FPGA BASED GLUCOMETER USING NANO STRUCTURED METAL OXIDE BIO SENSOR

Sundarraj Dorairaj* & Pradeep M**
* PG Scholar, ME VLSI, Department of ECE, Sasurie Academy of Engineering, Kariyampalayam, Sathy Road, Coimbatore, Tamilnadu
** Assistant Professor, Department of ECE, Sasurie Academy of Engineering, Kariyampalayam, Sathy Road, Coimbatore, Tamilnadu

Abstract:

Glucose (C6 H12 O6) is a carbohydrate [1] is a source of energy for human body and is a pre-cursor to the synthesis of ATP (Adenosine Tri Phosphate). In Human body, blood Glucose concentration is highly regulated by the hormones Insulin and Glucagon generated by Pancreas. When the pancreas fails to generate enough of these hormones at the required level, it causes Diabetes in the human body. Diabetes is a chronic disease that is characterized by high or low levels of Glucose in the blood stream. In order to control the disease, it is required to keep the blood Glucose levels within the specified limit. Glucometers are portable handheld devices used to measure the blood glucose with a specified range. This paper discusses about the steps taken to design a Glucometer using Nano structured metal oxide biosensors controlled by the Altera Cyclone based FPGA EP1C3T144C8. Attempts will be made to study the response time of Glucometer using the nanostructured metal oxide biosensors along with the Glucometer measurement circuits.

Index Terms: Diabetes, Nano structured, Biosensors & Glucometer

1. Introduction:

Diabetes Mellitus has affected large number of people over the last decade and the disease is characterized by the deficiency in the production of hormones like Insulin and Glucagon, which control the Glucose level in the human body. Insulin is generated when high levels of Glucose are detected in the blood stream. It is generated by Beta cells [1] of Pancreas. Glucagon is generated when low levels of Glucose are generated in the blood stream. Alpha cells of Pancreas generate it. If there is any deviation in this Glucose regulation process, it causes the Glucose level to go up or low. Because of this, measuring the levels of Glucose in the humans has become increasingly important.

Diabetes is of three types- Type 1, Type 2 and Gestational diabetes. Type 1 Diabetes is normally found in Children and young adults. People suffering from Type 1 diabetes have their human body does not produce Insulin at all. Type 2 Diabetes is found commonly among the majority of the population. Gestational diabetes is found during pregnancy.

Glucometers are devices, which are used to measure the Glucose level in the human body. There are several types of Glucometers available in the market, like Accu-check, Contour Next EZ, Freestyle Insulinx, Nova Maxplus etc. Some of the factors, which could differentiate between these Glucometers, are the materials used for sensing the Glucose level, accuracy of detection, size of the Glucose sample solution, sensitivity, reliability of monitoring and stability.

Nanotechnology [5] has opened greater opportunities for exploring Glucose Bio sensing applications through the use Nano structured materials. Nano structured metal oxides like ZnO, Cu Oxides, MnO2, TiO2, CeO2, SiO2, ZrO2 are materials, which can be used as Bio Sensors and they fall under one of the operating principles of Amperometric, Potentiometric, Impedimetric or Conductometric Glucose sensing. Each of these metals oxides is characterized by different sensitivity, fast response times and stability for the determination of glucose.

We will be studying the sensitivity and response times for these nano-materials and use them those materials to develop a Glucometer using Altera Cyclone based EP1C3T144C8 FPGA.

2. Literature Survey Overview:

Development of Glucometers started about 40 years ago [7] and since then there has been constant progress in the field of blood Glucose meters. The 1980s was an active period more number of Glucometers evolved based on various parameters and features like size, easy of use, design etc. Later, biosensor strip based Glucometers became available which binds with the instruments with the strips manufactured. These strips follow the electrochemical principles to measure the blood Glucose levels.

Emergence of metal oxide based Glucose sensors contributed to a highly sensitive, cost effective means by Glucose level could be measured. The last two decades [5] more effort has been made for the detection of glucose based on Nano structure metal oxides and their composites. These metal oxide based Glucose sensors has many functional properties like sensitivity, detection limit and response time which could be used appropriately to design an efficient Glucose sensing system.

3. Methodology:

3.1 Basic Block Diagram:

The Basic block diagram of the proposed Glucometer is shown in the figure below:

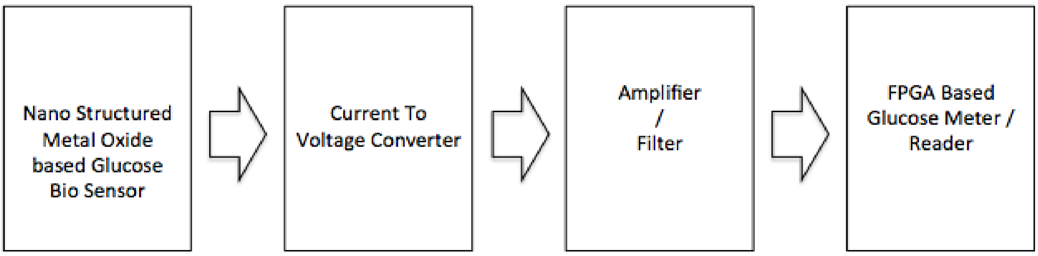

Figure 1: Basic Block diagram of Glucometer

Glucometer consists of mainly 4 blocks, which forms the complete system. They are:

i. Glucose Bio sensor
ii. Current to Voltage conversion
iii. Amplifier/ Filter (if required)
iv. FPGA Control unit

The Glucose biosensor block in the current work proposes to use the nanostructured metal oxide based biosensor. The detected current from the nanostructured biosensor from the Glucose will be converted to an analog voltage, which would be amplified and filtered. The resulting output will then be converted to digital format by the analog to digital converter and used by the FPGA module to do the control processing.

3.2 Metal Oxide based Nano Structured Glucose Bio Sensor:

Bio Sensor research [5] started with enzyme based Glucose Bio Sensor on various principles like Amperometric, Potentiometric and Impedimetric or Conductometric technique. Amperometric Glucose sensing works on the principle that GOx (Glucose Oxidase) catalyzes the Oxidation process of Glucose to Gluconic acid. The Glucose bio-sensing strip contains three Electrodes namely Reference Electrode (RE), Counter Electrode (CE) and Working Electrode (WE). Parameters like temperature, humidity and toxic chemicals bind the activity of enzymes in the enzyme-based sensors. In order to overcome this problem, enzyme free sensors are considered. But the enzyme free sensors have selectivity and sensitivity issues and hence highly selective and sensitive, reliable and fast enzymatic/non-enzymatic sensors are considered. Metal Oxide based sensors are very sensitive, relatively inexpensive and have advantage of rapid response associated with specific nanostructures such as nanowires, nanotubes, nanoparticles, nanofibres etc., [5].Attempts will be made to study these sensors combined with metal oxides in order to synthesize a highly efficient Glucose bio sensor.

3.3 Trans Impedance Amplifier:

The current from the Glucose Bio Sensor is converted into Voltage by the trans-impedance amplifier. This current is proportional to the Glucose concentration, which is provided as an input to Glucose Bio Sensor.

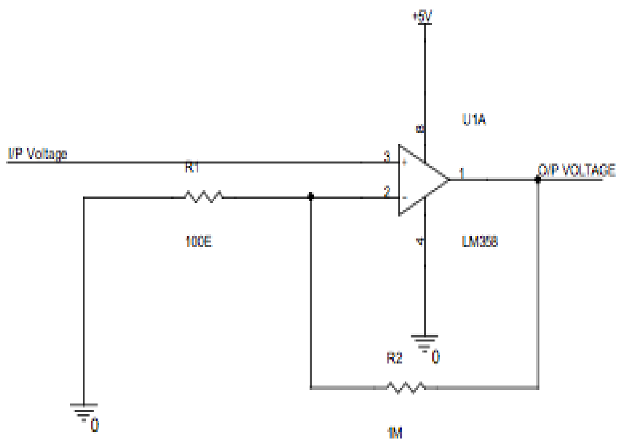

Figure 2: Circuit diagram for Trans-Impedance amplifier

The formula for the output voltage of the Trans Impedance amplifier is given by:

$$V_{out} = I \text{ Working Electrode} * \text{Resistance}$$

3.4 Analog to Digital Converter:

The Analog to Digital Converter is used to convert the Voltage into 8 bit data, which is provided as an input to the Altera Cyclone FPGA. The Circuit diagram of the ADC, to be used in the Glucometer, is shown below:

8 BIT ADC CIRCUIT

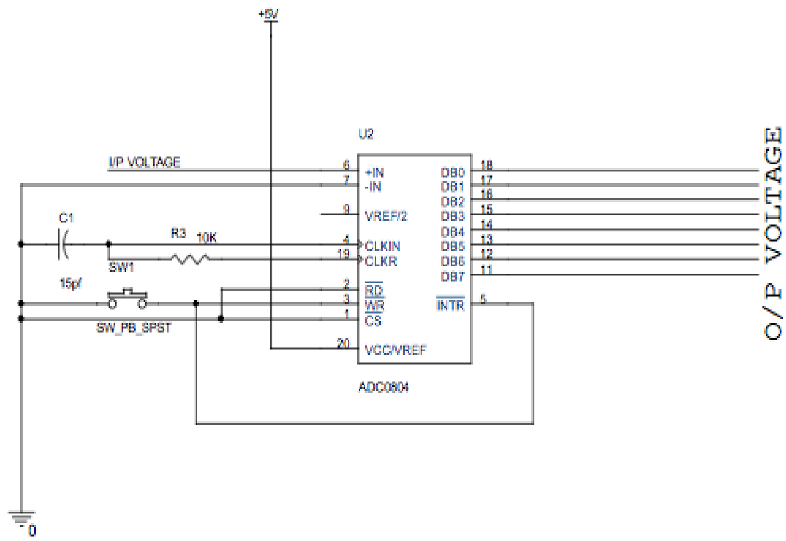

Figure 3: Circuit diagram for ADC

In the circuit shown, the analog input is given to the pin 6 of ADC 0804. The voltage $V_{out}$from the Trans Impedance amplifier is fed as an analog input to the ADC 0804. This analog input is converted to an 8 bit digital value and fed to the Altera FPGA for further processing.

3.4 Altera Cyclone FPGA:

Altera Cyclone FPGA (Field Programmable Gate Array) family is based on 1.5V, 0.13um, and all layer copper SRAM process with densities up to 20,060 logic elements (LEs) and up to 288 Kbits of RAM. Cyclone devices contain a two-dimensional row and column based architecture to implement any custom logic. Column and Row interconnects of varying speed provide signal interconnects between LABs and embedded memory blocks.

Altera Cyclone EP1C3T144C8 is 144 pins FPGAwhich provides the control functions of the proposed Glucometer. The block diagram of the proposed system is given below:

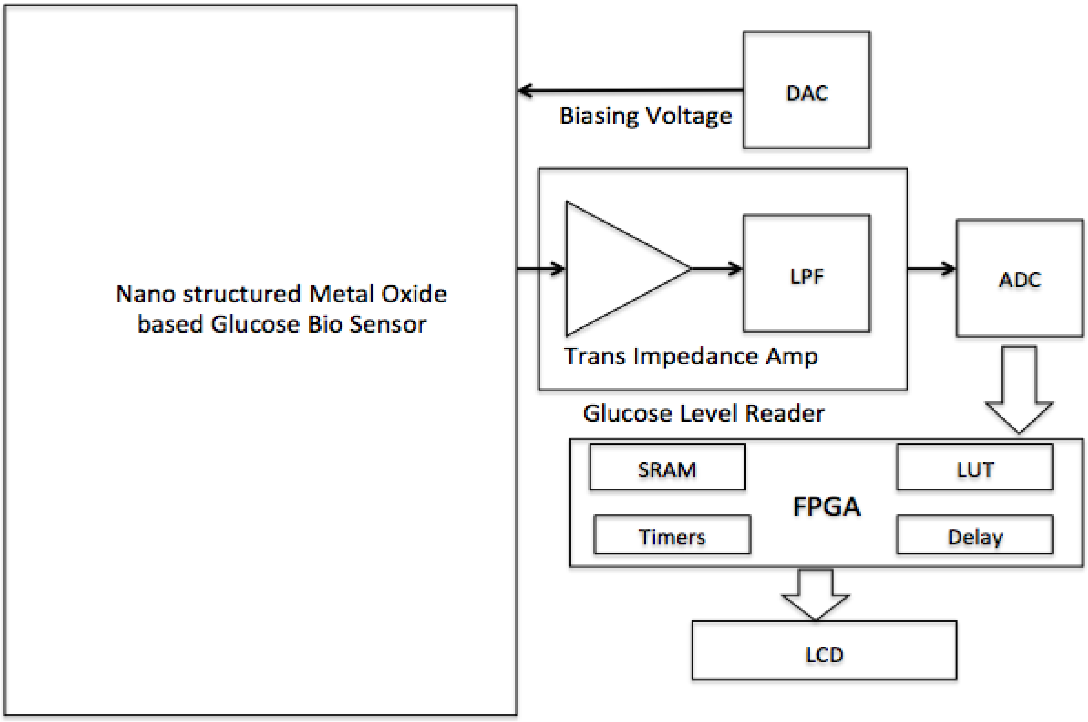

Figure 4: Block Diagram of the proposed Glucometer

The core elements of the Glucometer are the Nano structured Glucose Bio Sensor and the FPGA. The FPGA uses modules like Timers, LUT (Look up table), SRAM and Delay blocks in the control software. The timers are used whenever it is required to wait for stabilization time or during initialization. The SRAM block is used to store the previous read Glucose levels. The control software is written in VHDL, which is then simulated to check the functionality of Glucometer.

3.5 LCD Display:

LCD (Liquid Crystal Display) screen is an electronic display module and find a wide range of applications. A 16x2 LCD display is very basic module and is very commonly used in various devices and circuits.

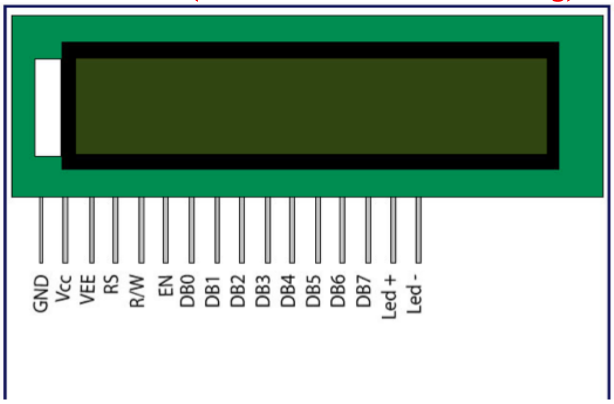

Figure 5: Pin out diagram of LCD Display

These modules are preferred over seven segments and other multi segment LEDs. The reasons being: LCDs are economical; easily programmable; have no limitation of displaying special & even custom characters (unlike in seven segments), animations and so on.

A 16x2 LCD means it can display 16 characters per line and there are 2 such lines. In this LCD each character is displayed in 5x7 pixel matrix. This LCD has two registers, namely, Command and Data.

The command register stores the command instructions given to the LCD. A command is an instruction given to LCD to do a predefined task like initializing it, clearing its screen, setting the cursor position, controlling display etc. The data register stores the data to be displayed on the LCD. The data is the ASCII value of the character to be displayed on the LCD.

3.6 Algorithm:

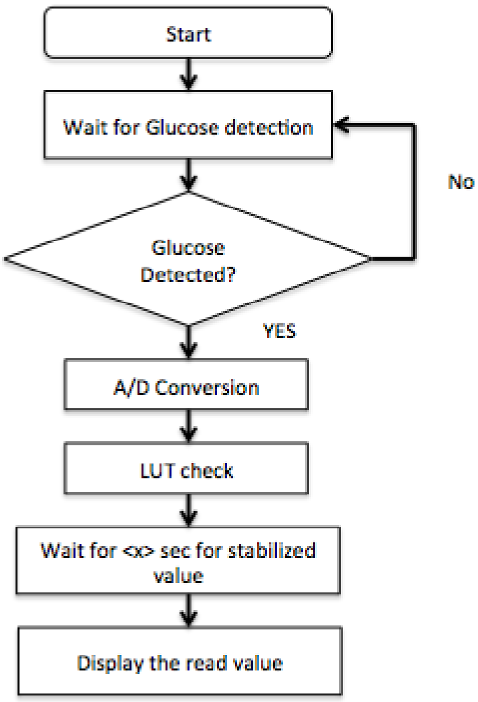

Figure 6: Flow chart for the Glucometer functionality

The flow diagram for the Glucometer functionality is shown below. Initially the Glucometer waits for the solution to start the detection. Till the Glucose solution is detected, it remains in the waiting mode. Once the Glucose solution is detected by the Glucose biosensor, the current will be generated from the biosensor proportional to the concentration of Glucose and this current will be amplified and converted to analog voltage using the trans-impedance amplifier. The voltage is then filtered to remove any unwanted noise.

This analog voltage is converted into a digital format using the ADC circuit and performs extrapolation using the Look up table. Once this is done the Glucose reading is obtained and displayed once the stabilization of the voltage reading is completed.

4. Result Analysis:

The C-V curve for the synthesized Glucose biosensor is taken and it is used as a reference for the design of ADC, Trans impedance amplifier and also to work on the FPGA Software design. Using the curve, the Current for various Glucose concentration levels are taken and a linear curve is constructed by plotting the values with ADC voltage on the x-axis and the Glucose level on the y-axis. With the resulting curve, the slope (m) and the constant (c) are calculated. Then for any glucose level concentration, the software extrapolates the reading of the Glucose level using the equation $y = mx + c$.

The table below shows the comparison of some of the parameters tried out by previous works [3] in the field of Glucometer.

Comparisons of Previouswork			
The differences	**MCU**	**PC**	**This Project**
Control Unit	ATMEG A 16L	PC & NI DAQ Card	ALTERA CYCLONE EP1C3T144C8
Controller Type	Micro Controller based	Micro Controller based	FPGA Based
Frequency	16 MHz	NA	66 MHz
Linearity and Accuracy	0.9715	0.9715	TBD
Measurement Time	15 seconds	15 seconds	10 seconds(expected)

Table 1: Comparison of Previous work

5. Conclusion and Future Work:

The ADC, Trans Impedance amplifier and FPGA software are designed and constructed, using the sample value of the C-V curve for the Glucose Bio sensor. The readings of the Glucose level will be displayed on to the LCD display module. The future work involves the development of Nano-structured metal oxide Glucose sensor. Using this sensor, the reading of the Glucometer will be obtained and verified against the existing products of Glucometers available in the market

References:

1. Miriam Garcia Yanez. "Glucose Meter Fundamentals and Design". Application Note: Free Scale Semiconductor.
2. NamrataDalvi. "Glucose Meter Reference Design". Application Note: Microchip Technology Inc.
3. Teddy Lesmana, Wen-Yaw Chung, Shih-Lun Chen. "Amperometric Glucose Sensing System Based on FPGA Platform"
4. JivanParab, Rajendra S Gad, Gourish M Naik. "Soft Core FPGA Platform For Blood Glucose Measurement"

5. Md. MahbuburRahman, A. J. SalehAhammad, Joon-Hyung Jin, Sang Jung Ahn and Jae-Joon Lee. "A Comprehensive Review of Glucose Biosensors Based on Nanostructured Metal-Oxides"
6. Materion Inc. "The Role of Thin Films in Blood Glucose and BioSensors "
7. S. F. CLARKE and J. R. FOSTER. "A history of blood glucose meters and their role in self-monitoring of diabetes mellitus"
8. [Online]. Available: http://www.electronics-eetimes.com/en/google-dexcom-partner-on-wearable-glucose-monitor.html?cmp_id=7&news_id=222925805
9. [Online].Available: http://www.mentor.com/products/fpga/multimedia/overview/handheld-glucose-meter-ui-built-with-nucleus-integration-of-tara-systems-embedded-wizard-ui-tool-082c58d3-e674-4349-91fa-389496072058
10. [Online]. Available: https://www.unigoa.ac.in/academic_staff.php?staffid=20
11. [Online]. Available: http://www.eetimes.com/document.asp?doc_id=1278181
12. [Online]. Available: http://www.electronicsweekly.com/news/components/passives/analysis-blood-glucose-meter-design-2011-05/
13. [Online]. Available: http://www.maximintegrated.com/en/solutions/medical/diagnostics-monitoring-therapy/blood-glucose-meters.html/tb_tab0
14. [Online]. Available: http://www.maximintegrated.com/en/app-notes/index.mvp/id/4659
15. X.W. Sun, Jianxiong Wang, A.W. Wei. "Zinc oxide nanostructured biosensor for glucose detection"
16. Sunil Govardhan. "A Cmos Switched Capacitor Based Amperometric Readout Circuit For Microneedle Glucose Sensor"
17. L.I. Boguslavsky, L. Geng, I.P. Kovalev, S.K.Sahini, Z.Xu, T.A.Skotheim, V.Laurinavicius, B.Persson& L. Gorton. " Amperometric thin film biosensors based on glucose dehydrogenase and Toluidine Blue O as catalyst for NADH electrooxidation.
18. Atsushi Seki, Syuu-ichi Ikeda, Izumi Kubo, Isao Karube. "Biosensors based on light-addressable potentiometric sensors for urea, penicillin and glucose"
19. Sejin Park, Hankil Boo, Taek Dong Chung. "Electrochemical non-enzymatic glucose sensors "
20. Anantha I. Gopalan, Kwang P. Lee. DhanusuramanRagupathy, Se H. Lee, Jong W. Lee "An electrochemical glucose biosensor exploiting a polyaniline grafted multiwalled carbon nanotube/perfluorosulfonateionomer–silica nanocomposite"
21. Haipeng Yang, Yongfa Zhu. "Size dependence of SiO2 particles enhanced glucose biosensor"
22. Xi-Liang Luo, Jing-Juan Xu, Wei Zhao, Hong-Yuan Chen "Glucose biosensor based on ENFET doped with SiO2 nanoparticles"
23. Christopher Batchelor-McAuley, Gregory G. Wildgoose, Richard G. Compton, Lidong Shao, Malcolm L.H. Green "Copper oxide nanoparticle impurities are responsible for the electroanalytical detection of glucose seen using multiwalled carbon nanotubes"
24. A.S. Poghossian. "Method of fabrication of ISFET-based biosensors on an Si–SiO2–Si structure"
25. Jeffrey D. Newman, Anthony P.F. Turner. "Home blood glucose biosensors: a commercial perspective "

26. Haipeng Yang, Yongfa Zhu. "Glucose biosensor based on nano-SiO2 and "unprotected" Ptnanoclusters "
27. Shaw-Hwa Parng Chih-Hsiu Yin Kun-Feng Lee Chuh-SuanChen ,Tsung-Che Chou Horn-Chin Lee, Yuh-Jiuan Lin. "Effect of temperature and glucose concentration on a glass-based sensor for long-term stability investigation"
28. CosiminoMalitesta, Francesco Palmisano, Luisa Torsi, and Pier Giorgio Zambonin "Glucose Fast-Response Amperometric Sensor Based on Glucose Oxidase Immobilized in an Electropolymerized Poly (o =phenylenediamine) Film"
29. Xi-hongZu, Zhi-huiJian, Guo-bin Yi, Hai-liang Huang, Ben-bin Zhong, Hong-sheng Luo, Jia-rong Huang and Cui Wang "Surface-enhanced Raman Scattering Effect of Ordered Gold Nanoparticle Array for Rhodamine B with Different Morphologies"
30. J. Wang, H.X. Zhao, L.P. Du, H. Cai, P. Wang. "Construction of a photovoltaic glucose sensor applying a metal-insulator-silicon structure in combination with ultra-thin polypyrrole-glucose oxidase film"
31. ZhenjingZhuang, Xiaodong Su, Hongyan Yuan, Qun Sun, Dan Xiao and Martin M. F. Choi. "An improved sensitivity non-enzymatic glucose sensor based on a CuO nanowire modified Cu electrode"
32. Rajesha, TarusheeAhuja, Devendra Kumar. "Recent progress in the development of nano-structured conducting polymers/nanocomposites for sensor applications"
33. Jian-Ding Qiua, Jing Huanga, Ru-Ping Lianga. "Nanocomposite film based on graphene oxide for high performance flexible glucose biosensor"
34. Kuo-Yuan Hwa, BoopathiSubramani. "Synthesis of zinc oxide nanoparticles on graphene–carbon nanotube hybrid for glucose biosensor applications"
35. J. X. Wang, X. W. Sun, and A. Wei, Y. Lei, X. P. Cai, and C. M. Li, Z. L. Dong. " Zinc oxide nanocomb biosensor for glucose detection"
36. S. Inbasekaran, R. Senthil, G. Ramamurthy, T.P. Sastry. "Biosensor using Zinc Oxide Nanoparticles"
37. Said Benramache, BoubakerBenhaoua and HamzaBentrah. "Preparation of transparent, conductive ZnO:Co and ZnO:In thin films by ultrasonic spray method"
38. SelvakumarPalanisamy, SrikanthCheemalapati, Shen-Ming Chen. "Enzymatic Glucose Biosensor Based on Multiwalled Carbon Nanotubes-Zinc Oxide Composite"
39. Syed Muhammad Usman Ali, Sara I Liin, Fredrik Elinder, BengtDanielsson. "An intracellular glucose biosensor based on nanoflakeZnO"
40. Kai Loong Foo, Muhammad Kashif, U. Hashim, Md. Eaqub Ali. " Fabrication and Characterization of ZnO Thin Films by Sol-Gel Spin Coating Method for the Determination of Phosphate Buffer Saline Concentration"
41. Hitoshi Muguruma, Atsunori Hiratsuka, and Isao Karube. "Thin-Film Glucose Biosensor Based on Plasma-Polymerized Film: Simple Design for Mass Production"
42. M. H. Habibi, M. KhalediSardashti. "Preparation and proposed mechanism of ZnO Nanostructure Thin Film on Glass with Highest c-axis Orientation"
43. [43] I. Nkrumah, F.K. Ampong, B. Kwakye-Awuah, R.K. Nkum, F. Boakye "Synthesis and Characterization of ZnO Thin Films Deposited By Chemical Bath Technique"

44. SitiNurAkmarMohdYazid, IllyasMd Isa, Suriani Abu Bakar, NorhayatiHashim&SazeliAbGhani. "A Review of Glucose Biosensors Based on Graphene / Metal Oxide Nanomaterials"
45. I. K. Battisha, H. A. Wahab, A. A. Salama, A. A. El Saeid, M. Willander, O. Nur. "Semiconductor ZnO Nano-Rods Thin Film Grown on Silver Wire for Hemoglobin Biosensor Fabrication"
46. Zhigang Zhu, Luis Garcia-Gancedo, Andrew J. Flewitt, HuaqingXie, Francis Moussy and William I. Milne. "A Critical Review of Glucose Biosensors Based on Carbon Nanomaterials: Carbon Nanotubes and Graphene"
47. Chunyang Zhou, Lin Xu, Jian Song, Ruiqing Xing, SaiXu, Dali Liu &Hongwei Song. "Ultrasensitive non-enzymatic glucose sensor based on three-dimensional network of ZnO-CuO hierarchical nanocomposites by electrospinning"