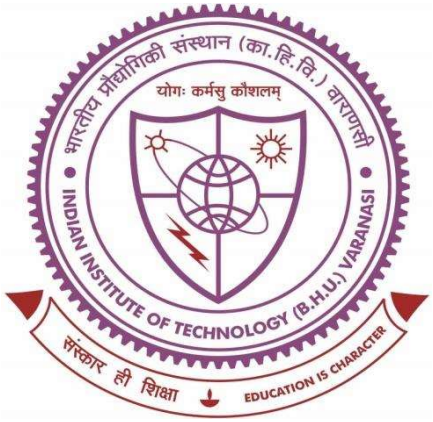
Fabrication and Characterization of Thin Film Nanomaterials based Biosensing Devices for Assessing Dynamic Behaviour of Mammalian Cells



Thesis submitted in partial fulfillment for the Award of Degree

Doctor of Philosophy

By

Uvanesh K.

SCHOOL OF BIOMEDICAL ENGINEERING
INDIAN INSTITUTE OF TECHNOLOGY
(BANARAS HINDU UNIVERSITY)
VARANASI – 221005
INDIA

ROLL NO: 15021002

2020

Chapter 6

Summary and Future Scope

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6.1 Summary

The main objective of this thesis is to provide some insights into the fabrication and characterization of thin-film nanoomaterials based biosensing devices for assessing dynamic behaviour of adherent mammalian cells. This chapter presents the chapter-wise major observations and findings of the thesis as well as future scope releted to present work as described in the following section.

Chapter-1 introduces the basics about biosensor, cell-based biosensor (CBB), and types of CBB currently being used. Different types of CBB based on its transduction principle are discussed. Strategies for the design and characterization of CBB and fundamental behaviour of cells in electric field are also discussed. A detailed literature review on cell-based biosensors (electric cell-substrate impedance sensing system, and thin-film based sensor) is carried out. Based on the observations from literature survey, the problem statement is identified and the scope of the present study is defined.

Chapter-2 describes the investigation of functional behaviour of myoblast (C2C12) cells using a co-planar silver metal electrode system integrated to a low-cost ECIS system. The major observations and finding from the chapter are summarized below:

- Typically, a low-cost ECIS sensor is developed using silver metal. The Ag is thermally coated on the conversional glass substrate to construct metal-insulator-metal (MIM) structure *via* shadow mask method, to achieve an active layer's dimensions of 1.5 mm wide and 4 mm length.
- At the same time, to develop a ECIS system, we used the electronic components locally available at the laboratory to construct a low-cost impedance measuring

circuitry and calibrated the developed circuit, against the standard commercial resistor. Further, the MIM device is integrated to the developed impedance measuring circuitry to construct a low-cost ECIS system.

- To increase the cell adhesion process, the MIM device is coated with 2% gelatin protein and the gelatin-coated MIM device is used as a platform to study the phenotypic change of adherent mammalian cells under the influence of applied electric field.
- The proposed system is working notably well with cell culture assembly designed for studying the cellular functions such as cell adhesion, spreading, migration and proliferation.
- The variation in physiological behaviour is well correlated with both changes in the electrical impedance and microscopic images data as well as using an equivalent electrical model.

Chapter 3 focuses on fabrication and characterization of metal-oxide thin film nanomaterials based biosensing devices for assessing dynamic behaviour of adherent mammalian cells. Typically, the Chapter 3 investigates the effect induced by cellular functional behaviour on the characteristic electrical properties of the e-beam deposited aluminium oxide (Al_2O_3) thin film nanomaterial-based metal-insulator-metal (MIM) device. The major observations and finding from the chapter are summarized below:

- The gelatin-coated MIM device is used as a platform to study the phenotypic change of adherent mammalian cells under the influence of applied electric field.
- The proposed device is working significantly to determine various cellular functions such as cell adhesion, spreading, proliferation, and differentiation.
- The effect induced by cellular functional behaviour is well correlated with both

changes in the characteristic electrical property and microscopic observation of the cells as well with an equivalent electrical model used.

- Hence, the proposed device could be used for various bio-sensing applications wherein dynamic changes of the biological cells play a vital role and need to be essentially examined.

Chapter 4 investigates the effect induced by cellular functional behaviour on the characteristic electrical properties of the sol-gel synthesized spin coated zinc oxide (ZnO) thin film nanomaterial-based metal-semiconductor-metal (MSM) device. The major observations and finding from the chapter are summarized below:

- we have demonstrated that modulation of the dynamic behaviour of the adherent mammalian cells using electrical properties of the ZnO based semiconducting nanomaterial.
- This work reports the analysis of cellular processes using the fabricated gelatin functionalized ZnO based MSM device with respect to the change in electrical response using a unique biosensing platform.
- The obtained results based on the electrical parameters are well in correlation with the functional changes in the cellular processes as observed through microscopic images and MTT assay.
- Further, the dynamic behaviour of adherent mammalian cells is analyzed by optimizing the appropriate cell density.
- Therefore, the ZnO thin film based MSM biosensor could be used for various biosensing applications wherein dynamic changes of the cells play a vital role.

Chapter 5 investigates the effect induced by cellular functional behaviour on the characteristic electrical properties of the sol-gel synthesized spin coated zinc oxide (ZnO)

thin film nanomaterial-based larger area heterojunction device. The major observations and finding from the chapter are summarized below:

- The work exposes the demonstration of change in characteristic electrical properties of the poly-L-lysine coated extended large area heterojunction device, due to the change in the progression of cellular processes that is being exhibited by the neuronal cells.
- We analysed that an increase in the conductivity with a decrease in the magnitude of impedance is due to the formation of cell-substrate interaction and also due to the formation of synaptic junction after neuronal differentiation between the neuronal cells across the surface.
- Further, we also found that the characteristic electrical properties is well in correlation with the observed microscopic and SEM images.
- Hence, we anticipate that the fabricated extended large area heterojunction device could be used in the *in vitro* cell-substrate sensing application where the recording of the dynamic behaviour of the mammalian neuronal cells is adequately important.

6.2 Future Scope

- ❖ Novel biosensors can be fabricated using other metal-oxide such as CuO, MoO_3, etc. available for cell-substrate study.
- ❖ Doped ZnO nanomaterials using metals such as Al, Ti, Sn, Ag, etc. can be investigated for constructing cell-based biosensor.
- ❖ The real-time functional behaviour of various other cells can also be investigated using the prototype circuit developed.
- ❖ The real-time functional behaviour of various other primary and secondary cells can also be investigated using the biosensors developed.