جامعة القاهرة

Biological sensors

Submitted to:

Dr. Mohamed Ahmed Mounir Islam

Submitted By:

BN	Section	Name
3	1	أحمد سيد أحمد البدوي
27	1	حسن فتحي شلقامي صالح
48	1	عمار السعيد محمد محمد

SBE202B

Contents

Abstract

Sensing technologies are a rapidly growing subject in science and product design, and have evolved in the fields of electronics, photonics, mechanics, chemistry and biology. Their participation was important in biomonitoring and medical applications. This is due to the increased demand for stable, lightweight portable sensors to satisfy the needs of many applications. In this report, we will show some of these sensors, electrical circuits and electronics used in them, such as sweat rate sensor, Cantilever-based bio-MEMS and Heart rate sensor.

Introduction

Biosensors are devices that collect important data about a biological system, such as measuring concentrations of a biomolecule, or measuring vital signals like heart rate and EEG. one of the very first biosensors that measured concentrations of a biomolecule was Clark's electrode, which was used for oxygen detection, and was named after it's inventor Leland C. Clark back in 1956.

Biosensors have some general characteristics which are a must in any of them, for example, any biosensor must be selective in what it measures, so if a biosensor is said to measure glucose levels, it must measure glucose levels only without being affected by concentrations of other biomolecules. The results of any biosensor must be very accurate to be reliable, and it should also be reproduceable, stability is also an important feature of biosensors, as they are used in many different biological environments, so they must not be affected by ambient disturbances. In addition, biosensors must be very sensitive, because the signals and biomolecule concentrations

in a biological environment are usually very low, i.e. sometimes it is required to measure concentrations in ng/ml.

Biosensors are used in a wide range of applications, ranging from environmental monitoring of humidity, to disease detection such as measuring the concentration of prostate-specific antigen, which indicates prostate cancer if its concentration in blood is higher than 4ng/ml.

Discussion

In this study we will be looking at 3 types of sensors, which are:

- Sweat rate sensor.
- Cantilever based bio MEMS.
- Heart rate sensor.

1. Sweat rate sensor

1.1 Introduction

The rapid development of wearable sensors is due to the high need for them in sectors such as sports, fitness, and clinical medicine and one of the most important of these sensors is Sweat rate sensors. We use it to Monitor the sweat rate. There are different techniques for measuring the rate of sweating, so we will show and explain in this research two types of sensors used to monitor the rate of sweating

1.2 Skin Conductivity Sensor

Human skin is a good electrical conductor and its electrical properties can be sensed and directly linked with the production of sweat. Human skin consists of three main layers:

I. Epidermis
II. Dermis
III. Subcutaneous layer

The epidermis is the outer layer of the skin and its 100μm thick and It is constantly replenishing and its function is protecting the skin from the external factors. Dermis is thicker its about 2 mm thick and the sweat glands are located in it. The subcutaneous layer consists of connective tissue and elastin and it acts as a barrier to protect the internal organs. Epidermis has the lowest electrical conductance, but the epidermis conductance increases according to the model of Edelberg when sweat ducts fill. Conductance changes are called electrodermal activity (EDA) and Its unit of measure is micro siemens (μS). EDA recordings using an external current are defined as axosomatic. Two types of skin conductance may be distinguished: tonic and Phasic. The skin conductance level (SCL) is the reference standard representing the average skin conductivity overtime periods. This usually depends on the degree of humidity in the upper epidermal layer. EDA can be seen as peaks that occur in SCL when there is a stimulus. It largely depends on the number of sweat gland ducts that are filled with sweat for moments. Each peak represents a specific skin conductance response (SCR).

SCR is quantified by four parameters: latency, time increase, half recovery time, and amplitude (Figure 1.1).

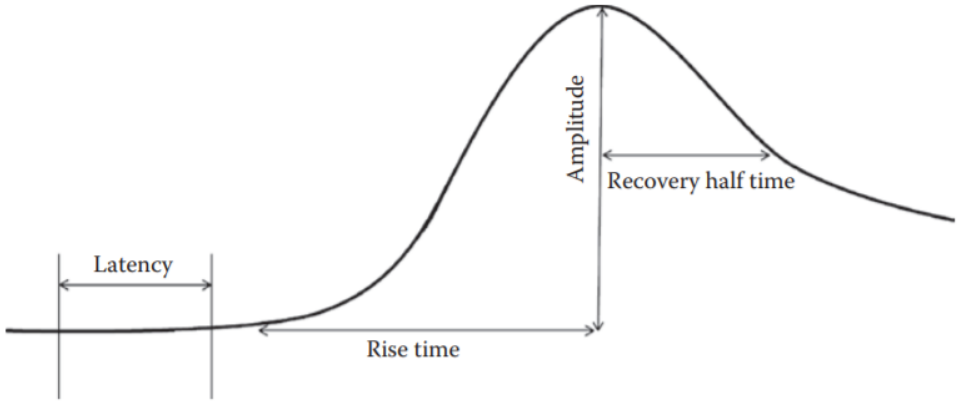

Figure 1.1: Raw SCR showing the parameters used to characterize SCRs.

SCL and SCR can be estimated by direct applying of Ohm 's law. By applying a DC power source between two electrodes, the conductivity of the skin is equal to the current flowing through the skin divided by the voltage on the skin. The circuit suggested by Lowry for measuring EDA is shown in Figure 1.2.

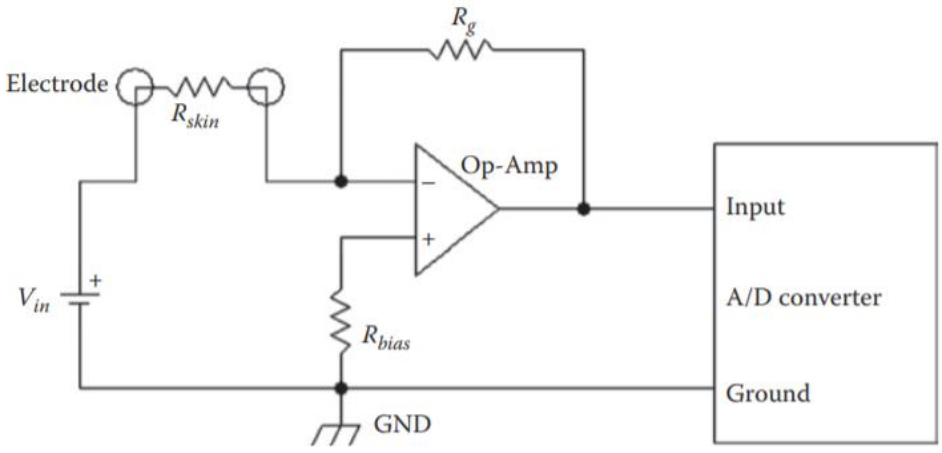

Figure 1.2: A basic circuit for the sensor

The input voltage V_{in} is set to 0.5V as Edelberg recommends. This voltage must be precise and constant to ensure accurate readings, so we use voltage divider. The circuit consists of DC voltage source with a voltage divider consisting of two resistors. The output voltage, Vout which calculated form the eq $V_{out} = -V_{in}\frac{R_g}{R_{skin}}$ is preamplified with Op-Amp and sent to an analog- to - digital (A / D) converter and R_{skin} is the resistance of the skin . A bioamplifier with high input impedance, normally based on an instrumentation amplifier, should be used instead of an Op-Amp to improve the signal - to - noise ratio (SNR) and signal integrity. Although DC recording circuits are simple, there are many disadvantages. They induce polarization of the electrodes and electrolyzing the skin electromotive forces (EMFs) in the circuit may affect the results.

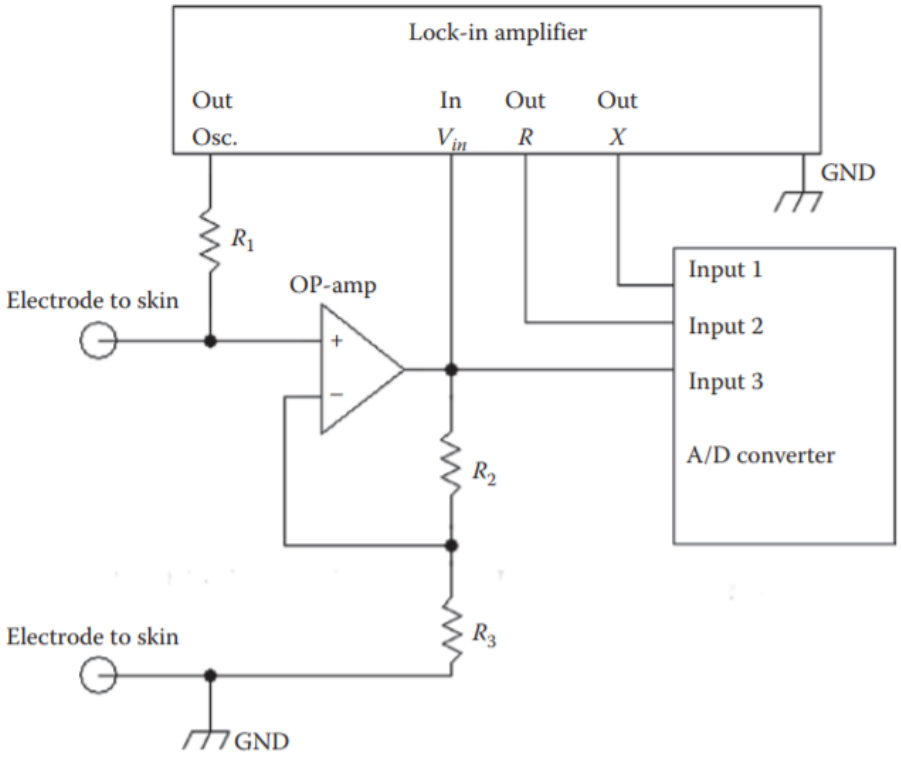

Figure 1.3: the modified circuit for the sensor by using AC voltage

Figure 1.3 shows the suggestion made by Grimnes et al. where the complex impedance (Z) is measured by substituting DC voltage with alternating current (AC) voltage. A signal output (2.5V rms at 22Hz) is given by a lock-in amplifier, combined with the measuring electrode by the resistor R1 (100MM). The measured signal is sent to a non-inverting Op-Amp and multiplied by 100. The output of the Op-Amp is combined with an A / D converter and the lock-in amplifier. AC conductance, G, is calculated from equation: $G = \frac{R}{R^2+X^2}$

Where:

R is the AC resistance (Ω)

X is the reactance (Ω)

EDA is an important method for providing indirect sweat rate monitoring. But skin conductance can change in reaction to parameters not generally associated with an increase in sweat rate. Factors such as strong emotions, startling events, demanding tasks such as mental workload, humidity, cold or relaxation of the skin can alter the sensor output. So, we must use a highly controlled test to ensure that EDA variations depend only on sweat gland activity.

One factor that should not be overlooked with respect to the skin electrodes. The impedance of the electrode to the skin can be modelled as seen in Figure 1.4 To eliminate the difference between the skin and the impedances of the electrode and avoid movement errors so use a gel is often added to the skin in many applications, such as ECG and electroencephalography.

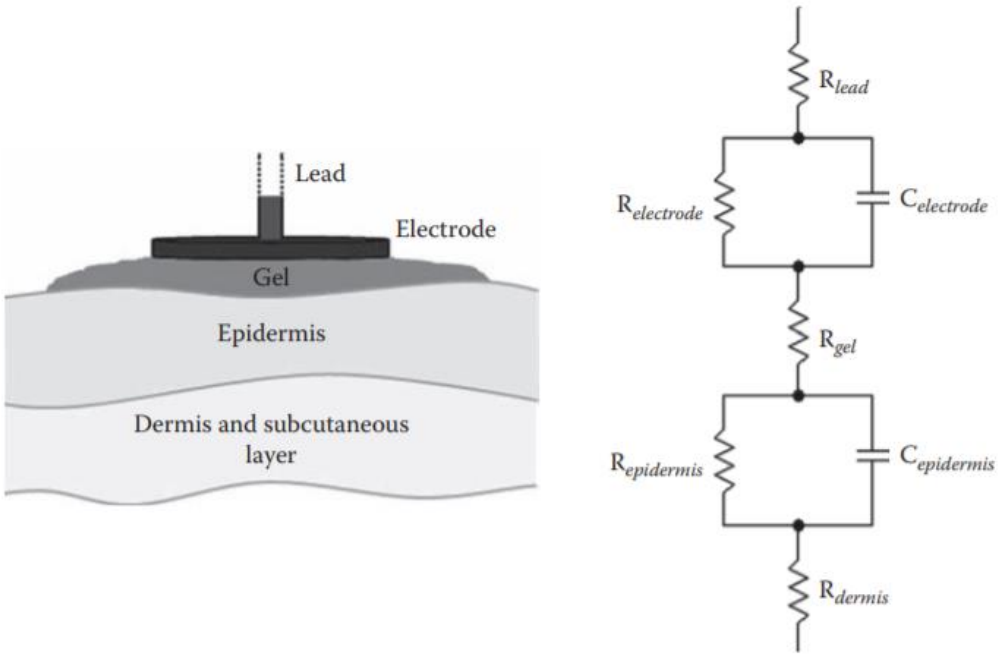

Figure 1.4: Equivalent circuit of the skin–electrode interface

The use of wet electrodes could not be suitable for monitoring sweat rate because it would change the moisture in the skin. The use of dry electrodes is the solution. Dry electrodes could be platinum, stainless steel, anodized aluminium, and silicon oxide or silicon nitride. There is a group of insulating electrodes lies within dry electrodes. These consist of a metal or semiconductor, such as TiO2 and Ti2O5, with a thin dielectric surface layer, such that the interaction with the bioelectric signal is greatly capacitive. The major problem of dry electrodes is that they need to add a high input impedance active buffer because of the absence of the intermediate layer formed by the gel. This makes the circuit more complicated, increases power consumption and increases sensor size.

1.3 Resistive Wristwatch

Resistive Wristwatch is an application of sweat rate measurement. The design resembles a wristwatch and is meant for diabetic use. The unique aspect of this device is that the electrodes don't contact the skin directly, but they detect the increase in the thickness of the layer of sweat on the skin. As the amount of sweat on the user 's skin reaches a defined threshold amount, the layer of sweat comes into contact with the electrodes and an audible alarm is issued by a speaker. The electronic circuits illustrated in Figure 1.5.

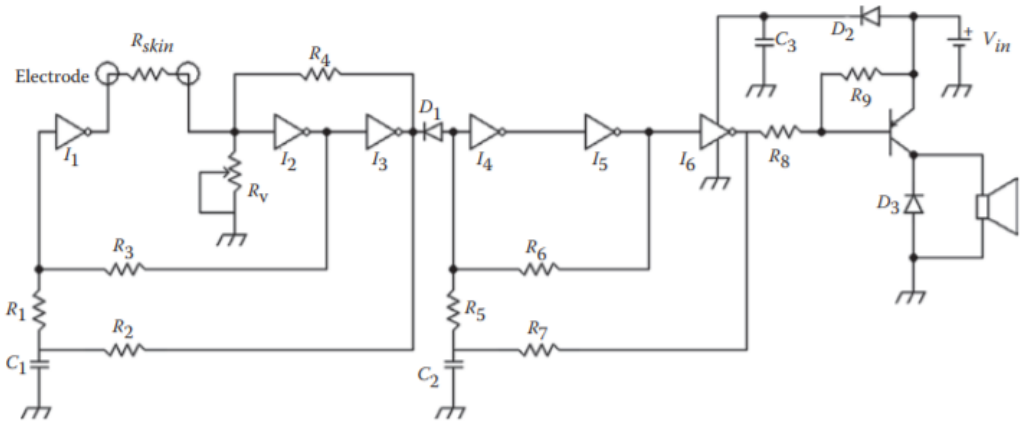

Figure 1.5: the circuit of the wristwatch for diabetics

When the R_{skin} resistance is very high between the electrodes, the inverter I3 output is low and is fed back to the inverter I2 input through R4. So, the I2 output and the I3 input are high. The I1 inverter has a high output. Low impedance between skin electrodes is observed when sweat rate increases so output of I2 is low, whereas I3 output is high. Capacitor C1 begins charging at a rate determined by the R2 and C1 RC time constant. When I1 input exceeds the threshold, its output is low. Thereafter, I2 output is high, and I3 output is low and This sequence is repeated. The circuit of the oscillator involving I1, I2, and I3 works at 5Hz and the oscillator composed of the

I4, I5, and I6 inverters turns on and off at 2.5KHz. this oscillator contacts to the base of a PNP transistor that has an audio transducer contacted to its collector. Three or four 1.5 V batteries supply the power to the circuit. The delivered voltage is filtered by D2 and C3 to prevent fluctuations of battery voltage from affecting the circuit.

2. Cantilever-based Bio-MEMS

2.1 introduction

Bio-Mems are a special category of biosensors based on Micro-Electro-Mechanical systems, their main purpose is to detect and measure amounts of certain biomolecules, which in turn is necessary for disease diagnosis and drug detection, hence each sensor should measure the amounts of a unique molecule with good precision. Cantilever-Based Bio-MEMS are one type of this category, they are capable of detecting certain molecules even at very low concentrations and can be used in ambient or aqueous environments.

Cantilever-based Bio-MEMS rely on a simple mechanical concept, that is when a fixed rod is subjected to force that would cause moment, the rod will bend and deflect and its surface tension will increase, since the rod is fixed and cannot rotate. Cantilever-Based Bio-MEMS are designed to be capable of reacting to a unique biomolecule (this process is called functionalization), this reaction changes the surface tension of the cantilever because of the new bonds formed between neighbouring molecules, which causes a bending moment. The more the amount of the measurand there is, the more reactions that would happen, resulting in more bending of the

cantilever, so the amount of the measurand can be determined by determining the deflection of the cantilever.

2.2 Functionalization

Functionalization of the cantilever-based bio-MEMs is the process of adding a layer of matter on the top of the cantilever, that uniquely reacts with one biomolecule, that is the biomolecule we wish to measure. functionalization layers could be made of proteins, nucleic acids, or antibody/antigen complexes. For our current example we will use gold, which is also a bio sensitive material used in many biosensors.

2.3 Measuring deflection

bio-MEMS are used in different biological environments and are required to be of small size (micrometres), and of low price so that they can be used in daily medical diagnosis. In addition to that, cantilever-based bio-MEMS are subjected to very low stresses and show very low deflection, usually in nanometres. The previous design considerations made the traditional methods of measuring deflection impractical for the case of bio-MEMS, i.e. capacitive methods of measuring deflection cannot work in electrolytes, because of the faradic current generated between plates, Another example is Optical detection method which cannot be implemented in this very small size, also, the interferometric method which utilizes interference of different waves is not sensitive in liquids.

An electric method was developed to measure the nanometric deflection of the cantilever, it utilizes two polysilicon electrodes with a very small gap between them, we will discuss it in the next paragraph.

2.3.1 Electrical method for measuring deflection

To measure the deflection of the cantilever two electrodes are placed, one on the non-sensitive side of the cantilever, and the other is placed under it with a very small distance, when the cantilever is subjected to forces that would cause deflection, the two electrodes come in contact and current passes through, the bigger the force acting on the beam the higher the deflection is, which results in a bigger contact area between the electrodes, hence less contact resistance and more current flow. In that manner, attachment of the measurand biomolecule causes deflection of the beam which in turn is transduced into electrical current.

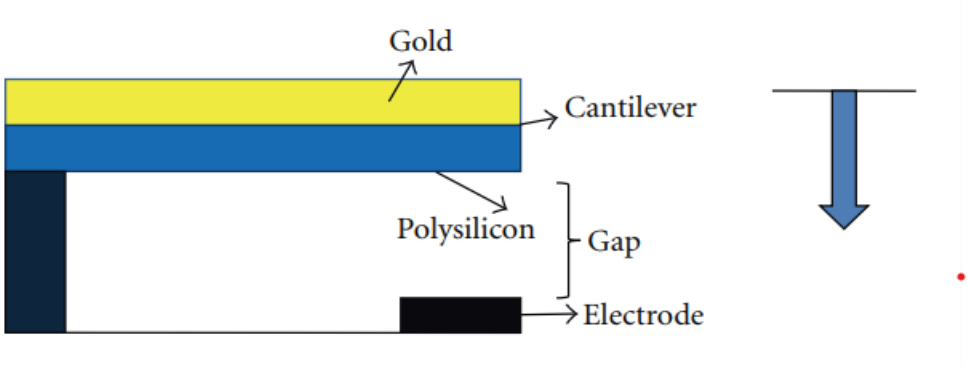

Figure 2.1: Simple layout of the cantilever-based bio-MEMS

This method does not require expensive hardware, and the bio-MEMS can be manufactured in very small sizes. However, there is still one design challenge to consider, that is the gap between the two electrodes, it should be very small in order to sense the nanometric deflections, but it is very hard to fabricate such a device. A solution to this problem is designing two electrodes that

are 2 micrometres apart (which is easy to fabricate) then bringing them closer by electrostatic forces, this process uses a control circuit that determines the voltage causing pre-deflection.

2.3.2 Voltage and deflection analysis

The cantilever we will study is made mainly of poly silicon with dimensions 100×35×0.5 micrometres and a gold layer for bio sensing of 0.3 micrometre thickness.

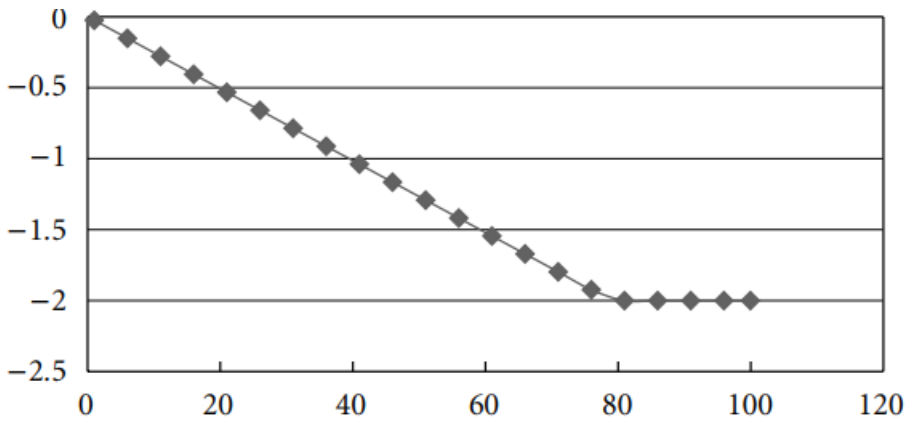

Figure 2.2: Load vs displacement

The following figure shows displacement of the cantilever on y axis (in micrometres), versus a load of 0.005 N/m to 0.5 N/m converted to a scale of 1 to 100.

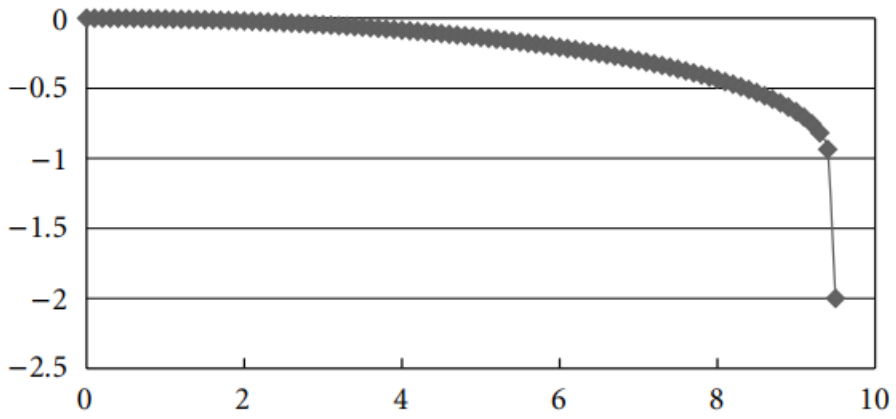

Figure 2.3: Voltage vs displacement

While this figure shows the displacement of the cantilever on the y axis (in micrometres), due to an applied voltage varying from 1 to 10 volt (on the x axis), the voltage difference between the two electrodes is responsible for electrostatic actuation, i.e. closing the big gap between them, note that when the gap between the two electrodes gets smaller, the device becomes more and more sensitive, i.e. small amount of measurand can produce enough force to close the gap so that the current flows and there is an output indicating the amount of measurand.

One more thing to note from the previous figure, is that at around 9 volts the gap is closed, the voltage difference between the two electrodes causes pre-deflection of the cantilever, and should be placed in a point where very low stress on the cantilever causes the gap to collapse and the current to flow, hence making the device more sensitive. The pre-deflection voltage is found using a feedback control circuit.

2.4 Feedback control circuit

The feedback control circuit main function is to determine the pre-deflection voltage, i.e. create the optimal gap between the two electrodes to increase the sensitivity of measurement.

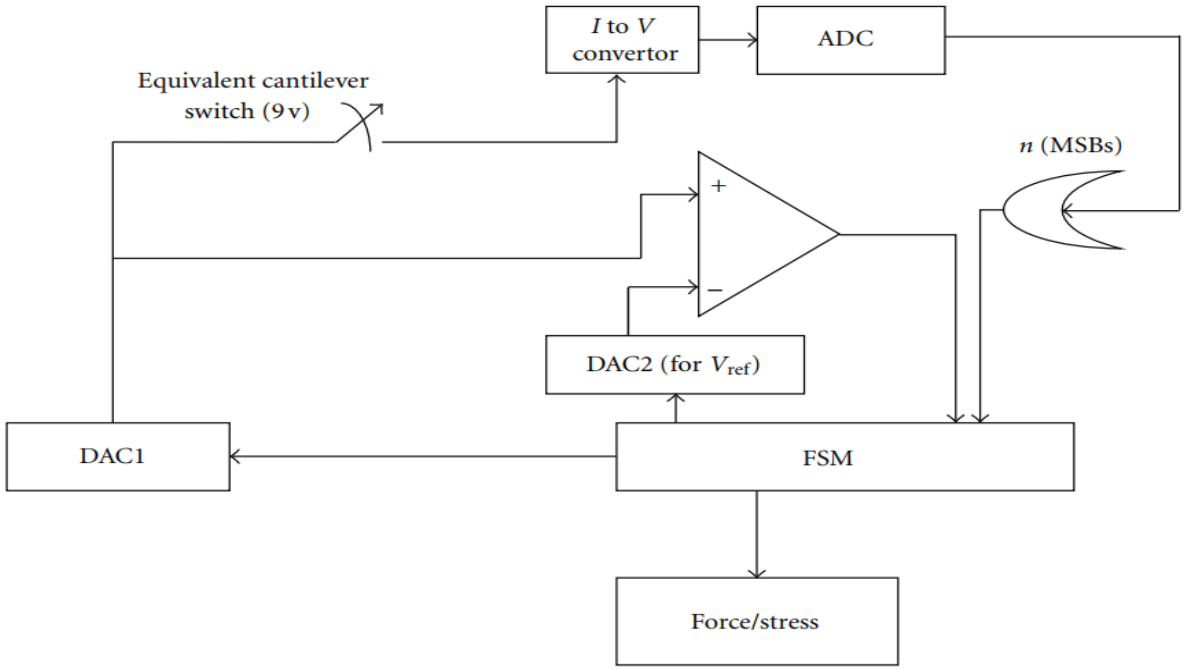

Figure 2.4: Schematic of the feedback control circuit

Initially, the gap is 2 micrometres long and there is no voltage applied on the electrodes, and there is no current flowing through them, so there is no current flowing through the transimpedance amplifier in the current to voltage converter, and the output voltage is zero according to the following equation $Vout = I \times R_F$, this value is input to an analog to digital converter (ADC) and produces a digital zero as well. This digital output is input to an OR gate, the OR gate produces a logic 1 if any of its inputs is at logic 1, if none of the inputs is at logic 1, it outputs zero. The output of the OR gate is input to the finite state machine (FSM) which behaves differently according to its input state, when the input to it is zero, it increments its

digital counter value by one, this digital value is then converted to an analog voltage, by means of a digital to analog converter circuit (DAC1) that could utilizes an amplifier in the weighted summer configuration where V1 to Vn are the bits of the counter, and Vo is the resulting analog voltage.

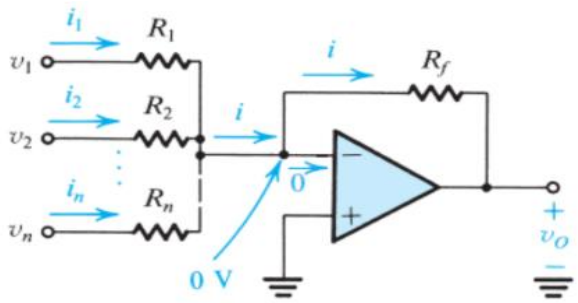

Figure 2.5: Weighted summer configuration of the amplifier

The resulting analog voltage value is supplied to the cantilever, causing the two electrodes to become closer together and the gap to become smaller. This process keeps repeating until the two electrodes come in contact and current flows through them. When there is current flow in the electrodes, this current is converted into voltage then supplied to the ADC to convert it to a digital 1. The pre-deflection voltage is the value supplied by DAC1 prior to current flow by one step. This value is stored in the FSM. The FSM now starts decreasing the voltage supplied to the cantilever through DAC1 until its zero and initial conditions are reached again. Next, FSM will supply the digital value equivalent to the pre-deflection voltage to DAC2, this value will get converted into an analog voltage then supplied as a reference input to the comparator. The comparator is an amplifier with high open loop gain operating with either no feedback or positive feedback, two analog voltages are input to a comparator (in our case they are DAC1 and DAC2 voltages), and the amplifier output saturates either on the positive side (Vcc) or the negative side (-Vcc) according to which of its inputs has a higher magnitude. In summary, the

comparator's function is to compare the two analog voltages input to its positive and negative nodes, compare them, and produce an output that behaves digitally to indicate which value is higher.

The FSM starts to increase the voltage supplied by DAC1 to the cantilever, the comparator's output is digital zero as long as DAC1 is less than DAC2, once DAC1 reaches the pre-deflection voltage the comparator's output becomes 1 and the FSM will display that now the system is ready to interact with biomolecules and measure the current resulting from the stress, i.e. measure the very low concentrations of the measurand.

The device is calibrated so that the current flowing through the electrodes can indicate the concentration of the attached biomolecules on the functionalized surface of the cantilever-based bio-MEMS sensor.

One important advantage that the feedback control circuit gives this electric deflection measuring circuit over other deflection measuring methods, is that it is not affected by variations in dimensions of the cantilever that may happen as results of device uncertainty during fabrication process.

3. Heart rate sensor

3.1 introduction

Heart rate measurement is very important and useful. We often need to measure heart rate for exercise safety and to create the ideal exercise routine, and to measure levels of anxiety or event

to diagnose heart diseases. Luckily the growth of technology has allowed us to measure heart rate easily using heart rate sensor.

Heart rate sensor is the sensor that allows us to measure the number of beats of the heart in one minute (bpm) to monitor the patient's state.

3.2 Way of measurement

The way the sensor measures the heart rate is using two main components: the infrared light-emitting diode (IR LED) and phototransistor.

- The IR LED: is solid state lighting device, it emits light the range of infrared of the electromagnetic spectrum which is from 700 nm to 1 mm.
- The phototransistor: is just as the ordinary bi-polar transistor, it is an electronic switch and current amplification device, and used to detect the pulses of the light and convert these pulses into digital signals. It is also used to convert light energy into electric energy. Like the ordinary bi-polar transistor it has NPN and PNP types, and it has the different configurations, common base, common emitter, and common collector. Back then the semi-conductor materials that were used were germanium or silicon, but in the modern phototransistors materials like gallium or arsenide are used for more efficiency. But there are differences, the main difference is that the phototransistor operates when in it is exposed to light as when the light falls on the junction a revers current flows within it and the that current is directly proportional to the luminance. So, the main function if the phototransistor is to emit current when exposed to light. It acts as a variable current source and depends on the intensity of the received light.

Combining these two main components and other components, the basic idea of the heart rate sensor is shining a light through or at one's finger using the IR LED, and measure how much light is absorbed or reflected using the phototransistor. Of course, the intensity of the light emitted from the IR LED is fixed, so, what makes the variation of the readings of the phototransistor? The answer to this question is easy and kind of obvious, as we said, the light goes through the finger, and inside the finger there are blood vessels, these blood vessels are of course flexible, they expand when fill with blood and shrink when drained from blood. The expansion of the vessels when fill with blood represents systole, and the shrinking represents diastole. A heartbeat consists of one systole and one diastole. When the volume of the blood increases inside the blood vessel and it expands, it absorbs more light than when the blood vessel shrinks and when the volume decreases. The difference in the intensity of the light when the vessel expands and when it shrinks represents the pulse (heartbeat).

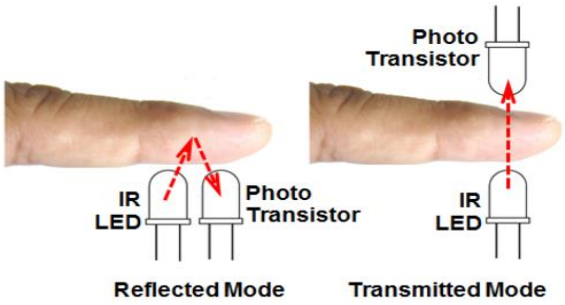

Figure 3.5: the position of the finger for the measurement

As more efficient way of designing the sensor, it takes the shape of a clip, it is placed on the finger tip of the patient, as the patient mostly is not conscious to hold his finger between the IR LED and the phototransistor like in Figure 3.1.

3.3 Circuit of the heart the rate sensor

To get an accurate output, the input signal must pass through few circuits as shown in Figure 3.2.

- Preamplifier: the output of the heart rate measurement components (*node A)* is coupled through a capacitor put in series *C1* and amplified using negative feedback resistor *R3* in the first amplifier *A1*.
- Low-pass filter: an RC filter for the high frequencies (noise).
- Voltage follower: the amplifier *A2* buffers the output of the low-pass filter.
- Inverting amplifier: *A3* amplifies the voltage signal and acts as a second stage low-pass filter.

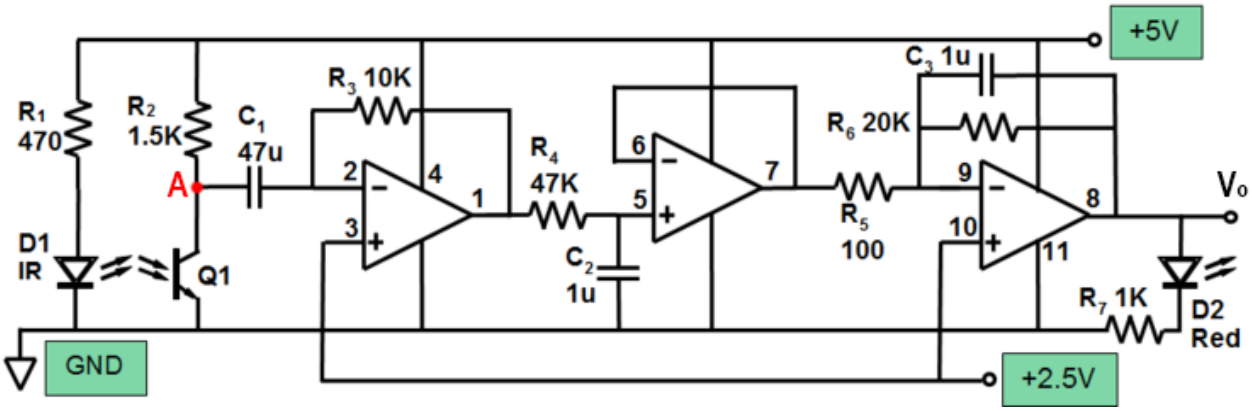

Figure 3.6: schematic of the heart rate sensor

Following the schematic from the very first input:

- IR LED: to protect the IR LED from any damage from the current we put a resistor *R1* in series with it to limit the current. The intensity of the light emitted from the IR LED depends on the operating range as I = $\frac{5 - Vled}{R1}$.

- Phototransistor: a common-emitter amplifier is used. When *Q1* is illuminated by IR LED it emits an output dependent on the intensity of the light. This output is created by the series resistor *R2* between the voltage supply and the collector of the phototransistor, and the value of *R2* is determined experimentally.
- Preamplifier: the input signal from the heart rate sensor at the node A is connected to a differentiator amplifier (*C1 – A1 – R3*). The capacitor *C1* filters any DC signal. *R3* and *C1* acts as a high-pass filter with cut-off frequency $F_{c1}= \frac{1}{2\pi R3C1}$. Also, this amplifier takes the input current and generates an output negative voltage based on the negative feedback resistor *R3*: *V = - I * R3.*
- Active low-pass filter: it is like a simple RC low-pass filter, both of them block high frequencies. But they differ in the active components. The active filter has operational amplifiers and draws its power from external power sources and uses it to amplify the signal.

  The active low pass filter (*A2 – C2 – R4*) has a simple passive RC filter, a path for the low frequencies to pass the input to the non-inverting op amp.

  The heart rate cannot exceed 180 bpm, and according to this equation: $F = \frac{bpm}{60}$ we conclude that frequencies higher than 3 Hz must be filtered. We can design the RC low-pass filter using the following equation: $F_{c2} = \frac{1}{2\pi R4C2}$.

  The op amp is configured to be a buffer (voltage follower) with DC Voltage gain 1. this configuration gives stability to the filter as the high input impedance prevents excessive loading on the output and the low output impedance protects the cut-off frequency point from change due to the changing in the impedance of the load. But this configuration has

one major disadvantage is that it cannot obtain more voltage gain above 1. The power gain however is high because the output impedance is lower than the input impedance.

- Final inverting amplifier: the final stage configuration is an AC operational amplifier integrator. It is a low pass filter (*R4 – C2*) it filters the remaining signals that are higher than the maximum frequency of the heart pulses, these are unnecessary frequencies (noise). And it amplifies the useful signals with a gain Av and it can be determined as follows: Av = $-\frac{R6}{R5}$. And the cut-off frequency is determined by this equation: $F_{C3} = \frac{1}{2\pi R6C3}$.
- LED *D2*: it blinks with each beat.

Conclusion

Measuring the vital signs is the backbone of healthcare nowadays, no doctor can make an accurate diagnosis without measuring the vital signs that are concerned with the case. We have illustrated three types of sensors: sweat rate sensor, cantilever-based bio-MEMS and heart rate sensor.

- Skin conductance It can be estimated by direct applying of Ohm 's law. By applying a DC power source between two electrodes, the conductivity of the skin is equal to the current flowing through the skin divided by the voltage on the skin.
- cantilever-based bio-MEMS are a special type of bio-MEMS biosensors that utilize a mechanical cantilever and a deflection transduction circuit to measure the concentration of a certain biomolecule. The device’s selectivity is achieved by inserting a functionalization layer that reacts with one specific molecule which we desire to measure its concentration, functionalization layers can be made of proteins or antigen/antibody complexes for example.

  The devices sensitivity is enhanced by a feedback control circuit that applies a voltage between the two electrodes which causes electrostatic forces between them (electrostatic actuation). The circuit not only increases the devices sensitivity, but also diminished the effect of uncertainty of dimensions that may occur during device fabrication, which is a bonus this device has over other devices. The circuit also made device fabrication easier, as gaps of nanometric size is not needed, and a gap of 2 micrometres between the electrodes was utilized along with this feedback circuit.

- Heart rate sensor is used for patients as well as healthy people, athletes use it to keep track of their exercise and to create the ideal exercise routine, and to keep updated with the patients' status.

  Heart rate sensor uses two main components, IR LED and phototransistor, the finger is put between or opposite to them, and the phototransistor measures the blinks of the light through the finger or reflected on it, due to the changing in blood vessels' volume hence absorbing more light. The signal passes through a series of resistors, capacitors and amplifiers to obtain the most accurate measurement.

References

- Krzysztof Iniewski, Biological and Medical Sensor Technologies, 2012
- R. Edelberg, Electrodermal recovery rate, goal-orientation and aversion, Psychophysiology, 9:512–520, 1972
- B. Figner and R. O. Murphy, using skin conductance in judgment and decision-making research, in M. Schulte-Mecklenbeck, A. Kuehberger, and R. Ranyard (Eds.) A Handbook of Process Tracing Methods for Decision Research, Psychology Press, New York, pp. 163–184, in press.
- R. Lowry, Active circuits for direct linear measurement of skin resistance and conductance, Psychophysiology, 14(3):329–331, 1977
- Kalambe, J., & Patrikar, R. (2012). Design of Microcantilever-Based Biosensor with Digital Feedback Control Circuit.
- Sedra, A., & Sedra, A. (2011). *Instructor's solution manual for microelectronic circuits, International 6th edition*. Oxford University Press.
- Op-amp Comparator and the Op-amp Comparator Circuit. (2020, April 13). Retrieved from https://www.electronics-tutorials.ws/opamp/op-amp-comparator.html
- Activity: Heart Rate Monitor Circuit [Analog Devices Wiki]. (2020). Retrieved 27 May 2020, from https://wiki.analog.com/university/courses/alm1k/alm-lab-heart-rate-mon
- Heartbeat Sensor Circuit Diagram Working with 8051. (2020). Retrieved 27 May 2020, from https://www.elprocus.com/heartbeat-sensor-circuit-daigram-working-with-8051/

- Phototransistor-Circuit Diagram, Construction and Its Applications. (2020). Retrieved 27 May 2020, from https://www.elprocus.com/phototransistor-basics-circuit-diagram-advantages-applications/
- What is IR LED (infrared light-emitting diode)? - Definition from WhatIs.com. (2020). Retrieved 27 May 2020, from https://whatis.techtarget.com/definition/IR-LED-infrared-light-emitting-diode