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Analysis of Normal and Infected Bio-cell by Using Dual Nanoprobe

Md. Akter Hossain[1], Md. Hedayet Ullah[1], Muhammad Ahsan Ullah[1]
[1]Department of Electrical and Electronic Engineering, Chittagong University of Engineering and Technology, Chittagong-4349, Bangladesh.
Email: polar.cuet@gmail.com, raifull0@mail.com, and ahsan@cuet.ac.bd

***Abstract*— Knowledge of nanoprobe based bio-cell analysis method can be used to diagnostically difference between healthy and infected bio-cells. This method is made possible by using nanotechnology, a new field of science that provide a technology for human to interact with nanoscale life form organism specially cell. The electrical behaviors of healthy and infected cells are different. This paper analyses yeast cell, liver cell, and blood cell in both healthy and infected conditions to observe the differences in electrical behaviors. A dual nanoprobe is used for supplying electrical power from source to bio-cell. The voltage can be applied by two ways across the cells. One is penetrating the cell wall and another is keeping the nanoprobe in closed contact with the cell membrane. After simulation the current was measured about 2.7 times larger for liver tumor cell than healthy liver cell including cell membrane. The current flow through the healthy cell is 1.9nA whereas the current flow through a dead cell is 34pA. It is expected due to the conductivity of cytoplasm of healthy cell is greater than that of dead cell. The current is measured for a leukemia affected cell is 21.2nA. It is 2% less than the current for a white blood cell.**

Keywords: Dual nanoprobe, Leukemia affected WBC, Yeast cell, Liver cell, Electrical properties, Conductivity.

I. INTRODUCTION

Nanoprobe based bio-cell analysis method is a very newer form of method. For example single cells electrical characterizations using nanoprobe via ESEM-Nano-manipulator System, one of the cell viability detection methods, was invented by a group of researchers in 2009 [1].

This method introduces the cell analysis in nanotechnology, a new field of science. In the analytical procedure, a single cell is analyzed by measuring the current through the cell by the application of a dc voltage using dual nanoprobe. Penetration (see in Figure 1) and without penetration (only contact with cell membrane; see in Figure 2) of the nanoprobe into the cell are the two processes for applying voltages across the cell. It is best to simulate the method first since the method is still new. For this purpose, ABAQUS 6.10 CAE, powerful finite element software has been used to simulate the experimental method.

It is observed that, a bio-cell shows various types of electrical behavior. Among them two behavior are taken into account for cell analysis. One is, conductivity of cytoplasm of cancerous or infected cell is lower than healthy cell. Because when the cell is dead or cancerous, the amount of ions becomes lower than healthy cell [2]. Another behavior is the conductivity of cell including membrane shows higher conductivity in case of cancerous or infected cell than the healthy one [3, 4], since the permeability of membrane increases, when the cell becomes cancerous. As a result more ions can flow into the cell [3, 5]. Moreover cancer cells have altered membrane composition and membrane permeability, which results in the movement of potassium, magnesium and calcium out of the cell and the accumulation of sodium and water into the cell [3, 5], results the flow of more ions into the cell.

The conventional method of cell viability and cancer detection is done by using chemical substance [1]. Colorimetric or florescent dyes are used for cell viability detection. The limitation of this method is the lack of capability to produce instantaneous and quantitative result but nanoprobe based cell analysis method is much better in terms of producing instantaneous and quantitative result [6].

Bone marrow aspiration is a conventional type of biopsy used to diagnose leukemia. In open biopsy, the bone is taken out and stitches are given to the patient. For this, the patient has to stay back in the hospital for few days. Patient may experience bleeding after the procedure. The nanoprobe based testing method may be better in this case for leukemia detection.

In this paper, section-I was discussed about theoretical background, analytical procedure and the advantages of this nanoprobe based novel analysis process in comparison to the conventional method; in section-II process of implementation is discussed; the simulation procedure is discussed in section-III and section-IV, V and VI are discussed about result and analysis, discussions and conclusions respectively. Here the result and analysis section represents the simulation output and compares the output data with previous data.

II. METHODOLOGY

A dual nanoprobe is needed to supply an electrical power from source to the bio-cell. The one end of nanoprobe has to be connected with 2V dc source shown in Figure 1 and the another end of nanoprobe has to be penetrated into the cell wall for both yeast and blood cell or have to be in closed contact with the cell membrane for liver cell shown in Figure 2.

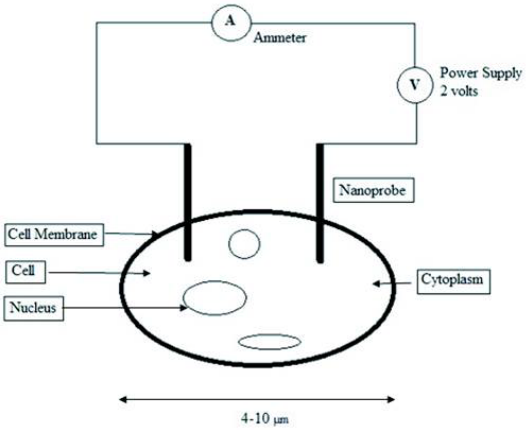

Figure 1. Schematic diagram on penetration of duel nanoprobe into a cell [1].

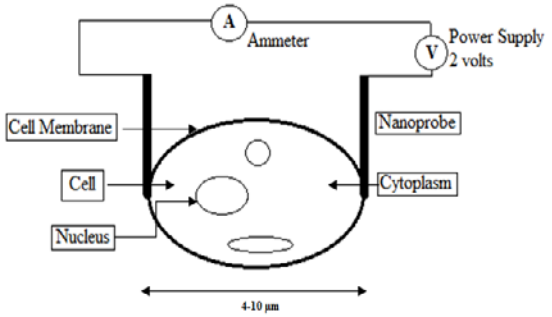

Figure 2. Schematic diagram of edge contact of dual nanoprobe into a cell.

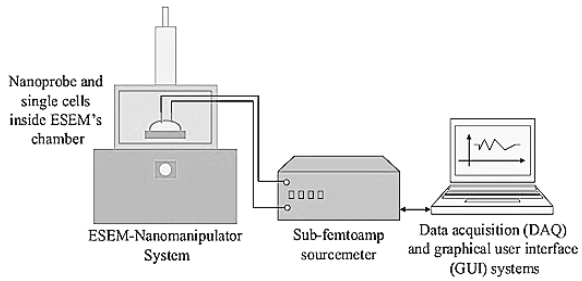

Figure 3. Experimental setup [1].

The cell can be analysed via ESEM-Nano-manipulator System. The output current is measured using sub-femto ampere source meter. This analog current is converted into digital by data acquisition (DAQ) and this digital data is then represented by graphical user interface (GUI) systems shown in Figure 3.

III. SIMULATION PROCEDURE

ABAQUS 6.10 computer aided engineering (CAE) software that provides strong platform to design and simulate any type. This software has the ability to use in nanoscale level simulation. Figure 4 shows the simulation setup designed in ABAQUS platform that shows two nanoprobes touching the cell-membrane. The properties of basement and the probe martials has to be the same.

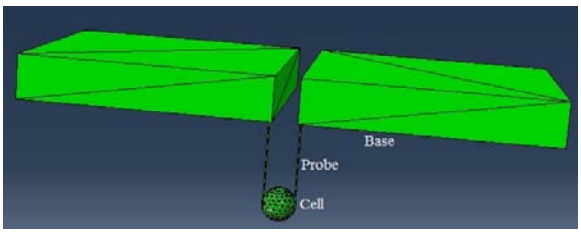

Figure 4. Simulation Setup.

Otherwise result will be varied due to dissimilar materials junction's conductivity of the system. The steps of simulation procedures are represented by a simple flow chart shown in Figure 5.

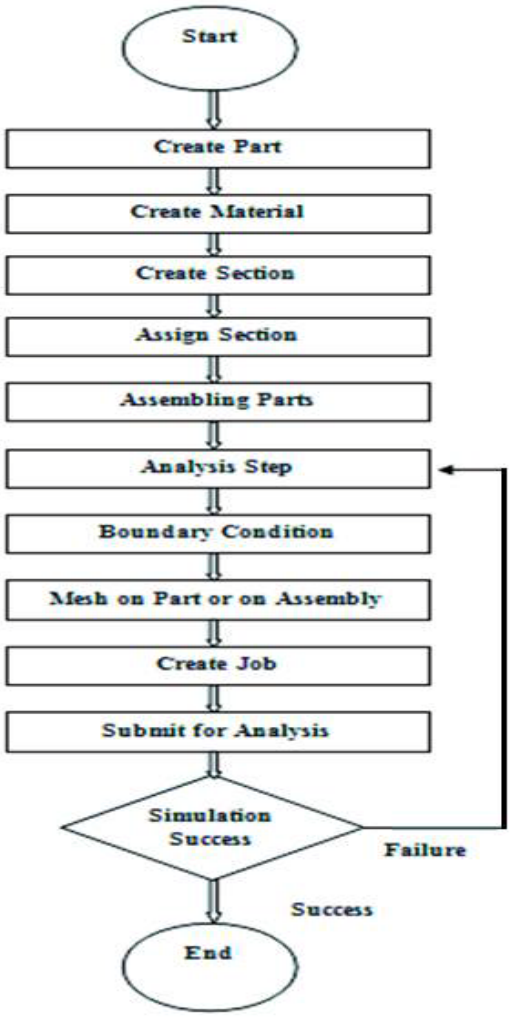

Figure 5. Flowchart of simulation procedure.

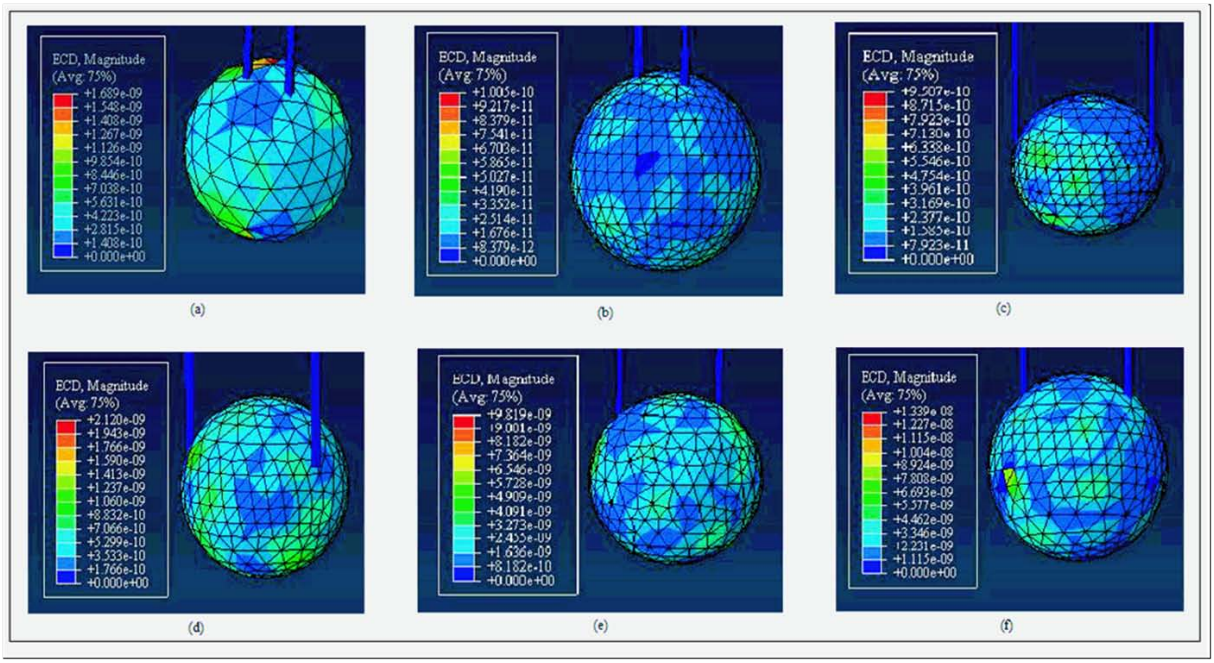

Figure 6. ECD value for different cell model. (a) healthy yeast cell, (b) dead yeast cell, (c) liver cell, (d) liver tumor cell, (e) white blood cell, (f) leukaemia affected WBC cell.

The major part of the study is to characterize the nanoprobe based on type of material and cross section. Resistance is the main factor of the probe. Many types of materials can be used to construct the probe but that material can provide the best result which low resistance and no loading effect on load (cell). The size of nanoprobe used is 15µm long and 200nm ×200nm cross-section area. The probe is made of gold. Cell characterization and simulation is the basic part of this study. A cell model is designed as close as real cell. Different mechanical and electrical properties are given to approach a model, which is seemed to be a real cell.

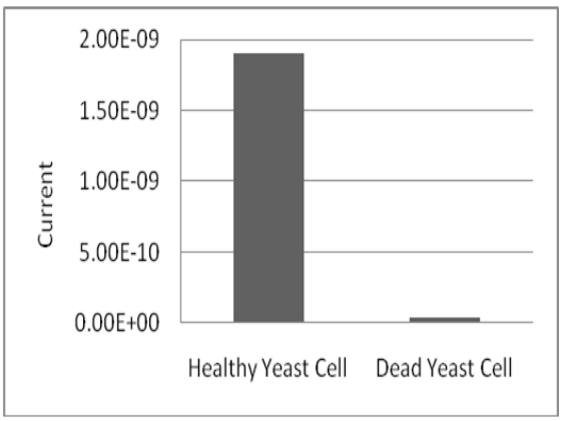

Figure 7. Current in a healthy and dead yeast cells.

IV. RESULT AND ANALYSIS

The current flows through the cells are represented by electrical current density (ECD). The output current is found by the product of average cross-section area of the cell and average electric current density (ECD) which is given by the equation (1).

$$I = J_{ECD} \times A \quad (1)$$

Where I is the current, J_{ECD} is the electric current density in the cell and A is the cross-sectional area of the cell under the probes. Figure 6 represents the electric current density for different cell model. The resultant J_{ECD} are 268pA/µm^2, 4.80pA/µm^2, 162.6pA/µm^2, 443.4pA/µm^2, 3037.0pA/µm^2 and 3000pA/µm^2 for healthy cell, dead cell, normal liver cell, liver tumour cell, white blood cell and leukaemia affected white blood cells, respectively.

By using resultant ECD magnitudes, a current that flows through the cell can be drawn according to the equation (1). Simulation outputs of the calculated current values become 1.9nA and 34pA for healthy and dead yeast cells shown in Figure 7. It is obvious that leaving yeast cell is highly conductive than a dead cell.

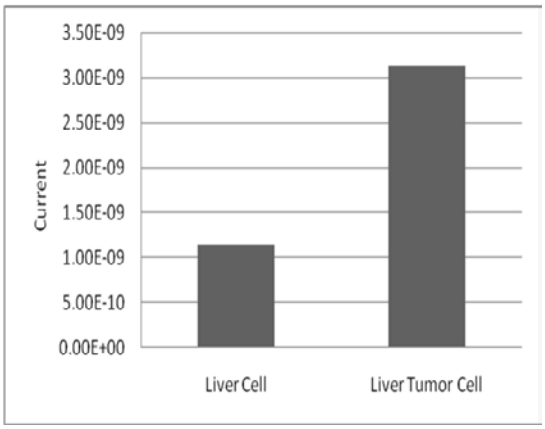

Figure 8. Current in a healthy liver cell and liver tumour cell.

On the other hand a healthy liver cell conducted current 1.1486nA and the liver cell with tumour conducted current 3.1327nA which is shown in Figure 8. The current level of a liver tumour cell increases due to increasing the ions in the liver tumour cell.

Figure 9 represents the currents for healthy WBC and the leukaemia affected WBC. The healthy WBC conducted the current 21.457nA and the leukaemia affected WBC conducted the current 21.2 nA, respectively. In this case leukaemia reduces the conductivity of the WBC.

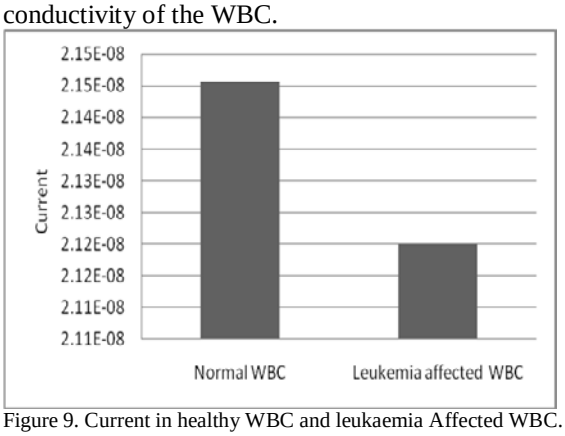

Figure 9. Current in healthy WBC and leukaemia Affected WBC.

The main approach of this study is to segregate the current value in between normal and infected cell. The current flow through the healthy cell is 1.9nA and dead cell is 34pA for yeast cell, which is expected. This is because; the conductivity of cytoplasm for healthy cell is greater than that of a dead cell. On the other hand the current was measured about 2.7 times larger for liver tumour cell than that of healthy liver cell. For measuring the current against WBC should be more precise, because the current as well as conductivity difference is only 2%.

Table 1, Results comparison between experimental and simulation

Types of Cell	Experimental result with 2V supply and with (probe + base + cable) resistance 1kΩ	Previous simulation result with 2V supply and with (probe +base) resistance 37.46Ω	Present simulation result with 2V supply and (probe + base) resistance 107.2Ω
Healthy (yeast ell)	262pA current	54mA current	1.9nA current
Dead (yeast ell)	2pA current	0A current	34pA current

Table 1 and Table 2 show the comparison among experimental data, previous simulation and present simulation done in this analysis. The probe gap was taken 1.46µm for penetration. The current values for present simulation are high compare to experimental result because resistance is low as there is only probe and base is considered.

Table 2, Results comparison between experimental and simulation for Yeast cell.

Properties	Experimental Result	Previous Simulation	Present Simulation
Resistance ,Ω	1k	37.46	107.2
Sensitivity, mA/V	1	27.6	9.3
Voltage, volt	2	2	2

V. DISCUSSIONS

The test may give perfect result if the cells are tested in same environment, keeping same probe gap and same depth of penetration because the conductivity between probes across the cell may vary with probe gap, depth of penetration and environmental condition surrounding the cell. More than one sample of blood cell having WBC should be tested for better confirmation of the presents of immature WBC as the conductivity difference between normal WBC and leukemia affected WBC is only 2%. As well as for other cells detections, same tasks should be taken.

VI. CONCLUSIONS

This nanoporbe based analytical process may have better opportunities, when it will be practically implemented. For detection of healthy, death and cancerous cells (leukemia), this process may give instantaneous and better results. Solution of process of analysis provides more accurate result then conventional ways as nanoprobe deals with any change of result in nanoscale level. A long way left to completion the research in this method. This project is only a small portion of a big idea. Simulation is one of the universal approach that researcher use in their research. This novel nanoprobe based detection process may introduce with versatile opportunities for researchers and a revolutionary change can occur in medical science specially in the section of detection, analysis and treatment of diseases.

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