MEMS Based Viscometric Biosensor to Continuously Detect Glucose Level of a Diabetic Patient

Abhishek Mallik, Diptyajit Das, Soumyajit Routh, Satyajit Bhowmick, Anik Karan, Sauvik Das Gupta

Abstract— In this paper a MEMS viscometric sensor is produced for glucose monitoring.Glucose sensing mechanism is based on affinity binding principles using solution of dextran residues on the nanospheres and Concanavalin-A (Con A).The sensing is based on the vibration measurement of the micro cantilever placed in the microchamber.The microchamber is filled with the proposed Glyconanospheres which is used for higher affinity towards glucose. The sensor design,sensing mechanism,fabrication process is reported. Sensor design using L-EDIT is shown.

Index Terms— Viscometric, MEMS, Glyconanospheres, Biosensor, Diabetic, Micro-cantilever, L-EDIT

1 INTRODUCTION

Diabetes is a metabolic disease that is characterized by high glucose level (hyperglycemia) which is resulted from defects in insulin production. Continuous assessment and necessary control of the blood sugar level is highly recommended for diabetic patients. It keeps them a check about their glucose level and timely taking of the insulin which is required to check the diabetic related issues. The various diseases that may result to a diabetic person is heart disease and stroke, blindness, kidney disease, high blood pressure. [1]

So Glucose monitoring sensor has always been an important device which has a strong social relevance. A biosensor is an analytical device which can be used to measure the glucose level in the blood. It converts a biological response into an electrical signal. [2]

The main components of a biosensor are-

a) **A biological element**: this is the glucose sensitive element that reacts with glucose. Mainly for glucose detection enzymes are used but there are various other biological elements like cell receptors, organelles etc.
b) **Transducer**: this transducer is the detector element. It converts the reaction of the analyte (here glucose) with the biological element into electrical signal. It works in various physiochemical ways like piezoelectric, optical etc.
c) **Associated Electronics**: This electronic circuitry is used to amplify the transducer signal and remove the noise from it.

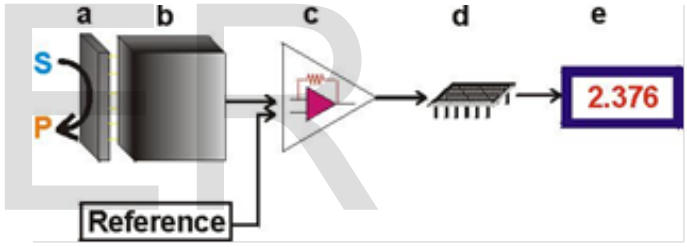


Figure 1: Schematic diagram showing the main components of a biosensor. The biocatalyst (a) converts the substrate to product.This reaction is determined by the transducer (b) which converts it to an electrical signal. The output from the transducer is amplified (c), processed (d) and displayed(e).[2]

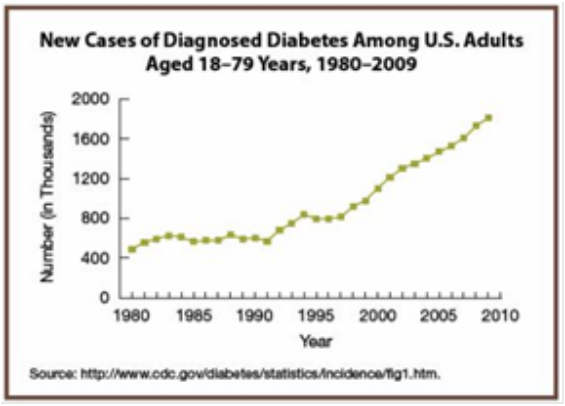


Figure 2: Chart representing the increase in diabetes in the USA.[3]

- *Authors [Abhishek Mallik & Sauvik Das Gupta] -School of Electrical and Computer Engineering, Oklahoma State University, Stillwater, OK, USA.*
- *Authors [Diptyajit Das, Soumyajit Routh, Satyajit Bhowmick & Anik Karan]- West Bengal University of Technology, Kolkata, West Bengal, India.*

2 SENSOR SELECTION:

Existing sensors for glucose are mainly based on electromechanical detection of enzyme-catalyzed reactions [4]. There are certain drawbacks of this type of sensor:

a. Glucose in irreversibly consumed during detection which may result in change of the equilibrium of the glucose concentration of the tissue.

b. The rate of glucose consumption is diffusion limited. The change in diffusion may limit the sensitivity.

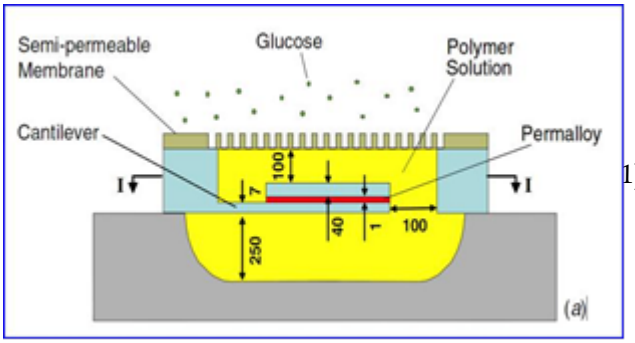
c. Frequent inaccuracy causing large drifts are observed and frequent calibration is required.[5]

A lot of research is going on to remove this limitations specially focusing on the use of non-consumptive, competitive affinity of binding of glucose.

So MEMS based Continuous Glucose Monitoring sensor has a lot of market in present days because of its increase in demand due to growth rate of diabetic patients.So in this paper a MEMS viscometric sensor is proposed that is used to monitor glucose based on the affinity binding principles. Glyconanospheres containing luminescent CdSe-Zns Quantum dots are proposed for higher affinity towards the glucose.

Further MEMS sensors can be batch fabricated which allows the manufacturer to reduce the cost and also integrate multiple functional components for metabolic monitoring.
It results in improved measurement and time response.[6]

3 SENSOR FACETS AND DESIGN:



1)

Figure 3: Schematic diagram of MEMS viscometric glucose sensor.

The sensor contains a semi permeable membrane from where the glucose can come in and go out of the sensor.Use of Glyconanospheres containing luminescent CdSe-Zns Quantum dots is proposed in place of normal polymer solution.A MEMS vibrational cantilever is present to detect the change in the viscosity of the liquid. It is anchored to one side. Permalloy strips are laid over the cantilever. They are covered with a thick reinforcement polymer layer to prevent the curling of the cantilever beam because of the internal stress.Thus a micro chamber is formed between the substrate and the membrane. [7]

The sensor top view was designed using L-EDIT. The input output channel was mentioned. The dimensions are taken 500 according to the reference paper.

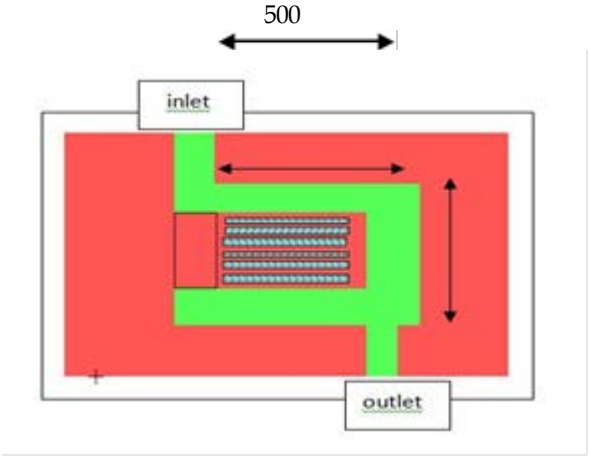


Figure 4: The top view of the sensor.

4 SYNTHESIS OF THE GLYCONANOSPHERES:

Negatively charged luminescent CdSe-Zns QD's can be incorporated into luminescent Glyconanospheres through electrostatic interactions with CM Dextran and polylysine. Covalent amide bonds were introduced to cross link the QDs with the polysaccharide matrix to further stabilize the Nano spheres. The dextran residues on the surface of the nanospheres show high affinity towards glucose binding protein-Concanavalin A(Con A). [8]

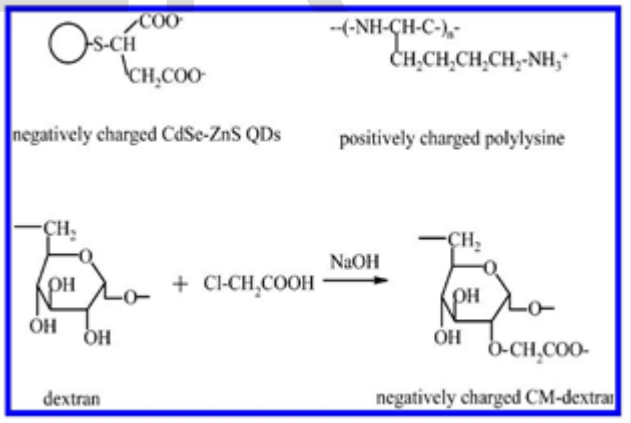


Figure 5: Structures of the different material used. [8]

5 SENSING MECHANISM:

The chamber contains the Glyconanospheres. Con-A which is attached to the dextran nanospheres can bind up to 4 glucose units reversibly. When a free glucose permeate through the membrane a partial de-crosslinking of the dextran-Con A complex. This results in the decrease of the viscosity of the solution.

It's a reversible process.When the glucose concentration on the

outside of the chamber decreases the glucose will unbind from Con A causing the dextran crosslink to recover and thus increase the viscosity.

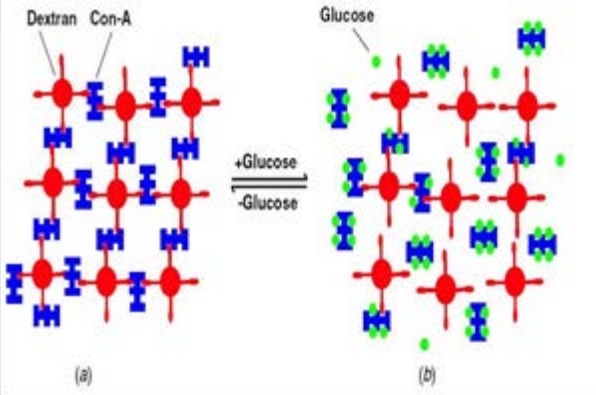


Figure 6: Affinity glucose sensing principle

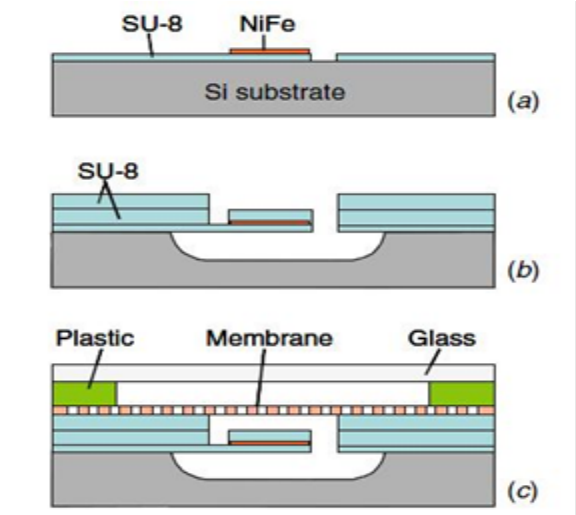


Figure 7: Device fabrication and Assembly process.

The viscosity of the sensing solution is detected by the cantilever vibration. A torque is given to the Permalloy by placing the device in a magnetic field. The torque is directed along the width of the cantilever. The cantilever vibration is effected by the elasticity of it and the vibration induced flow of the solution. The damping of the vibration is directly proportional to the viscosity of the solution. The measurement of the damped vibration is therefore the measure of the viscosity.

The solution viscosity is dependent on the glucose concentration of the subcutaneous tissue and is independent of the diffusive transport of the glucose.

6 Fabrication Process:

The initial step will be deposition and patterning of a layer of SU-8 to form the cantilever. A Permalloy will be deposited using sputtering and patterned. This will be followed by a spin coating and patterning of two SU-8 layers. This layer along with the other SU-8 layer forms the side wall of the chamber. Plasma etching can be used to release the cantilever by etching the silicon directly underneath it. The resulting chip will be packaged to form a complete device assembly. Epoxy can be used as an adhesive in all bonding steps. Two PEEK tubes will be affixed at the grooves that connected the microchamber and an edge of the substrate. A semi permeable membrane will be bonded to form the top wall of the microchamber. Finally the whole chamber will be etched into the silicon substrate.[9]

A test flow cell can be formed on the top of the membrane by bonding a plastic spacer disk and a glass cover slip.

7 Conclusion:

MEMS have shown a big advancement towards high sensitive and low cost sensors. Diabetes is a major problem in the society which can be restricted by handshaking with MEMS.
A new concept of Glyconano spheres is studied and depicted in the paper. It was a good learning experience going into detail about the concept.

References:

[1] National Diabetes Fact Sheet. http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2_005.pdf
[2] Report on Biosensors. London Southbank University. http://www.lsbu.ac.uk/biology/enzte ch/biosensors.html
[3] Center for disease control and prevention. http://www.cdc.gov/chronicdisease /resources/publications/AAG/ddt.htm
[4] Heller A 1999 Implanted electrochemical glucose sensors for the management of diabetes Annu. Rev. Biomed. Eng. 1 153–75.
[5] Dex Inc .
[6] Ballerstadt R and Ehwald R 1994 Suitability of aqueous dispersions of dextran and concanavalin A for glucose sensing in different variants of the affinity sensor.
[7] A MEMS viscometric sensor for continuous glucose monitoring Yongjun Zhao, Siqi Li, Arthur Davidson, Bozhi Yang, QianWang and Qiao Lin. Received 17 July 2007, in final form 23 October 2007 Published 14 November 2007.
[8] Synthesis of Glyconanospheres Containing Luminescent CdSe-ZnS Quantum Dots.
[9] L-EDIT Manual.