected to the current-to-voltage amplifier.
- **Reference electrode:** Held at a constant voltage with respect to the working electrode to push the desired chemical reactions.
- **Counter electrode:** Supplies current to the working electrode.

Most of the glucose meter designs use only two electrodes, reference electrode and working electrode.

A precise reference voltage (V_{REF}) is applied to the reference electrode and a precise bias voltage (V_{BIAS}) is applied to the op amp. This way the precise potential difference is maintained across the working electrode and the reference electrode. This voltage is the stimulus which drives the test strip's output current. The magnitude of the output current is then used to calculate the number of electrons produced.

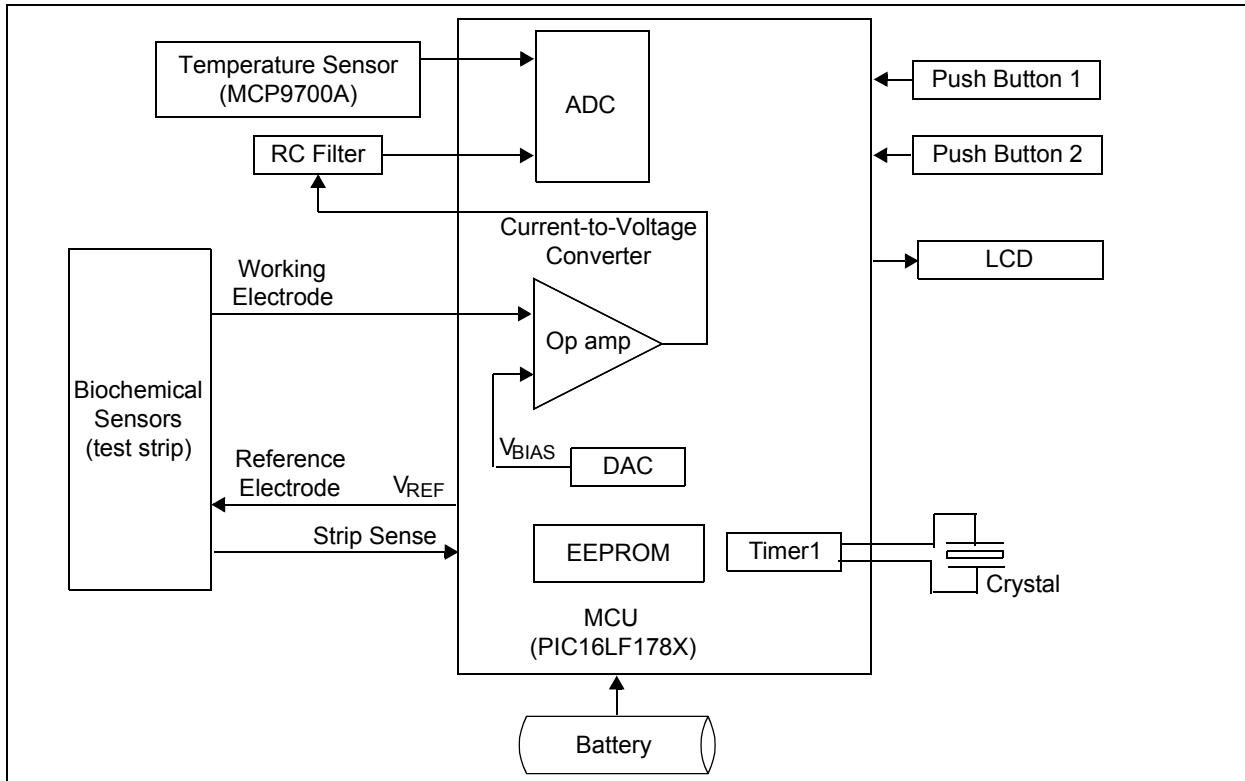
The solution sample is placed on the test strip and the reaction of the glucose with the enzyme takes place. Electrons are generated during the chemical reaction. Flow of electrons will correspond to the flow of current through the working and the reference electrode. This current will change according to the glucose concentration. The current is measured using a transimpedance amplifier (current-to-voltage converter) for the measurement with an Analog-to-Digital Converter (ADC).

The output of the transimpedance amplifier will be seen as a variation in the voltage with varying glucose concentrations in the solution.

DIGITAL IMPLEMENTATION OF GLUCOSE METER USING THE PIC16LF178X DEVICE

This section details the hardware design and the software development of the glucose meter using the Amperometric method.

FIGURE 2: GLUCOSE METER BLOCK DIAGRAM



The following are the features of the PIC16LF178X device and some of the peripherals in its integrated measurement engine:

- Extreme low-power (XLP) operation
- Two op amps
- 2x8-bit DAC
- 12-bit Successive Approximation (SAR) ADC, up to 11 channels
- Internal EEPROM
- Inter-Integrated Circuit (I^2C)
- 16-bit Timer1

When the solution sample is placed on the test strip, glucose undergoes a chemical reaction and electrons are produced. The flow of electrons (i.e., the current flowing through the working electrode) can be measured. This current will change according to the glucose concentration. The current is measured with the help of the current-to-voltage conversion using the internal op amp of the PIC16LF178X device and the filtering of high-frequency signals. The filtered signal is fed to the 12-bit ADC module of the device.

Figure 2 illustrates the block diagram of a typical glucose meter. The glucose meter can be implemented using the PIC16LF178X device.

The PIC16LF178X device starts capturing the voltage at the ADC channel after about 1.5 seconds of placing the solution sample. An average of about 2048 ADC readings is taken. This average value is substituted into the regression equation.

The glucose concentration is determined using this regression equation and the value is displayed on the LCD in units of mg/dl or mmol/l. Up to 32 glucose readings can be stored in the internal EEPROM and can be viewed later on the LCD. The power to the Glucose Meter Demo Board can be supplied from the on-board lithium battery (3V 225 mAH CR2032).

Note: The time to start capturing the ADC values (i.e., one second to 1.5 seconds) and the number of ADC readings taken should be modified to match the type and characteristics of the test strip to be used.

GLUCOSE METER REFERENCE DESIGN HARDWARE

This section provides the hardware design details of the glucose meter.

Design Specifications

- Glucose measurement range: 20 mg/dl to 600 mg/dl (1 mmol/l to 33 mmol/l)
- Test result is displayed within five seconds
- Automatic storage of last 32 glucose readings with date and time stamp
- No test strip coding: Generic regression equation will be implemented and can be modified based on the test strip characteristics

Hardware Design Features

- Number of boards: Single board
- PIC16LF178X Device: 28-pin device
- Debug/program: In-Circuit Serial Programming™ (ICSP™) connection provided
- Monitoring/indication: Test points
- Test strip connection: Terminals/connector provided
- RTCC (using internal Timer1): Date and time stamp for the glucose meter
- Internal EEPROM:
 - Record last 32 readings of the glucose meter
 - Store any parameters or calibration data related to the test strip
- LCD:
 - Display the solution glucose content in units of mg/dl or mmol/l
 - Display the messages: "Insert Test Strip", "Strip Inserted Place The Sample", "Faulty Test Strip"
- Test strip sensing: To detect insertion of the test strip
- Temperature sensing: Provision given to consider temperature variation for the glucose calculations. If relation between the temperature and the glucose concentration is known, it can be incorporated in the regression equation to take care of any changes in the glucose concentration due to temperature variations.
- Battery voltage sensing: Battery health sensing and low battery indication
- Two push buttons: To read previously stored data on the LCD, and to set date and time
- Battery: CR2032: 3V, 225 mAH lithium battery

GLUCOSE METER FIRMWARE IMPLEMENTATION

Firmware Features

- Sensing of test strip current using the internal op amp, DAC, and ADC of PIC16LF178X
- Captures ADC readings after the test strip is inserted and checks for a rise above 450 mV
- Starts recording the ADC readings, 1.5 seconds after the test sample is placed on the test strip and calculates the average
- Calculates the glucose concentration using the regression equation and the average ADC reading

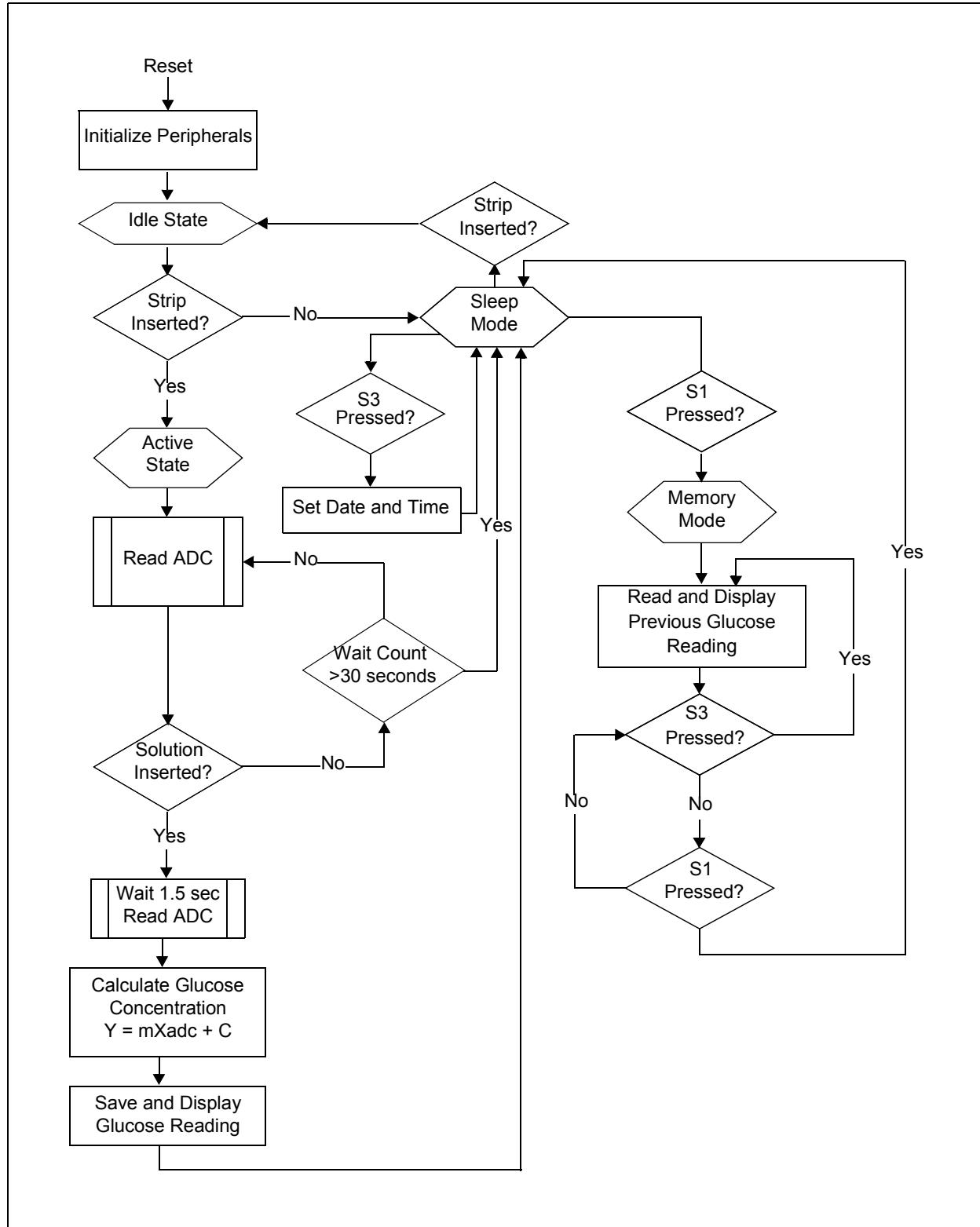
Firmware modules are available for the following features:

- LCD interface and display routines
- Configuration of op amp
- Configuration of DAC
- Store glucose readings into the internal EEPROM
- Reading the ADC channel
- Calculation of glucose concentration
- Implementation of the RTCC using Timer1 for time-stamping

Firmware Flowchart

Figure 3 illustrates the firmware flowchart.

FIGURE 3: FIRMWARE FLOWCHART



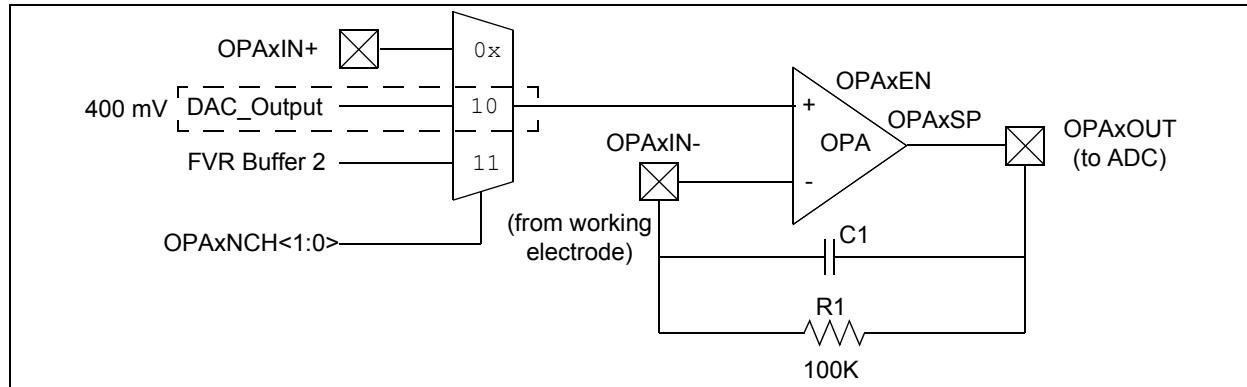
DAC Configuration

The voltage reference of the DAC is connected to the internal Fixed Voltage Reference (FVR) buffer 2, configured for the 2.048V. The DAC output voltage is set to be 400 mV.

Op Amp Module Configuration

As shown in [Figure 4](#), non-inverting input channel of the op amp is connected to the DAC output set at 400 mV. The inverting terminal of the op amp is connected to the working electrode. The current-to-voltage converter is formed with the help of the external resistor and the capacitor. The output of op amp is connected to the ADC channel of the PIC16LF178X device.

FIGURE 4: OP AMP CONFIGURATION



ADC Configuration

The op amp output (i.e., current-to-voltage converter output) is measured with ADC channel 0 (RA0/ AN0). ADC channel 3 (RA3/AN3) is used to measure the battery voltage to indicate the low battery condition. Output of the temperature sensor (MCP9700A) is connected to the ADC channel 8 (RB2/AN8) to read the temperature.

EEPROM

Glucose readings are stored in the internal EEPROM. During Sleep mode if the switch S1 is pressed, the PIC16LF178X device enters Memory mode and the stored glucose reading is displayed on the LCD. To view the previous glucose readings, the switch S3 has to be pressed. Press the switch S1 again to exit Memory mode.

LCD Interface

A 16 x 2 character LCD "NHD_C0216CZ-FSW-FBW-LCD" from NHD is used for displaying the glucose reading and text messages. Power to the LCD is cut off during Sleep mode by controlling the Vss of LCD through the port pin of the microcontroller.

RTCC

Timer1 along with the external 32.768 kHz watch crystal is used to implement the RTCC. The current date and time can be set for the RTCC using switches S1 and S3.

Determining Regression Equation

The following steps were used to determine the regression equation for the design of the Glucose Meter:

1. Using solutions with different glucose concentrations, the voltage profiles at the ADC output were captured.
2. Moving average of about 2048 ADC readings were taken, approximately 1.5 seconds after the sample was placed on the test strip. The average ADC reading was found to give a linear variation with respect to the glucose concentration of various test solutions (multiple ADC readings at short intervals can be taken and averaged to get more accurate results).
3. Determine the best fit equation using the poly-fit function in MATLAB®, regression feature in Microsoft® Excel or any other math tool. For example, a linear equation yielded good results, and was selected. See [Equation 1](#).

EQUATION 1: GLUCOSE REGRESSION EQUATION

$$Y = mX + C$$

Where,

Y = Glucose concentration in mg/dl

m = Slope

X = Average ADC reading of op amp output voltage

C = Constant

GLUCOSE METER CURRENT CONSUMPTION

The current consumption of the glucose meter in Active mode is approximately 1.1 mA, and it consumes 3 μ A during Sleep mode. The glucose meter will be in Sleep mode most of the time. We can consider Sleep mode time to be approximately 99.5%. The average current consumption of the glucose meter can be calculated as shown in [Equation 2](#).

EQUATION 2: AVERAGE CURRENT CONSUMPTION

$$0.995 \times 0.003 + 0.005 \times 1.1 = 0.008485 \text{ mA}$$

(i.e., 8.485 μ A)

Expected battery life for the 3V, 225 mAh coin cell is 26517 hours (i.e., 3.03 years).

FIGURE 5: GLUCOSE METER DEMO BOARD (FRONT VIEW)

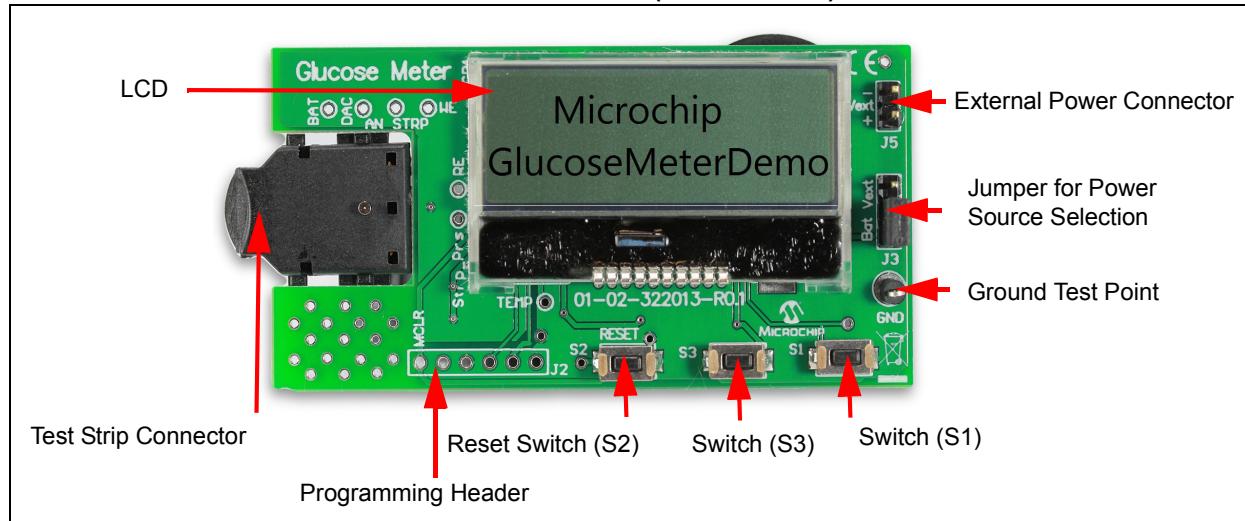
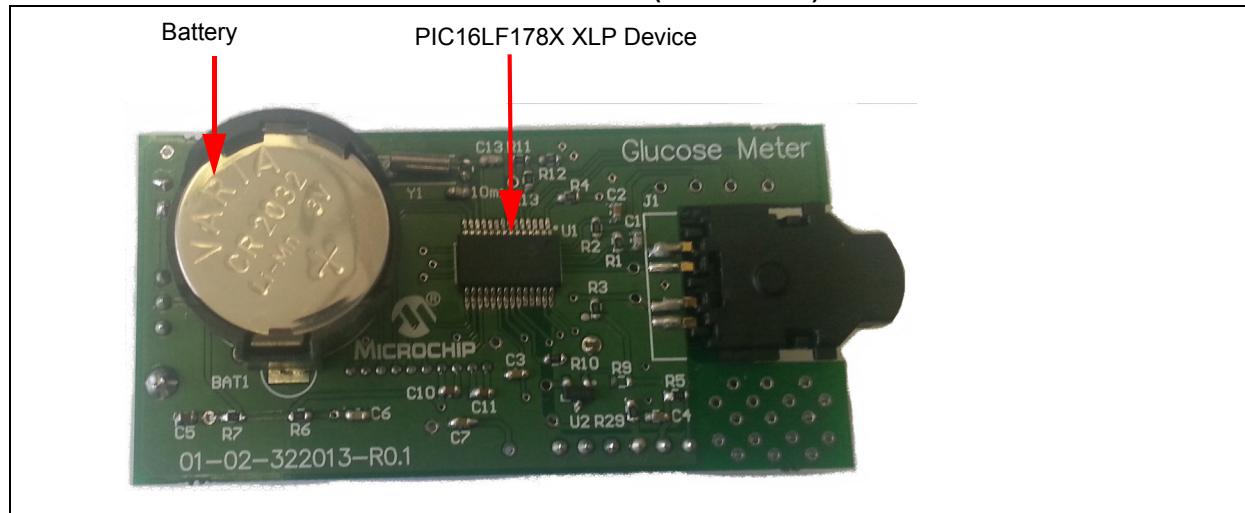


FIGURE 6: GLUCOSE METER DEMO BOARD (REAR VIEW)



DEMONSTRATION OF GLUCOSE MEASUREMENT USING THE GLUCOSE METER BOARD

This section describes the process involved in the measurement of glucose using the Glucose Meter Demo Board. For the test purpose, a standard test solution with a known concentration of glucose can also be used.

[Figure 5](#) illustrates the front view of the Glucose Meter Demo Board. [Figure 6](#) illustrates the rear view of the Glucose Meter Demo Board.

The current date and time for the glucose meter can be set using switches S1 and S3.

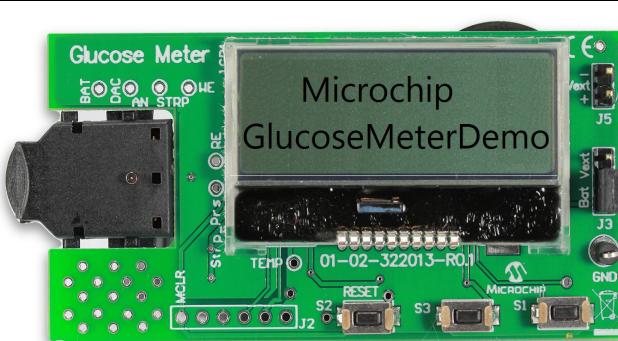
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Measuring Glucose using Glucose Meter

Perform the following steps for measurement of the solution glucose using the Glucose Meter Demo Board:

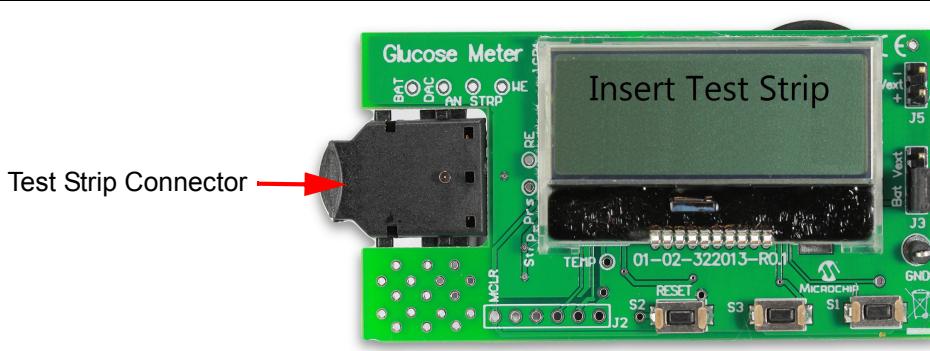
1. Power-up the Glucose Meter Demo Board, or press the switch S2 to reset the demo board. The start-up display will be as shown in [Figure 7](#).

FIGURE 7: GLUCOSE METER DEMO BOARD AFTER RESET



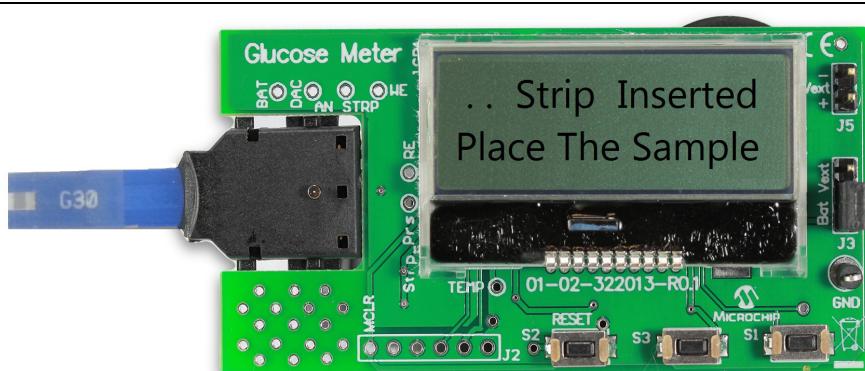
2. After about two seconds, the "Insert Test Strip" message will be displayed, see [Figure 8](#).

FIGURE 8: GLUCOSE METER DEMO BOARD WAITING FOR TEST STRIP INSERTION



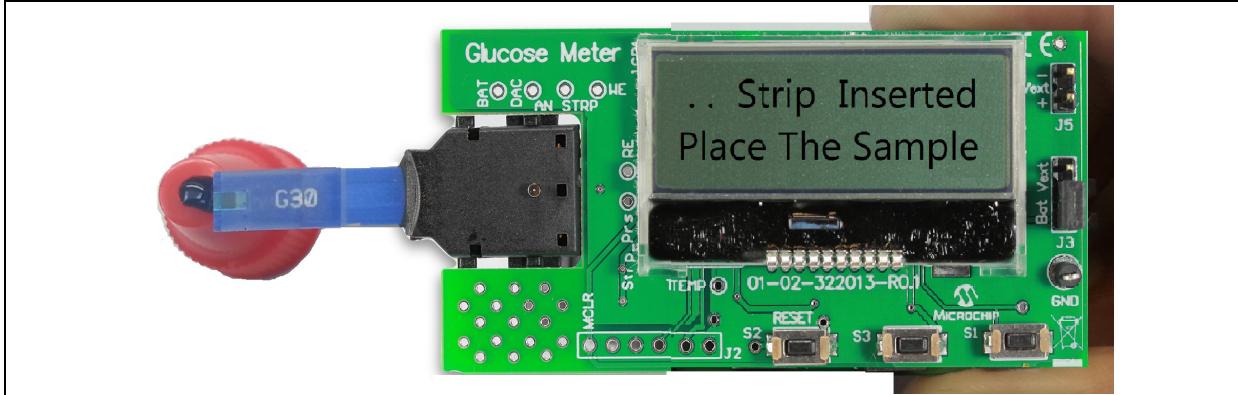
3. Insert the test strip into the test strip connector. When the test strip is inserted, the "Strip Inserted Place The Sample" message will be displayed, see [Figure 9](#).

FIGURE 9: GLUCOSE METER DEMO BOARD WAITING FOR SOLUTION SAMPLE



4. Place the solution sample or standard test solution on the test strip, see [Figure 10](#).

FIGURE 10: GLUCOSE METER WITH STANDARD TEST SOLUTION PLACED ON TEST STRIP



5. The glucose meter starts capturing the output voltage profile of the transimpedance amplifier, and then calculates the glucose content in the solution.
6. The concentration of glucose will be determined in 4 to 5 seconds, and displayed in units of measurement (mmol/l with time in hh:mm (24 hour) format and mg/dl with the date in mm/dd/yy format), see [Figure 11](#). The solution glucose reading will be saved in the internal EEPROM of the glucose meter.

FIGURE 11: GLUCOSE METER DEMO BOARD AFTER CALCULATING THE GLUCOSE CONCENTRATION IN THE SOLUTION



7. Remove the test strip after the glucose measurement. The PIC16LF178X device will enter Sleep mode after removing the test strip.
8. To measure another solution glucose reading, insert a new test strip in the test strip connector. The PIC16LF178X device will wake up from Sleep mode, then repeat Step 4 through Step 7 to measure the concentration of solution glucose.

Setting Date and Time for the Glucose Meter

Perform the following steps to set the current date and time for RTCC of the glucose meter:

1. Press the switch S3 to set the current date and time for the RTCC. Enter date in mm/dd/yy and time in hh:mm (24 hour) format, see [Figure 12](#).

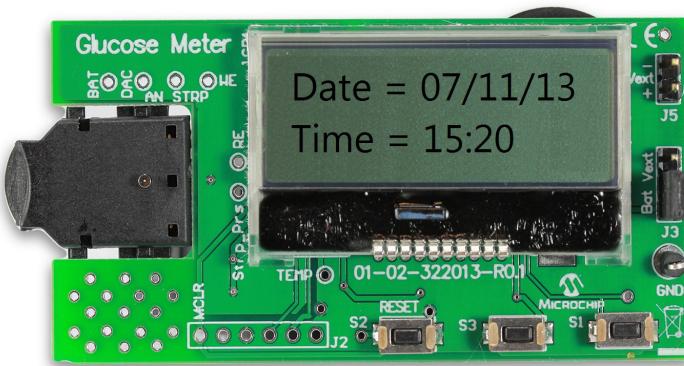
Note: To set the month as November (i.e., 11th month), press switch S1 once to set “1” as the first digit, and then press switch S3 to move to the next field entry. Press switch S1 once to set “1” as the second digit, and then press switch S3 to move to the next field entry (i.e., date). Repeat the procedure to set date, year, hour and minute for the RTCC. If the field to be set is zero, then press switch S3 directly to navigate to the next field entry.

FIGURE 12: GLUCOSE METER DEMO BOARD FOR SETTING DATE AND TIME



2. LCD will display the set date and time (for example, the date is set as 11th July 2013 and time is 3:20 p.m.), see [Figure 13](#).

FIGURE 13: GLUCOSE METER DEMO BOARD AFTER DATE AND TIME SET



CONCLUSION

The glucose measurements are affected by the external factors such as temperature, humidity, altitude and so on, because the rate of the enzyme reaction depends on these and other factors. In addition, test strips with different chemistries will require variations in the regression equation determined using MATLAB or Microsoft® Excel. These factors must be considered when designing a glucose meter to use any particular test strip.

The PIC16LF178X MCU is equipped with op amp, 12-bit ADC, DAC and EEPROM, which makes a great combination for this type of battery operated application needing precision measurement and lower current consumption.

As this application note demonstrates, the Microchip PIC16LF178X MCU can be used to implement a flexible and low-cost glucose meter design.

REFERENCES

"PIC16(L)F1784/6/7 28/40/44-Pin 8-Bit Advanced Analog Flash Microcontrollers" (DS41637).

APPENDIX A: CURRENT-TO-VOLTAGE CONVERTER OUTPUT WITH VARIOUS GLUCOSE CONCENTRATIONS

This appendix provides the scope captures of the current-to-voltage converter output which is measured with ADC to determine the concentration of the glucose. [Figure A-1](#) illustrates the current-to-voltage converter output with high control solution for the glucose reading of 17.5 mmol/l (i.e., 315 mg/dl).

FIGURE A-1: CURRENT-TO-VOLTAGE CONVERTER OUTPUT WITH CONTROL SOLUTION HIGH

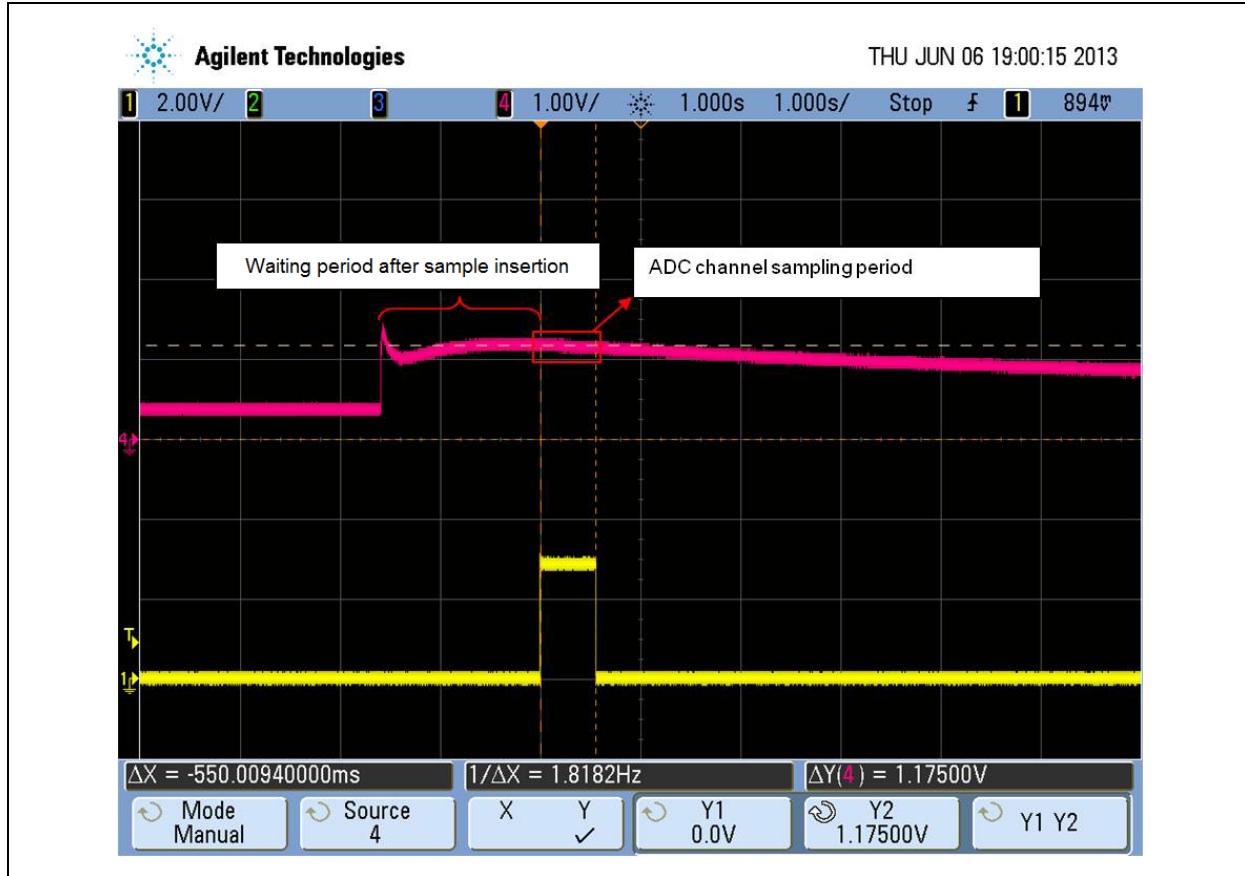
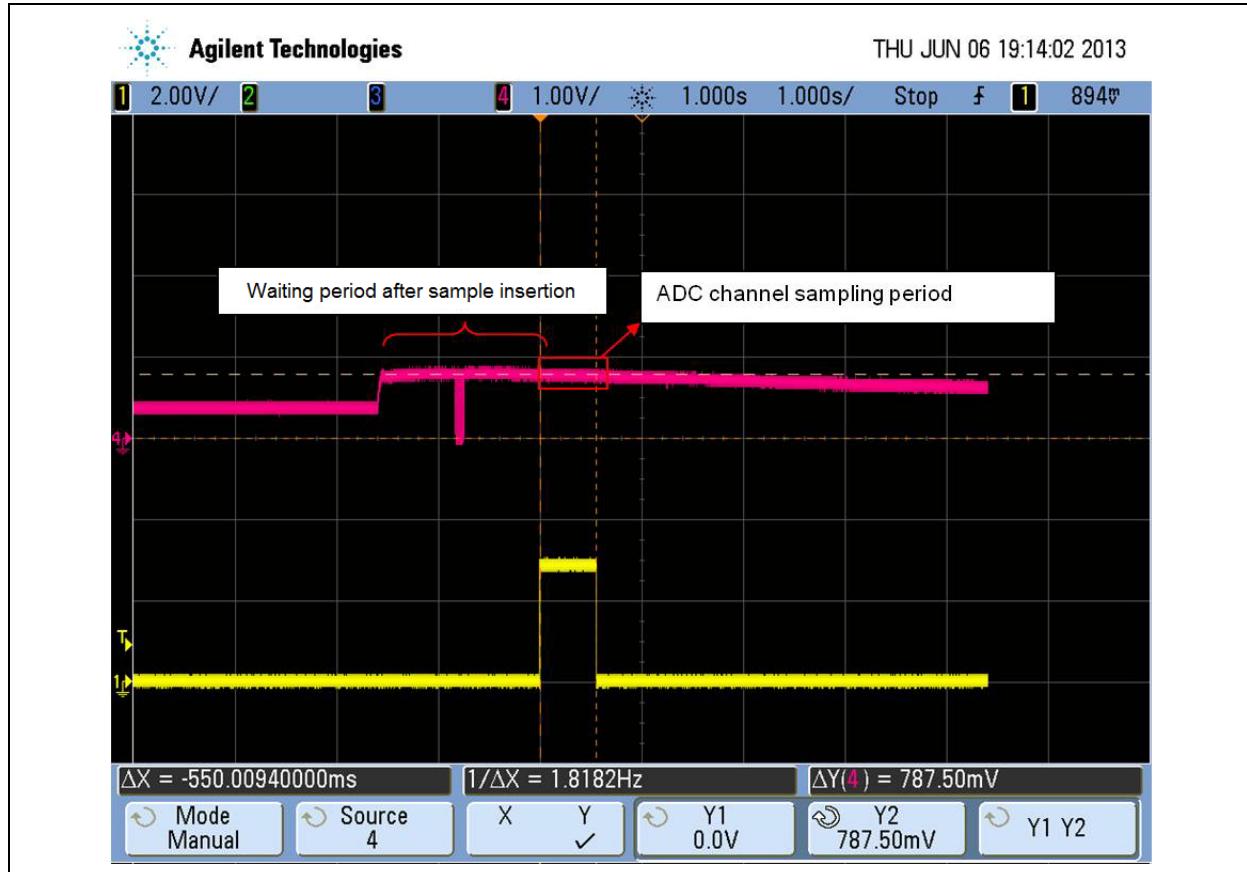


Figure A-2 illustrates the current-to-voltage converter output with normal control solution for the glucose reading of 5.3 mmol/l (i.e., 95.4 mg/dl).

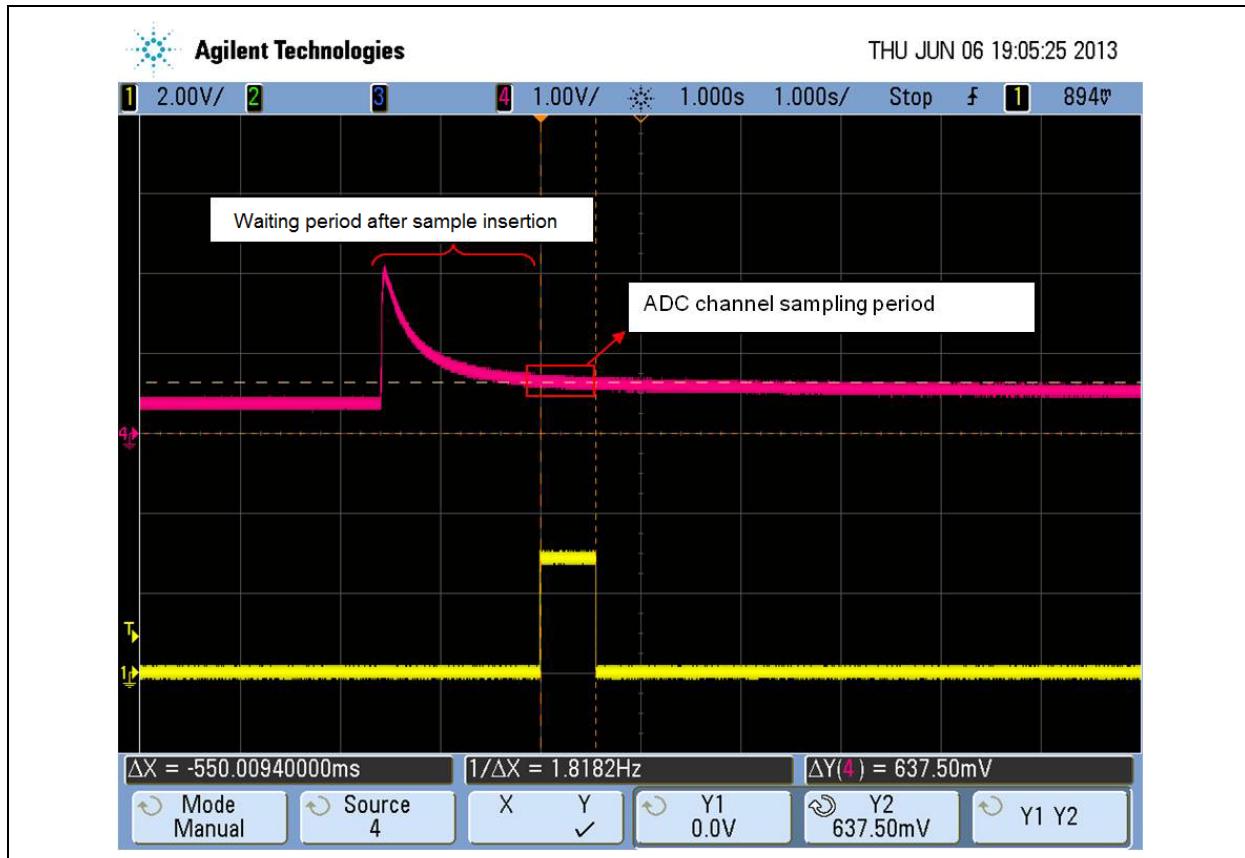
FIGURE A-2: CURRENT-TO-VOLTAGE CONVERTER OUTPUT WITH CONTROL SOLUTION NORMAL



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Figure A-3 illustrates the current-to-voltage converter output with low control solution for the glucose reading of 1.9 mmol/l (i.e., 34.2 mg/dl).

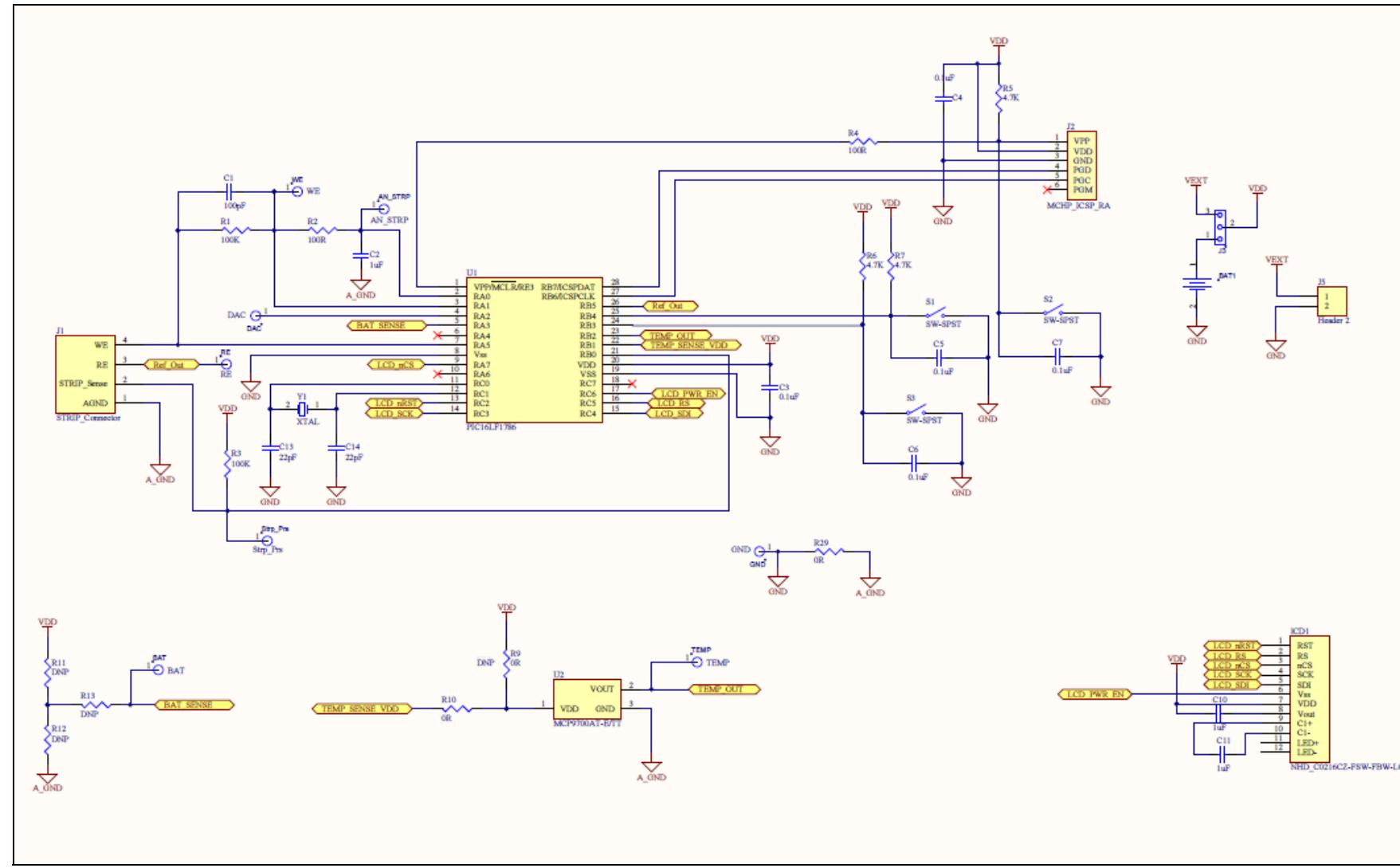
FIGURE A-3: CURRENT-TO-VOLTAGE CONVERTER OUTPUT WITH CONTROL SOLUTION LOW



APPENDIX B: GLUCOSE METER REFERENCE DESIGN CIRCUIT SCHEMATICS

Figure B-1 illustrates the glucose meter reference design schematics.

FIGURE B-1: SCHEMATIC

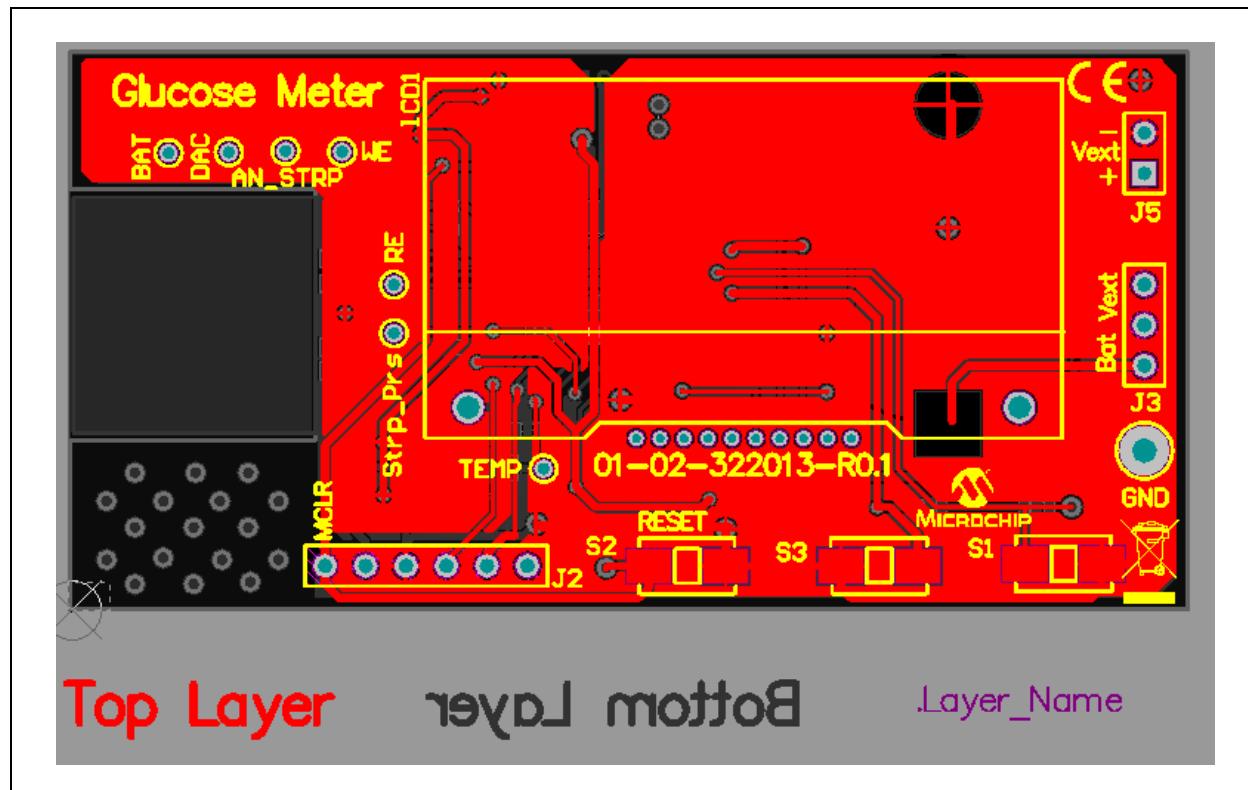


APPENDIX C: GLUCOSE METER REFERENCE DESIGN PCB LAYOUT

C.1 PCB Layout Top Layer

Figure C-1 illustrates the top layer of the glucose meter reference design PCB layout.

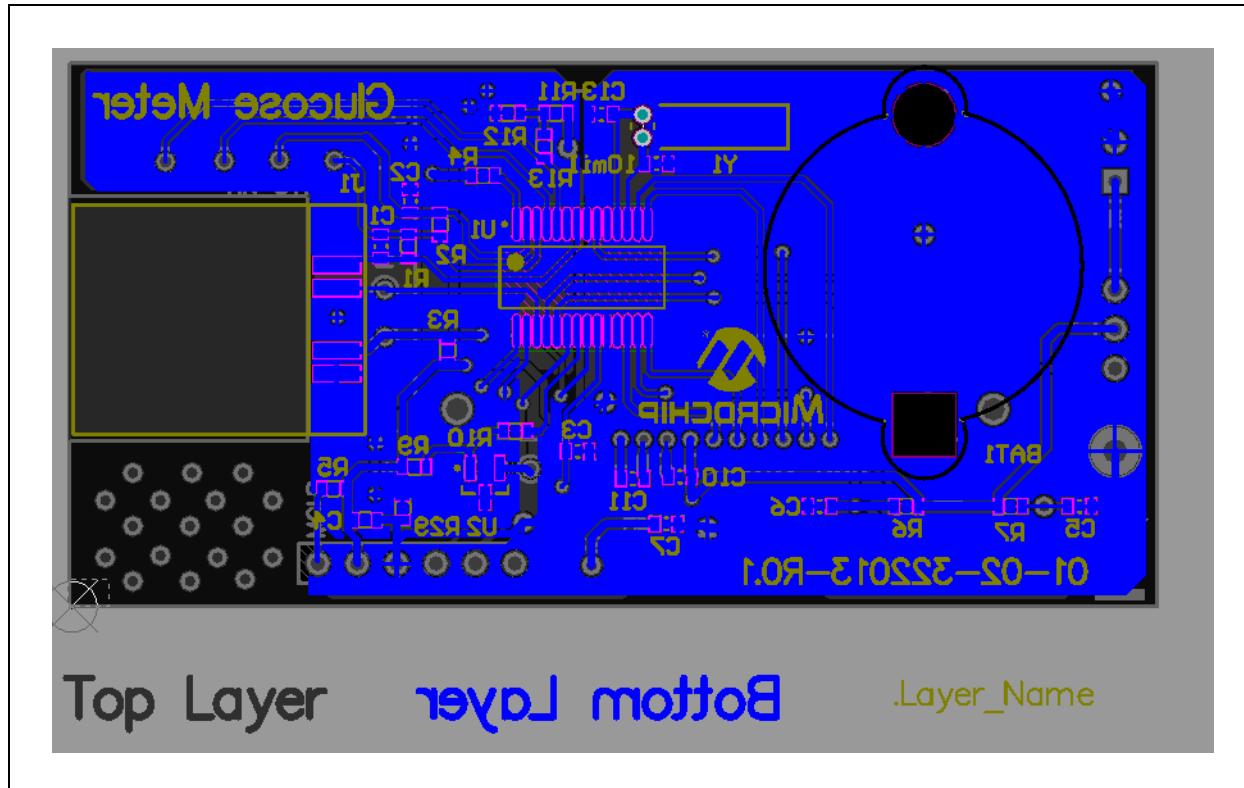
FIGURE C-1: PCB LAYOUT TOP LAYER



C.2 PCB Layout Bottom Layer

Figure C-2 illustrates the bottom layer of the glucose meter reference design PCB layout.

FIGURE C-2: PCB LAYOUT BOTTOM LAYER



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NOTES:

Note the following details of the code protection feature on Microchip devices:

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