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Nano Bioelectronics for Disease Diagnostics

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***Abstract*: New microelectronic systems offer and develop powerful circuits for innovative biochips responsible for sensing at the molecular levels to detect diseases, biomarkers, and therapeutic components. However, there are challenges in meeting the requirements of reliability, sensitivity, and specificity provided by the biomedical applications. The innovative chips have the ability to sense the minor therapeutic elements in the human body. It is worth noting that nanotechnology provides the solution for improving the sensing process's surface properties. The study is relevant for revealing the extent to which there are improvements in the Nano Biotechnology in the electrochemical systems responsible for detecting the molecules in carrying pout therapy and monitoring the human cell culture.**

***Keywords*: Disease diagnostics, Nano bioelectronics.**

1. Introduction

Personalized therapy is critical in injecting the drug doses in the recommended amount based on the patient's metabolic conditions. Different people have distinct cytochrome P450 isoforms because of having different genotypes. Notably, the Cytochrome P450 is a protein in nature and play an important role in human metabolism (Iijima 1991). The existence of the different patient's genotypes is known for causing the plasma concentration variation when patients are injected with the same drug amount. For this reason, AmpliChip is a genetic test developed by Roche to detect the genes responsible for expressing the 2D6 and 2C19 as components of the cytochrome P450. The AmpliChip identifies the various four patient classes by providing the genetic predisposition that metabolizes the drugs. On the other hand, human metabolism includes a significant number of P450 isoforms. Additionally, individual metabolism is associated with the genetic predisposition and changing patients' conditions. Eminently, there are specialized drug monitoring laboratories where there is modernized equipment for serving the function. Remarkably, cell therapy and regenerative have been used to replace the damaged tissues through the engineering processes (Johnson 2003). The magnetic fields are regarded as the modern fields for the engineered tissues' fabrication, improving cell feeding. Nonetheless, there are missing biochemical mechanisms during the cell differentiation that become a challenge detecting the minor tissues, thus understanding the cell metabolism in tissue engineering. The arising demand for knowledge about metabolism creates a desire to have the microchip technology to provide a circuit for addressing the issue. Having poor specificity, sensitivity, and unstable systems limits the required tissue engineering techniques, hence requiring new efforts. According to Richard Philip Feynman, Nano-biotechnology gives a broader range of opportunities that will boost the nano-bio-chips (Joseph 2003). He suggests that there are strategies to have bio-materials under nano-scale control. In this study, there will be a consideration for having the biological and organic structures as the nanotechnological systems' main pillars. Therefore, the zero, one, and two-dimensional systems will be considered in coming up with this discussion for attaining experimental investigations. The merits arising from the nano-biotechnology will be examined by comparing them with the bulk materials. The detection capability, sensitivity, and specificity will reveal the successful examples in the experimentation done. It is worth noting that there are many innovative ideas from the research on nano-bio-chip technology in cell biology and therapies.

2. Two-dimensional Nano-Structures Improving DNA and Immuno-Chip

Keeping one of the two dimensions in the nano-scale helps obtain the nano-structures' fabrication as one of the structures will be a nano-scale. For instance, the Langmuir Blodgett's molecular layers where a single layer is found in the water-air interface then turned into a solid substrate (Shumyantseva 2004). Repeating the step gives multiple layers with the primary nano-structures. To obtain a molecular layer, there will be leaving substrates in the molecular solution for the whole night to enable the molecules to gain a stable bond. Modern technology is proposed for DNA detection when measuring hybridization's capacitance and variation (Carrara 2009). The main emphasis is on specificity as most of the works involve low specificity that does not produce the desirable results. DNA hybridization is recommended for antigen and DNA detection despite lacking reliability. The main drawbacks in this experiment are seen in the non-insulated probe surfaces. When experimenting, there should be a consideration to have deep grooves across the whole film. It will allow the ions to pass through the film and be discharged at the electrode surface.

With the above set up, there are two limitations involving the undesired behavior of the film resistivity. Such a limitation affects the behavior of the film capacitance. Another limitation

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is the attainment of an unstable electrochemical structure that will affect the time required for measuring the capacitance. Remarkably, researchers have to avoid the two limitations by having critical strategies like establishing a means of close conducting the available pathways (Rahman 2009). It will be done by applying the blocking agents responsible for eliminating the drawbacks stated above. The blocking agents should be arranged to attain the desired results.

Another method that can be effectively employed in such a scenario will be to use the co-immobilization and blocking the molecules where the blocking agents like the mercaptoethanol are used. Furthermore, researchers suggested new blocking agents to effectively gain the results with the redox reactions of potassium ferrocyanide. The current blocking agents provide reliable results in the probe films for DNA detection than the ancient agents that could not assure reliability (Huang 2007).

Using diethanolamine improves the electrochemical stability. Critically, using the ssDNA probes and lipoate-diethanolamine brings a reduced number of grooves seen in figure B above. The figure shows diminished errors when carrying out the measurements. The detection errors in the event the DNA probes are made into ethylene films will be negligible. The capacitance value will be reduced by one magnitude when ethylene-glycogen is used because it has a long chain of molecules. Notably, the capacitance changes lead to the opposite when the probe immobilization occurs due to the existence of distinct amphiphilic characters within the glycol components than the methylene groups (Chen 2000). The below structure is established to create a general understanding of the differences between the ssDNA probes immobilized in the gold and the one immobilized into the ethylene-glycol mono-layer.

3. One Dimensional Nano-Structures Improving Enzyme Chips

A single dimensional system results from the placement of the two dimensions on the nano-scale such that the whole system will be built along with one of the given three spatial dimensions. A good example of the one-dimensional nano-structures is the carbon nanotubes containing the carbon allotropes with cylindrical shapes containing either a single or multi walls. The multiwalled carbon nanotubes may go to as long as 60 nm or more. Such a character makes them suit their role in the given space regions (McEuen 2002). The confinement of the particular carriers causes the formation of amazing structure below.

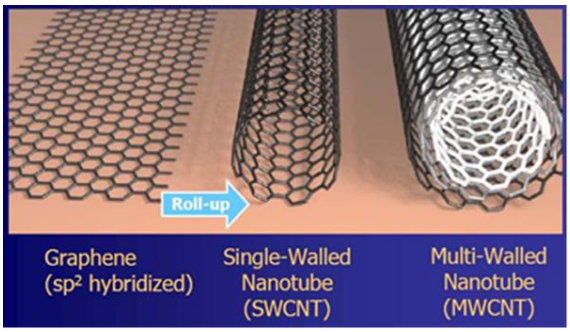

Fig. 1. 3. One dimensional nano-structures improving enzyme chips

The carbon nanotubes present in the maximum densities are used as sources for eliminating the linear fields under water molecule adsorption. The above properties aid in electron transfer to the enzyme probes with their sources placed in the biochip electrodes. Noteworthy, the enzymes, in this case, are protein in nature and transform the biochemical molecules through the redox reactions to facilitate the detection processes, hence an increase in its sensitivity (Kim 2001).

There is an improvement in case the enzyme detects benzenediamine. As stated earlier, the different isoforms have distinct substrates where there are exogenous compounds like the pharmacological drugs having many P450 proteins for catalyzing the various components available. Furthermore, the cytochrome may detect the already used anti-obesity drugs and inflammatory drugs. On the other hand, P450 11A1 helps in determining the cholesterol levels. Therefore, there is a variety of opportunities for biosensing applications when using the P450 enzymes. The sensitivity in the benzenediamine will be achieved by using the multi-wall carbon tubes. (Hone 1999). Similarly, oxidases may be used as the endogenous metabolites detectors because they speed up the redox reaction in the human metabolism with hydrogen peroxide as the end product. Hydrogen peroxide produced then releases the two electrons at the polarized electrodes used to detect the oxidase substrates. The hydrogen peroxide detection case causes an enhancement in the electron transfer until a two-magnitude order is attained. Moreover, there is a sensitivity improvement when the carbon nanotubes are used in the biosensors depending on the oxidases being applied at the given set up.

4. Zero Dimensional Nano-Structures Improving Enzymes Chip

It is a structure where the dimensions on the scale look like spaces where the particles are held, leading to the quantum dots formation. In contemporary nanotechnology, there are dots for fabricating the given particles using simple procedures and methods to ensure suitable outcomes (Wang 1998). There is a possibility of fabricating the nano-particles using the atom aggregation's physical processes by subjecting it to the liquid state. The Langmuir Blodgett films involve a mono-layer gained by pressing the amphiphilic particles to change the water into the solid substrate through the vertical dipping. By repeating the procedure, one will obtain multi layers of the arachidic acid used to develop the film's semiconducting nano particles (Riepl 1999). Aggregating the atoms into arachidic acid requires the hydrogen sulfide atmosphere, as seen in the figure below.

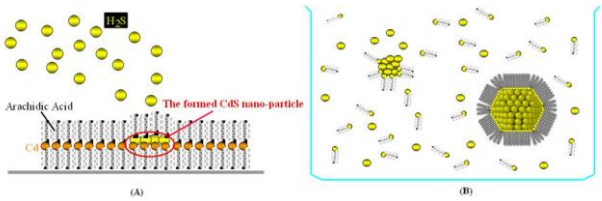

Fig. 2. (a) Hydrogen sulfide's role, (b) Role played by the alkanethiols

Fig. 2a above shows hydrogen sulfide's role in developing

the nano-particles having the semiconducting nature of the Langmuir Blodgett containing the arachidic acid. Sequentially, figure 2b shows the role played by the alkanethiols to have stable metallic nano-particles in the gold salts solutions (HAuCl4). The metallic nanoparticles may be obtained under the solvent conditions to acquire a nugget. Alkanethiols are added to the solution to eliminate the big particle formation. The alkyl develops an organic shell that will cover the solution to hinder the incoming atoms. Eminently, changing the salt - thiol ratio may determine the particle sizes (Radosavljevi 2001). The varying nano gold diameters are used in fabricating the particles while adjusting the ratio, as demonstrated in the figure below. The electron microscopy results reveal the image capped in the gold nano-particles having 5nm diameters. Simultaneously, the second structure shows the mass changes when the nanoparticles are forming under the influence of hydrogen sulfide in the Langmuir-Blodgett.

The above technique is regarded as the 'Brust method' where a scientist suggested an idea that could be essential in achieving the colloidal single gold nano-particles. The two methods above are critical in attaining a fast and low-cost fabrication in the zero-dimensional nano-structures. They are efficient because of using simple equipment as the expensive systems are avoided in such a case. The use of safe chemical protocols guarantees safety. The experiment will also take a short time to complete as the entire CDS particles are formed within thirty-five minutes. Removing the arachidic acid from the used solvents will provide semi-conducting particles (Carrara 2009). The electrostatic concept is applied in such a study to show that the small particles will be suitable for trapping the conducting carriers as the electrons can only be trapped when the electrostatic energy maintaining the electrons in dot form is greater than its heat. There is a possibility of dropping the electrons from their dots when the electrostatic energy holding them is small. Someone has to expect current suppression within the voltage curve for the bias voltages near the trapping event. There is a specific relationship between the electrostatic energy and the temperature leading to structure transformation (Zheng 2005). Therefore, the larger electrostatic energy arises from, the smaller dots making it easier to obtain the thermal excitation. From the two structures, one will note a first lower schematic curve in the staircase shape and the second curve having oscillations for charge trapping.

Charge storage will be enhanced by having the above carrier trapping. Similarly, the current transport and electron transfer will be boosted by the within the carriers. In the above setting, the gold nanoparticles will be used as the medium through which the electron transfer occurs between the electrodes and the cytochromes.

5. New Electrochemical Systems for Personalized Therapies and Cell Biology

Applying the drugs in the right amount is one of the critical strategies that can be put in place when personalized therapy is to be achieved. The process should be done by monitoring the disease progress, the victims' metabolism, and the drug efficacy (Carrara 2009). When measuring the biomarkers and drug concentration the biochips are made from the fully electronic capacitance technique to ensure reliability in every step taken towards detecting the molecular components. Some of the factors affecting the exercise include; low productivity and time drift. Therefore, there are changes in place to have proper resolutions from the nano-bio-science, like probe surfaces with the 2D glycol layers. Such structures will provide an improvement in the and portability of the devices in the cancer detection processes. Consequently, the concentration in the plasma's therapy values may vary based on the kind of drug being administered (Tsai 2007). There should be a strict measurement of the concentration range to have a successful bio-chip development for monitoring the drugs required in personalized therapy (Stagni 2006). Enzymes will be essential in catalyzing the chemical reactions; thus, new solutions must be considered when there is a need to have bio-chip sensitivity for the recommended drug concentration and electronic biochip development. Lactase and glucose will be the primary metabolites in the cellular metabolism where lactase is associated with cell suffering, and glucose is the cellular fuel. Nonetheless, the instrumentation required for carrying out the process is costly following the expensive equipment needed. Besides, the process is time-consuming, making it inappropriate because the spectrophotometer used in the experiment is unsuitable for real-time monitoring (Yang 2008). Off-line sample measurement will be relevant in such a scenario involving the colorimetric substrates. Another step that people have to adopt towards reducing the experimentation cost will be to use the many available oxidases and dehydrogenases that are naturally available for making the highly integrated sensors (Berggren 1998). Nowadays, integrating then enzymes is possible to create portable biosensors in diabetic patients to monitor and control the cell cultures.

6. Conclusion

In summary, the paper has exposed the multiple technologies necessary in developing the nano-structures where one, two, or three dimensions are made at the nano-scale. The nano-structures have new functionalities depending on the materials found on the respective scales. For instance, the ethylene-glycol two-dimensional nanolayers have amazing electrical properties that will ensure sensitivity enhancement. The zero-dimensional nanoparticles with metallic or semi-metallic features trap the carriers with the electric conduction capabilities when applied for the bio-detection functions. Importantly, nanotechnology has a significant contribution to the electrochemical system development to monitor cell biology and personalized therapy. Biological systems have to be improved by writing the information and doing something about it as far as scientific experiments are concerned. New opportunities will be identified in the biological field that will help determine the proper solution to problems affecting living organisms. It is worth noting that the nano-biotechnology provides several progresses that will enhance the growth of nano-bio chips with adequate control to have the working advantages considering that the current society requires much emphasis on the reliability, specificity, and applicability of the various modes of

disease detection and diagnosis.

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