Achieving Efficiency in Blood Glucose Meter Design

Cuauhtemoc Medina Rimoldi

Diabetes mellitus is a worldwide common health problem. According to World Health Organization statics, the global prevalence of diabetes mellitus is approximately 155 million, which is expected to increase to 300 million by the year 2025.

This disease is characterized by the body's inability to produce enough insulin or by the inability to properly metabolize the insulin hormone which is produced in the pancreas. Insulin is responsible for allowing cells to absorb glucose from food.

Type 1 diabetes is caused by an autoimmune disorder that mistakes beta cells for invaders and attacks them, this prevents the body from being able to take energy from food since no insulin is produced. Symptoms of diabetes appear when beta cells are destroyed en mass. For type 2 diabetes, the beta cells are still able to produce insulin, but the cells are not able to respond to the insulin or the naturally produced insulin might not be enough to meet the body needs. Type 2 diabetes is easier to deal with than type 1. Type 1 requires the patient to have insulin injections administered regularly while type 2 can be kept under control by losing weight, changing the patient's diet and increasing exercise. Eventually most of these patients will require insulin shots.

How Glucometry Helps Diabetes Patients

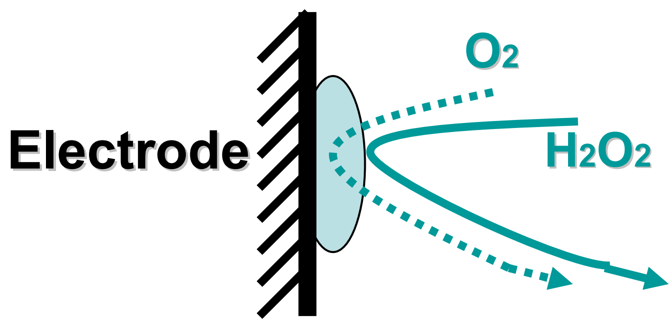
Glucometry is a technique for obtaining the value of concentration of glucose in peripheral or central blood. These values expressed either in mg/dl or mmol have important clinical value for metabolic disorders such as diabetes mellitus, denutrition, and some of their consequences like hyperosmolar coma, malabsorption syndrome and the most critical – hypoglycemia, lower than normal level of blood glucose.

A glucometer is a medical device for measuring levels of glucose concentration in the blood, depending on the level, administration of an hypoglycemiant drug might be required for the patient. A glucometer will use a test strip to interact with a patient's drop of blood. A chemical reaction is produced and the meter reads the level of glucose expressed in mg/dl or mmol/l. The glucometer is usually portable and is used at home for monitoring diabetic patients. A glucometer, and proper pharmaceutical treatment, is fundamental for a diabetic patient to maintain glycemic control at home.

The equipment should be portable and low power. For type 1 diabetes patients, the glucometer should include features that are easy-to-use and that enhance the experience. This could be attractive multimedia interfaces or video playing capabilities???. For older patients, may prefer a device that is easy to grab in order to avoid dropping and has larger numbers in the. These requirements directly impact technology and the glucometer niche market.

How It Works: Sensors and Amperometry

The first step to measure glucose in the blood is to convert the glucose concentration into a voltage or current signal, this is possible with special sensor strips for amperometry. The sensor uses a platinum and silver electrode to form part of an electric circuit where hydrogen peroxide is electrolyzed. The hydrogen peroxide is produced as a result of the oxidation of glucose on a glucose oxide membrane. The current flowing through the circuit provides a measurement of the concentration of hydrogen peroxide, giving the glucose concentration. It is important to highlight that the expressed relationship in the equation (see Fig 1.) is linear. This is different in reality since other biochemical substances might be involved in the reaction as well.



$$C_6H_{12}O_6 + O_2 \rightarrow C_6H_{10}O_6 + H_2O_2$$

Glucose Gluconic Acid

Fig 1. Electrodes reaction

The sensor used as a bloodglucose meter is based on a glucose oxide electrode. The glucose oxides are immobilized in a platinized activated carbon electrode. The enzyme electrode is used for amperometry determination by using an electrochemical detection of enzymically produced hydrogen peroxide. The sensor is composed of various electrodes: a glucose oxide membrane layer, a polyurethane film that is permeable by the glucose, oxygen, and hydrogen peroxide.

Amperometry measures electric current between a pair of electrodes that are driving the electrolysis reaction. Oxygen diffuses through the membrane and a voltage is applied to the Pt electrode reducing O_2 to H_2

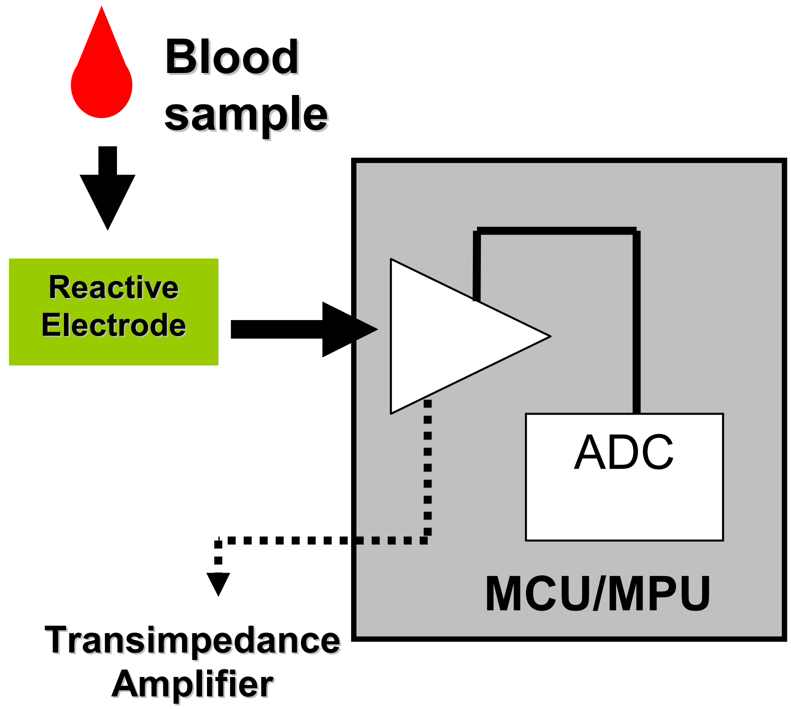


Fig 2. Test strip basic block diagram

These reactive electrodes are amperometric type sensors that use a three electrode design. This approach is useful when using amperometric sensors due to the reliability of measuring voltage and current in the same chemical reaction. Three electrode models use a working electrode (WE), reference electrode (RE), and a counter electrode (CE). After this current is produced, it must be changed to voltage for processing by the microcontroller (MCU). This action is performed by the transimpedance amplifier. Finally, the MCU detects and processes this signal with the ADC module.

For example, here is a practical way to explain amperometry. A voltage is applied in the WE and RE electrodes with a range of -200 milivots to 8 volts. This is used to define the voltage at which the sensor is able to perform at the maximum current. This value is around 4 volts with a current of 18 microamperes After selecting the 4 volts as an operating value, we obtain a stabilization time between 2 and 4 seconds. This means a reliable measurement can be obtained in this time since the maximum current is reached.

What to Look for

Glucometer System Characteristics

From a system perspective, the glucometer is formed by several elements that interact to deliver the necessary functionality.

A microcontroller is required as the main coordinator of the system. Depending on the scope of the application, internal or external Flash memory or SRAM might be selected. Memory is important since the measurements must be stored in order to provide data management and basic functionality as measurements average.

Low Power Consumption

Low power consumption must be observed. Today, most glucometer applications are battery powered, so microcontroller and LCD power consumption should be as low as possible. Glucose meters spend 99% of the time in a particular stop mode that allows it to track time, but it will wake up with an external interruption. Glucose meters manufacturers look at MCU operation frequency and wake up time in order to maximize battery life in run mode. Real time clock functionality is desired since most of the glucometers have an alarm system to alert the user when a measurement must be taken.

Keeping costs low is also important. This includes the cost associated with the device (glucometer) and future expenses made in additional components (strips). The glucometer itself should be cost effective since the user will continue to buy test strips.

Data Management

Connectivity through USB and wireless are also desirable since data management is key for the physician. It is very important to analyze the data of the patient who is using the glucometer and connecting to a computer to graph measurement information is a must. The interface should be easy for the patient to use but powerful enough to allow the doctor to obtain as much information as possible through the connectivity interfaces. Wireless connectivity is more important everyday -- not only for easy access to the information but also to connect with other devices which interact with the glucometer measurements -- such as an insulin pump to assist the user in administering the appropriate insulin dosage.

Keypads and a human machine interface can be implemented through buttons and segment LCD to touch sensing interfaces and graphical LCDs -- all which are also managed through the microcontroller.

Another basic component of the system is the measurement engine which is a group of analog and digital IP modules which interact with the sensors to deliver a voltage to the microcontroller and process the measurement. The proposed measurement engine consists of the following components:

a) Digital to Analog Converter (DAC): Provides the signal biasing. The DAC outputs specific voltages to bias sensors (strips). A critical parameter on the DAC is settling time, which must be lower or equal to 1 microsencondsfor high power mode and 5us for low power mode. Monotonicity must be guaranteed, this will allow the proper wave forms to bias the biosensor.
b) Transimpedance Amplifier: Used to convert the current inputs into voltages that can be read by the ADC, it performs signal conditioning. A critical parameter is bias current which must be below 500 picoamperes (typical at 25°C) to measure small changes produced in the biosensor during the chemical reaction.
c) Operational Amplifiers: Compare mode set for "greater than range" that initiates the measurement algorithm. The compare mode set for "inside range" easily identifies the peak of the chemical reaction. A critical parameter for general purpose amplifier is the bias current which must be below or equal to 2uA (typical at 25°C) to allow the proper design of unity gain buffers, low pass filter, gain amplifiers, inverter and non-inverter programmable gain amplifier (PGA)
d) Analog to Digital Converter (ADC): Add the intro line to explain ADC (for example, see the 1st sentence under DAC above. What does it provide?? The critical parameter on ADC is accuracy which should be above or equal to 13.5 bit effective number of bits (ENOB), this allows the measurement of small signals in the biosensor. Signal strength and value depend on manufacturer specifications and technology. Measurement techniques (customer Intelectual Property) influences the accuracy levels.
e) Additional modules (VREF, Programmable Delay Block and Time of Day): The VREF is a trimmable voltage reference used as a reference for analog peripherals. The Programmable Delay Block is the glue logic that controls the timing and trigger of ADC and DAC modules. The programmable delay block, along with the ADC, are used to perform measurements at preset time intervals and calculate glucose levels. A time of day module is used to keep track of time and therefore log the time at which a measurement was taken.

Embedded Measurement Engines

One advantage would be to have all of the measurement engines embedded in a microcontroller. The 8 bit 9S08MM128 and 32-bit MCF51MM256 from Freescale Semiconductor feature a measurement engine on-chip, reducing cost and minimizing component count. Need to add 1-2 more sentences explaining why this is beneficial.

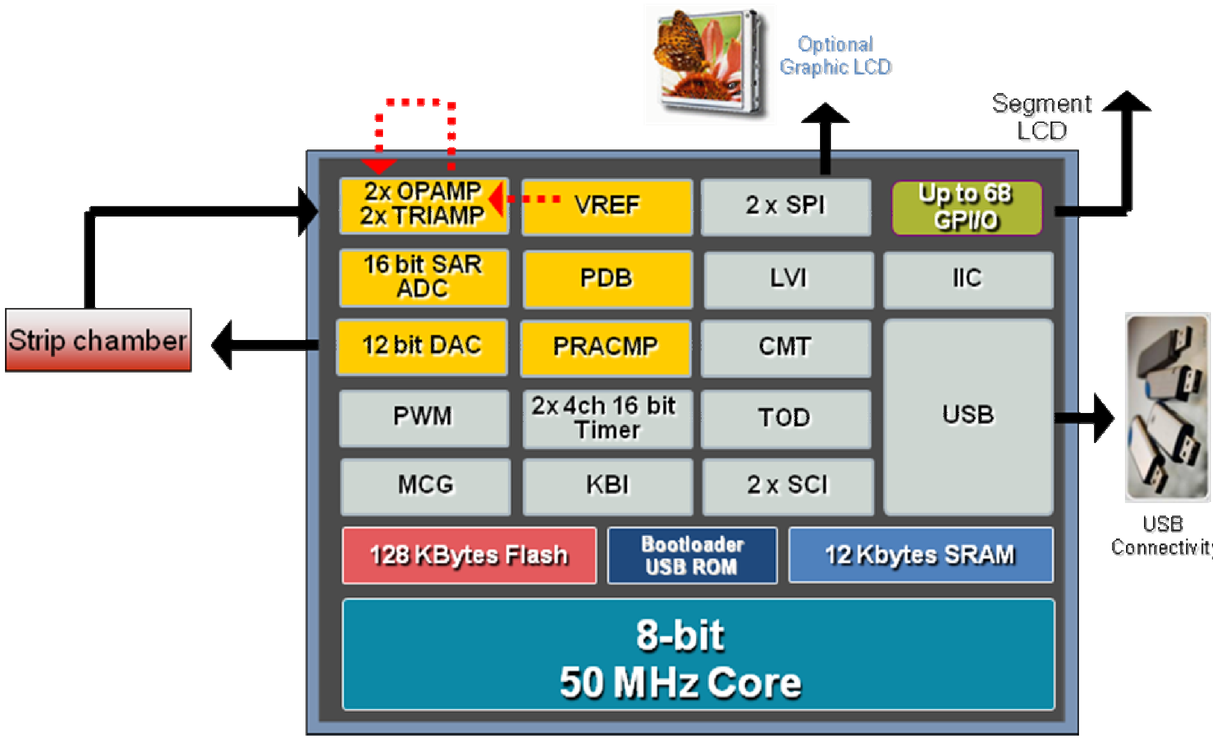


Fig 4. Glucometer system

Software and USB Connectivity

Software components are also vital for the development of the glucometer system. A glucometer can be more efficient depending on the software algorithm used. Complying with medical standards and organizations allows medical devices to interconnect even when they were made by different vendors.

One of the strongest organizations for standardizing of medical devices is the Continua Health Alliance (http://www.continuaalliance.org). This organization unites smart technology and medical devices with healthcare industry leaders to empower patients to not only exchange vital information, but to change the way they manage health and wellness.
When addressing USB connectivity, an important standard to consider is IEEE 11073. This provides structure to the communication interface by defining commands to access data, structuring data to be transmitted and defining communication states.

Another important standard is USB itself. The USB organization has defined the Personal Health Care Device Class (PHDC) which is a standard implementation of USB communication for medical devices in the industry.

These individual knowledge blocks provide the required tools for developing a particular implementation of medical USB connectivity to a specific vendor. Freescale provides these individual building blocks, making it easier to design for medical application, such as a glucometer.

Ready to use software for peripheral usage for the specific microcontroller reduces development time. These drivers would be used to control the LCD, the analog peripherals and the connectivity interfaces. If this is supplied when selecting the microcontroller, it is certainly an advantage for the medical application developer.

Getting Started: The Right Way

Diabetes is a world health problem and it is increasing. Fortunately glucometers ease diabetes patient care by measuring the amount of glucose in the blood so patients can make decisions about taking necessary medications.Glucometer strips interact with sensor circuitry and blood to produce a current that can be measured by the glucometer. Glucometers are differentiated by their accuracy, connectivity features, LCD displays and data management options. Key characteristics like low power functionality and medical software enablement are very important for glucometer design. The proper microcontroller that integrates digital and analog functionality , while balancing cost is recommended to implement small size, low power and high performance glucometers.

References:

Freescale Application Note: AN4025 - Implementing a Glucometer and Blood Pressure Monitor Medical Devices by Carlos Casillas and Roxana Suarez