Effect Of Glucose on Cell Capacitance: Simulation in MEMS

ARPITA GUPTA[1]
Assistant Professor,
Krishna Engineering College,
Ghaziabad, 201006, India

G. U. KHARAT[2]
Principal,
Sharadchandra Pawar College of Engineering,
Pune, 412409, India

ABSTRACT:
It is to be noted that membrane capacitance changes with diabetes, which is one of the fatal diseases in the world nowadays. Long term diabetes affects the immunity resulting to various disorders of the body. Fibrosis in the pancreas as well as myocardium is one of the major problems related with long term diabetes. Once fibrosis starts the capacitance of the cell linked to fibrosis will vary at different stages. The variation of the capacitance has been linked with the capacitance relaxation phenomena through simulation in MEMS. It is now well established that MEMS is diagnostic instrumentation for assessment of the status of diseases. The authors tried to measure the concentration of glucose with the help of Bio MEMS for establishing the fact that the capacitance of the living cell changes with the change in glucose in the body. The cellular transduction linked to capacitance relaxation phenomena has been focused through simulation in MEMS. The cellular transduction is also linked with growth of fibrosis in diabetic mellitus.

Keywords: Fibrosis, Diabetic Mellitus, Mems, Capacitance Relaxation, Diseases, Cellular Transduction.

Introduction:
Diabetes is a severe health problem that is increasing rapidly nowadays and is classified in two types, which are: type 1 diabetes also called juvenile onset diabetes, and type 2 diabetes, called non-insulin dependent diabetes [1]. Diabetes is distinguished by a very high level of glucose in the body that causes deregulation of the metabolism. Diabetes is the leading fatal disorder with severe consequences. With diabetes the body cannot regulate the level of insulin in the blood [2-5].Diabetes can change the status of blood vessels, and this can lead to cardiovascular disease. The lining of the blood vessels may become thicker, and this in turn can impair blood flow associated with heart problems [6]. Diabetes results to induce changes in cardiac structure with fat droplet deposition [7]. Myocardial fibrosis leads to extracellular matrix remodeling with the heart transplantation for survival. Reactive fibrosis is increasing in a variety of conditions though in the absence of ischemia [8-10]. Regardless of the etiology, fibrosis leads to increased myocardial stiffness therefore promoting cardiac dysfunction [11,12]. Various imaging modalities and collagen biomarkers have been used as surrogate markers to assess the presence, extent, and turnover of myocardial fibrosis. Techniques using echocardiography, cardiac magnetic resonance, and nuclear imaging have been developed to detect early features of systolic and diastolic left ventricular dysfunction and impaired contractile reserve [13,14]. Further identification of diffuse reactive fibrosis may be possible with evolving cardiac magnetic resonance and molecular techniques [15,16]. The goal of these approaches is to enable targeted therapy to be instituted earlier, leading to prevention of disease progression and

fibrosis accumulation. In addition, effects of type 1 diabetes are complicated by the concurrence of hyperglycaemia and insulin deficiency. Lack of cardiac insulin receptors reduces cell size, indicating the trophic effects of insulin. The insulin deficiency may thus be a major contributor to the LV mass and cell size. The use of appropriate diagnostic strategies for irreversible diabetic cardiomyopathy, which may help correctly identify the disease at early stages and implement suitable corrective therapies is imperative [17].

Brief Focus On The Change Of Membrane Capacitance with Glucose content:

Body capacitance is the absolute amount of energy storage of the body due to intact cellular membranes [18]. Capacitance measurements have revolutionized the study of exocytosis. In electrical terms, the lipid bilayer of cell membrane corresponds to a capacitor. The capacitance of the membrane can be measured fairly easily at high temporal resolution. Importantly, the capacitance (C) of the membrane is proportionally related to the membrane area (A) . The increase in cell surface area that results from fusion of secretory granules with the plasma membrane can therefore be monitored as an increase in cell capacitance. In cells the cell membrane is a leaky dielectric. This means that any condition, illness or change in dietary intake that affects the composition of the cell membranes and their associated minerals can affect and alter cellular capacitance [19].With diabetes the capacitance reduces in living cells. Changes in cell dimensions in the context of diabetes are a complex issue. In general, diabetes leads to apoptosis and a reduction in LV mass. . Body weight also decreases (or increases at a slower than normal rate). The LV mass/body weight ratio is often used as an index of cardiac pathology.

A Typical Simulation Of Cellular Transduction In Mems:

With the increasing use of MEMS (Micro-Electro Mechanical System) devices, the need to monitor the position of a moving MEMS component with high sensitivity is becoming more and more important. Not only in sensor applications, where the position of a moving part may be the variable to measure a certain physical property (like in acceleration sensors), but also in precise positioning systems [20-23].

The MEMS can be used to measure the capacitance of a living cell. The dielectric property of the living cell changes as the glucose content varies. The MEMS comprises capacitive electrode. The sample under test is sandwiched between the electrodes. With the glucose, the permittivity of the cell fluid changes with the capacitance of the cell. The capacitance is then measured which is proportional to the glucose content. The output of the MEMS is in terms of voltages [24-26].Different living cell with different dielectric constant (K1, K2, K3) have been taken and their capacitance is measured using MEMS where K1<K2<K3. The curve in Figure1 shows the relation between sensor output and concentration of glucose in the cell [27-32]. It is noticed from figure 1 that sensitivity increases with increase in dielectric constant. The experiment is done at a constant frequency (200Hz) and at room temperature.

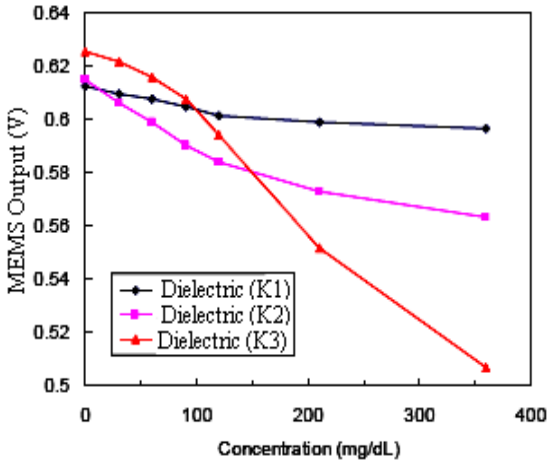

Figure: 1 Sensor output at 200 kHz plotted as a function of Glucose concentration.

The MEMS voltage output decreases consistently with increasing glucose concentration. The voltage at the output of the MEMS is proportional to the capacitance. This indicates that the permittivity of the cell decreases due to the increase in concentration of glucose. The relation between the change of capacitance with the permittivity is as shown in figure 2.

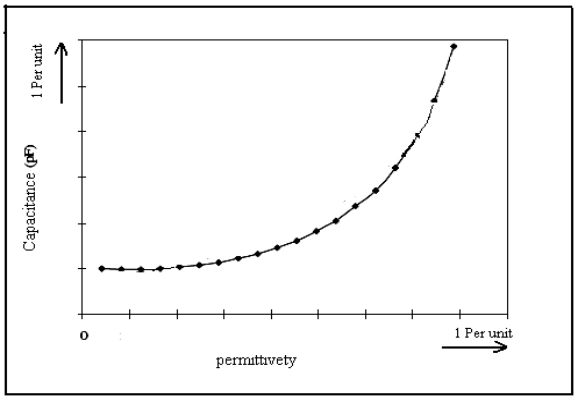

Figure: 2 Relation Of capacitance with permittivity

The curves have been simulated in Matlab Simulink 7.0. In this we have simulated capacitance of the cell of diabetic patients and this simulation is in agreement with the clinical values. We have simulated the curves in normalized way for projecting the status of the subject suffering from diabetes. There is a possibility of fibrosis with long diabetes [33-35]. A typical block diagram involved in simulink 7.0 is shown below in fig 3.

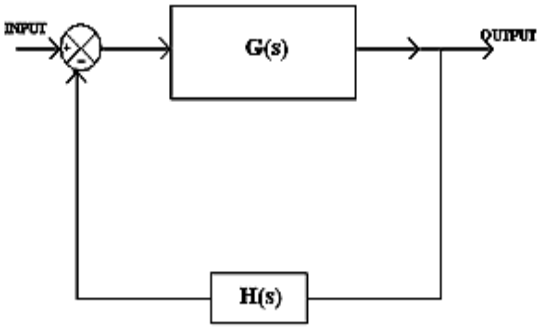

Figure: 3 Block Diagram in Simulink 7.0

The input is a step function, G(S) is a second order function in the forward path, H(S) is a first

order function in feedback path.

Discussion And Conclusion

The cellular transduction with the change of membrane capacitance of diabetic patient is very interesting and it is to be focused accurately for health care. The present paper in this respect has simulated the change of capacitance with cellular transduction concomitant with the change of glucose concentration of the cellular fluid. It is to further notice that with the increase of glucose concentration the permittivity of cell membrane decreases. The cellular transduction is linked with growth of fibrosis in the pancreas with capacitance relaxation phenomena. This growth is dependent on the insulin intake by the patient in long run. It is observed that in long run there is little effect of insulin consumed by the subject.

Acknowledgement

The authors are grateful to the authorities of Krishna Engineering College Ghaziabad. Prof. T. K. Basak is particularly indebted for inspiration received from his late wife, Mala Basak who is in the heavenly abode of Shree Shree Ramakrishna Paramhansa.

References

[1] A. Nygren, M. L. Olson, K. Y. Chen, T. Emmett, G. Kargacin and Y. Shimoni Propagation of the cardiac impulse in the diabetic rat heart: reduced conduction *reserve J Physiol 580.2pp* (2007) *543–560.*

[2] Kim TG, Jung J, Mysliwiec MR, Kang S, Lee Y Jumonji repressesalpha-cardiac myosin heavy chain expression via inhibiting MEF2 activity.*Biochem Biophys Res Commun* 329:544 –553 (2005).

[3] Lisa Juntti-Berggren, Essam Refai, Ioulia Appelskog, Mats Andersson, Gabriela Imreh, Nancy Dekki,Sabine Uhles, Lina Yu, William J. Griffiths, Sergei Zaitsev, Ingo Leibiger, Shao-Nian Yang, Gunilla Olivecrona,Hans Jo¨ rnvall, and Per-Olof Berggren Apolipoprotein CIII promotes Ca2_-dependent _ cell death in type 1 diabetes *10090–10094 _ PNAS _ vol. 101* (July 6, 2004*)*

[4] Erik Renstro¨m, Rosita Ivarsson,and Stephen B. Shears Inositol 3,4,5,6-Tetrakisphosphate Inhibits Insulin Granule Acidification and fusogenic Potential *the journal of biological* chemistry vol. 277, no. 30, issue of july 26, pp. 26717–26720,
(2002) printed in u.s.a.

[5] E. Neher and a. Marty Discrete changes of cell membrane capacitance observed under conditions of enhanced secretion in bovine adrenal chromaffin cells *Proc. Nati Acad. Sci. USA Vol. 79, pp. 6712-6716,(November 1982): Neurobiology*

[6] Wolf-Michael Weber, Andrei Segal, Anne Vankeerberghen, Jean-Jacques Cassiman and Willy Van Driessche Different activation mechanisms of cystic fibrosis transmembrane conductance regulator expressed in Xenopus laevis oocytes *Comparative Biochemistry and Physiology - Part A: Molecular & Integrative Physiology* Volume 130, Issue 3,(October 2001), Pages 521-531.

[7] Camelia R Ban, Stephen N twigg, Fibrosis in diabetes complications: pathogenic mechanisms and circulatory and urinary markers, *vascular health and risk management 4(3) (*2006) *575-596.*

[8] Christine Jellis, Jennifer Martin, Jagat Narul, Thomas H. Marwick 2010, Assessment of Nonischemic Myocardial Fibrosis, *Journal of the American College of Cardiology* Vol. 56, No. 2, 2010.

[9] Juan Asbun and Francisco J. Villarreal, The Pathogenesis of Myocardial Fibrosis in the Setting of Diabetic Cardiomyopathy, *journal of American college of cardiology*,47:693-00, doi:10.1016/ j.jacc.2005.09.050 (Published online 6 February 2006).

[10] Akar FG, Spragg DD, Tunin RS, Kass DA & Tomaselli GF Mechanisms underlying conduction slowing and arrhythmogenesis in nonischemic dilated cardiomyopathy. *Circ Res* **95**, 717–725 (2005).

[11] A. Nygren, M. L. Olson, K. Y. Chen, T. Emmett, G. Kargacin and Y. Shimoni, Propagation of the cardiac impulse in the diabetic rat heart: reduced conduction reserve, *J Physiol 580.2 (2007) pp 543–560*
[12] Laizuman Nahar, Farhana Alam Ripa, Abu Hasanat Md. Zulfiker, Md. Rokonuzzaman, Mahmuda Haque, Dr. Kazi Mohammed Shahariar Islam, Comparative study of antidiabetic effect of *Abroma augusta* and *Syzygium cumini* on alloxan induced diabetic rat agriculture and biology journal of north america issn print: 2151-7517, issn online:2151-7525, doi:10.5251/ abjna. 2010.1.6.1268.1272 (2010)
[13] Bollano E, Omerovic E, Svensson H.Waagstein F & Fu M Cardiac remodelling rather than disturbed myocardial energy metabolism is associated with cardiac dysfunction in diabetic rats. *Int J Cardiol* ***114****, 195–201* (2006).
[14] Candido R, Srivastava P, Cooper ME & Burrell LM Diabetes mellitus: a cardiovascular disease. *Curr Opin Invest Drugs* **4**, 1088–1094. (2003).
[15] Sugihara N, Genda A, Shimizu M,Diastolic dysfunction and its relation to myocardial fibrosis in essential hypertension. *J Cardiol; 18:353– 61 (*1988*).*
[16] Diez J. Mechanisms of cardiac fibrosis in hypertension. J Clin Hypertens (Greenwich);9:546 –50.Somashekar Bangalore Prakash and Pamela Abshire 2008 Tracking cancer cell proliferation on a CMOS capacitance sensor chip *Biosensors and Bioelectronics Volume 23, Issue 10,* (15 May 2008), Pages 1449-1457
[17] C.H.J. Lamers, J.W. Gratama, N.M.C. Pouw, S.C.L. Langeveld, B.A. Van Krimpen, J. Kraan, G. Stoter, R. Debets. Parallel detection of transduced T lymphocytes after immunogene therapy of renal cell cancer by flow cytometry and real-time polymerase chain reaction: Implications for loss of transgene expression *Human Gene Therapy. December 1, (2005) 16(12): 1452-1462. doi:10.1089/hum.16.1452.*
[18] Vonosuke kobatake, akihiko irimajiri, and nobuyoshi matsumoto, A Model Membrane Composed of a Filter Paper and a Lipid Analogue *biophysical journal Pubmed Central 10(8):* (1970) *728–744.*
[19] J Aoki and K Hara Detection of pattern of myocardial fibrosis by contrast-enhanced MRI: Is redefinition of uremic cardiomyopathy necessary for management of patients? *Kidney International* (2006) 69, 1711–1712. doi:10.1038/sj.ki.5000259
[20] C. Rembe, L. Muller, R.S. Muller, R. T. Howe, Full three-dimensional motion characterization of a gimballed electrostatic microactuator, *Proc. IEEE Annual International Reliability Physics Symposium (IRPS),* (2001) *p. 91 – 98*
[21] J. S. Burdess, A. J. Harris, D. Wood, R. J. Pitcher, D. Glennie, A systems for the dynamic characterization of microstructures, J*. MEMS* Vol. 6, (1997), p. 322 – 328
[22] M. R. Hart, R. A. Conant, K. Y. Lau, and R. S. Muller, Stroboscopic interferometer systems fpr dynamic MEMS characterization, *J. MEMS,* Vol. 9, (2000), p. 409 – 418
[23] W. M. van Spengen, R. Puers, R. Mertens, and I. De Wolf, Characterization and failure analysis of MEMS: high resolution optical investigation of small out-of-plane movements and fast vibrations, *Microsys. Technol.,* Vol. 10, (2004), p. 89 – 96
[24] M. Lei, et al., "A hydrogel-based implantable micromachined transponder for wireless glucose measurement," *Diabetes Tech. Therapeut.,* (2006). 8: 112-122,
[25] X. Huang, et al., "A MEMS affinity glucose sensor using a biocompatible glucose-responsive polymer," *Sensor Actuator. B Chem.,* (2009). 140: 603-609,
[26] S. Li, et al., "Development of novel glucose sensing fluids with application to MEMS-based continuous glucose sensing," *J. Diabetes Sci. Tech.,* (2009) 2: 1066,
[27] MiniMed Paradigm® REAL-Time Insulin Pump and Continuous Glucose Monitoring System, Medtronic MiniMed, Inc., San Antonio, (2006).TX, USA,
[28]. FreeStyle Navigator® Continuous Glucose Monitoring System, Abbott Diabetes Care, Inc. Alameda, CA, USA (2008).
[29]. R. J. Russell, et al., "A fluorescence-based glucose biosensor using concanavalin A and dextran encapsulated in a poly(ethylene glycol) hydrogel," *Anal. Chem.,* (1999).71: 3126-3132,

[30]. Xie H, Fedder G Vertical comb-finger capacitive actuation and sensing for CMOS-MEMS *Sensors & Actuators Physical* 95 (2002) p. 212-221
[31] W. C. Tang, M. G. Lim, and R. T. Howe, Electrostatic comb drive levitation and control method, *J. MEMS.* Vol. 1, No. 4, (1992), p. 170 – 178
[32] W. M. van Spengen and J. W. M. Frenken, A "Nano-battering ram" for measuring surface forces, *Proc. Micromechanics and Microengineering Europe 2006 (MME06),*Southampton, UK, (2006), p. 205 - 208
[33] TK Basak, T.Ramanujam, Rahul Dayal, V.Cyrilraj, Arpita Gupta, Poonam Goyal, Prachi Kulshreshtha 'Data mining of Nephropathy and parenchymal lesson in nephron' *has been accepted for presentation at the 2009 World Congress on Computer Science and Information Engineering* (CSIE 2009), to be held from March 31 to April 2, 2009, Los Angeles/Anaheim, USA. Paper ID: 950
[34] Xiao Z, Peng W, Wolffenbuttel W F, Farmer K R Micromachined variable capacitors with wide tuning range, *Sensors & Actuators: Physical* 104 *(2003) p. 299-305*.
[35] Sun Y, Piyabongkarn D, Sezen A, Nelson B J, Rajamani R A high aspect ratio two-axis electrostatic microactuator with extended travel range *Sensors & Actuators: Physical*. 102 (2002) p. 49-60.