Multi-Sensor Platform Measuring and Data Collection System for Risk Evaluation of Kidney Stone Formation

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ABSTRACT: The multi-sensor system presented in this paper is a complete stand-alone point-of-care test device which is used for measurement of key parameters in urine sample. The succeeding data analysis of these parameters will be used for risk evaluation for kidney stone formation. The system has its own local database for storage of the measured data while it can also synchronize the data with centralized database in cloud whenever the internet connection is available. The analysis of the big data collected by this system will ultimately provide the pattern required for early detection and prevention of kidney stone formation. The system measures the temperature using the semiconductor sensor. pH and concentration of Ca^{2+} are measured by FET-based sensors. Disposable biosensor is used for measurement of uric acid concentration. The total dissolved salt is measured by using conductivity biosensor. A semiconductor analog output temperature sensor is used for measurement and recording temperature. Temperature is an essential factor for calibration and improvement of system accuracy. Potentiometric, amperometric and conductometric type readout circuits of these sensors are developed in this paper. An ARM® based micro-controller with embedded multi-channel 12-bits analog to digital converter serves as digital back-end and control section of the system. A single-board computer is added to the system that serves as local database, graphic user interface and connectivity to the internet. The test results of this proposed system show its potential application for urolithiasis prevention.

1 INTRODUCTION

Medical diagnosis for formation of stone in the bladder or urinary tract, urolithiasis, could be predicted by the composition of stone (C.Y.C Pak et al. 2003). Study of 1000 patients in South Taiwan shows Calcium Oxalate and Calcium Phosphate as the most common components of the stone (Y.H. Chou et al. 2007). In another work, measurement of four parameters - pH, Calcium ion concentration, total dissolved salts and uric acid concentration – are used for assessment of urine sample to predict stone formation in early stages (A.A. Silverio et al. 2016).

The multi-sensor platform presented in this paper could be used as point-of-care solution. The system utilized by physicians, lab technicians, patients and other medical staff for measuring four key parameters in urine sample. The system provides convenient, reliable method of accurate measurement and records the data in both local and centralized databases. It provides practical tool for gathering large amount of data in short period of time. Such data will be essential in the machine learning training phase. The goal of this Artificial Intelligence (AI) algorithm is to evaluate the risk of kidney stone formation based on measurements of key parameters in the urine sample.

In the first layer, sensors, the system uses a semiconductor temperature sensor, an ISFET (Ion-Sensitive Field Effect Transistor) bio-sensor for measurement of pH, an EEGFET (Enzyme-Extended Field Effect Transistor) bio-sensor for measuring Calcium Ion concentration, a Uric Acid electrochemical disposable bio-sensor and a four-electrode conductivity bio-sensor for measurement of total dissolved salts.

The next layer of system, readout circuits, employs a potentiometric readout circuit for ISFET and EEGFET biosensors, an amperometric readout circuit for the uric acid bio-sensor and a multi-frequency bio-impedance readout circuit for conductivity bio-sensor.

The digital control layer uses an ARM® Cortex-M0+® core micro-controller as the heart of the system. It complements the readout circuits with control and timing sections, analog to digital conversion, digital filtering and implementation of the calibration process. The digital back-end also communi-

cates with the local server to receive user commands, setting, adjustments and firmware updates while sending the results, online information and acknowledgments back to the local server.

The top layer of the system, local server, is a single board computer. It accommodates the local database, Ethernet and Wifi for internet connectivity or an access point in the absence of internet, serial communication with digital back-end for sending commands, adjustment parameters and receiving the measured data, HTML server that acts as Graphic User Interface (GUI). It could be accessed by smart phone, iPad, tablet, laptop or personal computer.

2 SYSTEM DESIGN

The overall system is designed in four layers, sensors, readout circuits, digital control and local server. Block diagram of the system and interaction between the blocks are shown in Figure 1.

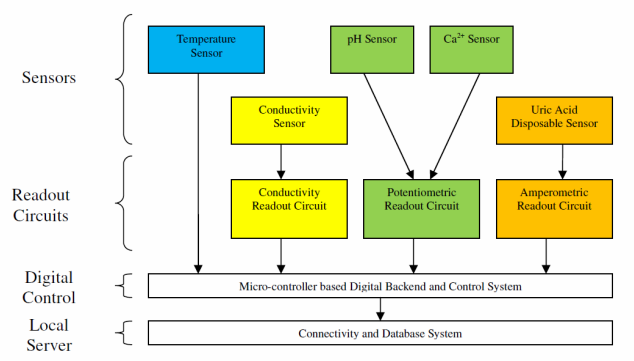


Figure 1. System Block Diagram

Three readout circuits apply the proper signal conditioning to convert sensor output into a voltage which can be measured by the Analog to Digital Converter (ADC) of the micro-controller. The amperometric readout circuit and uric acid sensor are used for measuring uric acid concentration. The potentiometric readout circuit is used for measuring pH and Ca^{2+} concentration while the ISFET pH sensor and EEGFET Ca^{2+} will be connected to the same readout circuit one at a time using analog switches or mechanical relay. The conductivity sensor and its readout circuit are used to measure the conductivity which is proportional to total dissolved salts in urine sample. The semiconductor temperature sensor is directly connected to the ADC. Since temperature sensor output does not require signal conditioning, it is able to be connected directly to the ADC.

An ARM® Cortex-M0+® microcontroller was selected for digital back-end. In addition to the strong 32-bit ARM® core it has an 8-Channel 12-bit ADC with conversion rate up to 1 Msps. Among the several other peripherals of micro-controllers few timer modules and serial communication peripheral are used in this work.

The single board computer on top layer has embedded Wifi and Ethernet for connecting to internet. When internet connection is not available the Wifi module will act as an access point to allow the user accessing the system with their Wifi enabled device. An HTML server on the single board computer becomes the GUI to view the results, control and adjust the system parameters. The local database storage and communication with micro-controller are other tasks of the single board computer.

3 POTENTIOMETRIC SUB-SYSTEM

The potentiometric sub-system includes two MOSFET based sensors with reference electrode, potentiometric readout circuit, ADC and digital calibration.

The ISFET and EEGFET sensors are working based on the principle of threshold voltage change. If the sensor MOSFET biased in linear region while Drain-Source voltage V_{DS} and Drain-Source current I_{DS} remain constant then the Gate-Source voltage V_{GS} will be proportional to internal threshold voltage (W.Y. Chung et al. 2010). The sensor internal threshold voltage is the difference between MOSFET structure inherent threshold voltage and electrochemically induced voltage. In that condition, the V_{GS} voltage is related to ion activity of the sample under test. Applying different proper membrane material, the ISFET sensor is used for measuring hydrogen ion concentration. The EEGFET sensor is used for measuring calcium ion concentration.

The readout circuit presented in this paper is modified version of the circuit introduced by W.Y. Chung et al. 2010. The floating-bridge constant voltage constant current CVCC circuit allows connection of multiple sensors while keeps the V_{DS} and I_{DS} constant. In addition, the value of V_{DS} and I_{DS} is selected in such a way that MOSFET operates in linear region. The circuit of floating-bridge is shown in Figure 2.

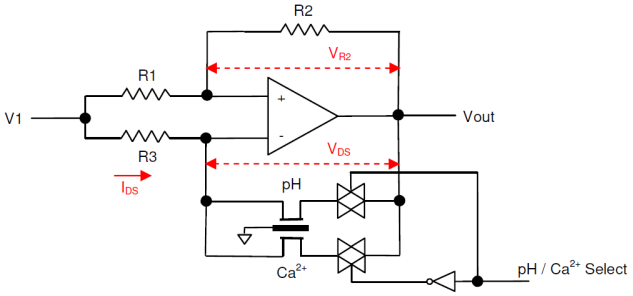


Figure 2. Floating-bridge circuit

In this circuit $V_{DS} = V_{R2}$ so we can achieve the desired constant V_{DS} by choosing proper value for

V_1, R_1 and R_2. In addition, the current I_{DS} could be adjusted by choosing proper value for R_3 resistor.

The additional circuit is required to keep the value of Vref = (V1 – Vout) constant in spite of variation of Vout. That could be achieved by adding a voltage adder with two inputs of Vref, and Vout and the output of V1 as shown in Figure 3.

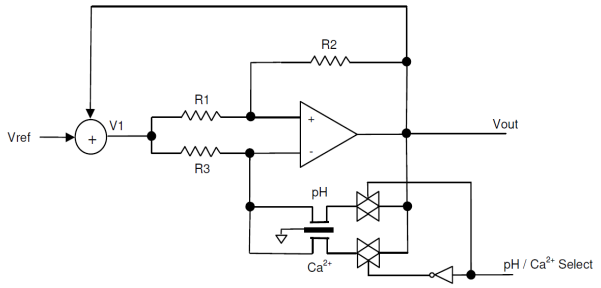


Figure 3. CVCC floating-bridge circuit

Furthermore, passive low pass filter is added in parallel with sensor for noise reduction purpose. The complete circuit is shown in Figure 4.

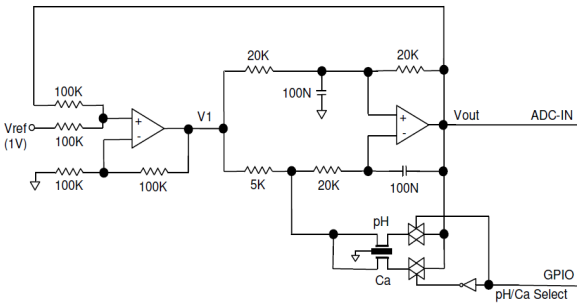


Figure 4. Potentiometric readout circuit

In the circuit of Figure 4 the resistors are calculated based on V_{DS}=0.5V and I_{DS}=100µA, while the V_{DD}=3.3V, analog ground is set on V_{DD}/2 and Vref=1V.

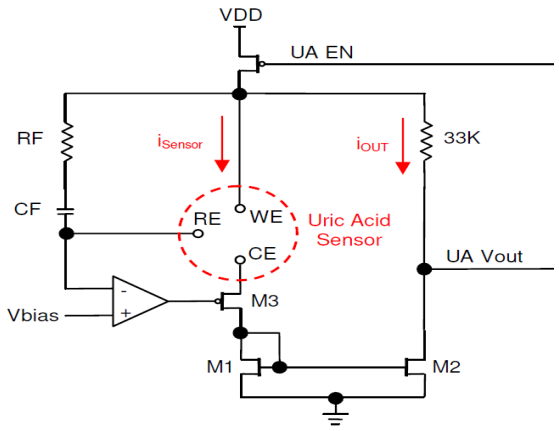
4 AMPEROMETRIC SUB-SYSTEM

The amperometric sub-system is used to measure uric acid concentration in urine sample. The sub-system includes disposable uric acid sensor, amperometric readout circuit, ADC and digital timing and calibration.

A simplified version of circuit presented by Chung et al. 2011 is used as amperometric readout circuit in this work. Specific oxidation voltage should be applied to the sensor and later the urine sample will be dropped on the strip. The readout circuit measures the sensor current which is related to uric acid concentration.

The schematic diagram of amperometric readout circuit is shown in Figure 5.

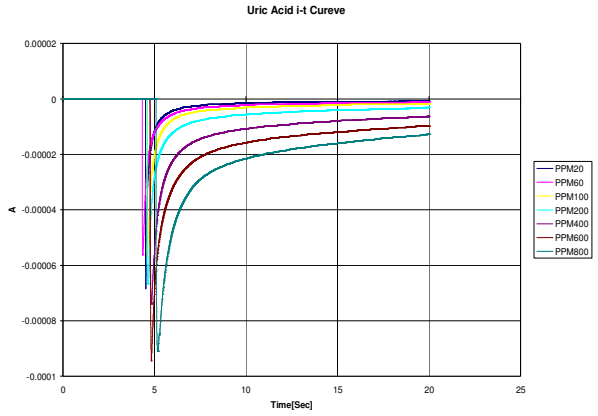
Figure 5. Amperometric readout circuit



The op-amp regulates M3 gate voltage in such a way that voltage in RE (Reference Electrode) becomes equal to Vbias. That applies oxidation voltage (Vox = VDD-Vbias) between WE (Working Electrode) and RE. The presence of urine sample combined with applied oxidation voltage creates the sensor current i_{Sensor} through WE and common electrode (CE). In two-electrode sensors CE and RE are connected together as short circuit. The sensor current i_{Sensor} passes through M3 and M1 drain-source. M1 and M2 are creating current mirror. If they are identical the out put current i_{OUT} become same as i_{Sensor}. The output resistor converts the current to proper voltage which will be measured by ADC.

The moment of sharp increase in current forms the time reference zero for the measurement. After certain period of time the measured current is proportional to the uric acid concentration in the sample.

Figure 6. Amperometric Sensor Output Current



The curves in Figure 6 are showing preliminary results of test. The sensor current versus time was depicted. The reference time for measurement is the sudden increase of current due to drop of sample.

5 CONDUCTOMETRIC SUB-SYSTEM

The conductometric sub-system includes conductivity sensor, readout circuit, ADC and digital timing, calculation and calibration section. A four-electrode conductivity sensor is formed by gold coated PCB as shown in Figure 7. The outer electrodes are used for feeding the constant sinusoidal current and the voltage is measured through inner voltage electrodes.

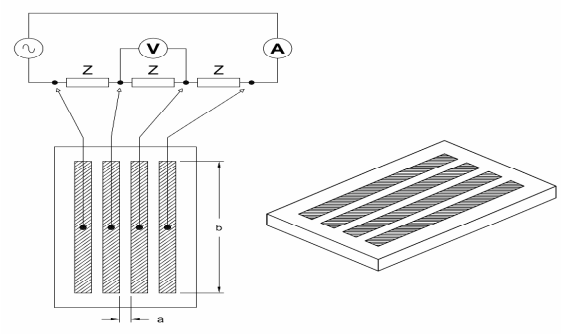


Figure 7. Conductivity Sensor

The block diagram of the conductometric system is shown in Figure 8.

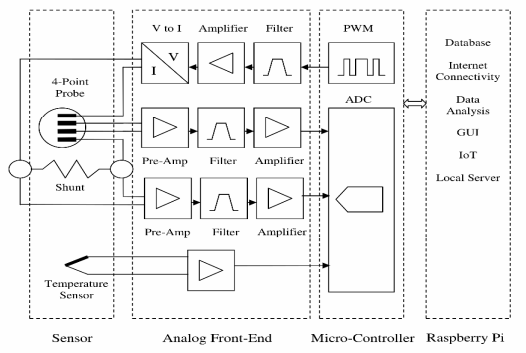


Figure 8. Conductometric sub-sytem

The desired PWM frequency generated by microcontroller passes through a band-pass filter. The filter outputs a sinusoidal wave that is coupled to an amplifier. Then, the voltage signal is converted to a constant current and fed to the outer probe of the sensor. Such current passes through the urine sample and creates a voltage proportional to its resistance measured between the inner probes. Resistance is function of conductivity and geometry of the sensor. The voltage signal will pass through pre-amplifier block formed by a high CMRR (Common Mode Rejection Ratio) instrumentation amplifier (IA). The output of the IA passes through a band-pass filter. The succeeding block is a signal conditioning amplifier which brings the signal to the level of ADC input. The microcontroller uses the ADC measured value for calculating the amplitude of impedance of the sample.

The system measures the impedance in several frequencies and the linear regression line of the impedance in different frequencies is calculated. The Y-intercept of the linear regression (at zero frequency) is the sample resistance. Conductance is obtained by inversing the resistance, and after multiplying it by the cell constant, the conductivity is calculated.

6 CONCLUSION

This paper presents the electronics system of multisensor platform that successfully developed for measuring and data-collection of four key parameters in urine sample to evaluate the risk of kidney stone formation in early stages.

7 ACKNOWLEDGEMENT

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