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Review on CNTFET: Recent Developments in Biosensors for Health Care Applications

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Abstract: With the increasing use of high-performance component circuits (VLSI) in biosensing, there has been remarkable progress in the field of nanotechnology. The carbon nanotube is basically made of graphite sheets wrapped to form a tube-shaped structure, with a periodic boundary structure that makes a hexagon that never breaks. Carbon nanotube field-effect transistors (CNTFETs) have lower latency and power consumption compared to compatible CMOS devices, so they are considered a viable option to switch CMOS devices to VLSI circuits with very low power. Biomedical sensors have received a lot of attention in the field of health care. CNTFETs have a high potential to drive many technological advances in the industry due to their unique electrical structures of CNTs. In this review, we focus on the use of CNT-based FET (CNTFETs) in biomedical systems. It starts with the introduction of the device and discusses four applications where CNTFETs are used, namely covid-19, hearing aid, cholesterol, and cancer. Finally, we conclude the review with an overview of CNTFET in the medical field.
Keywords: Biosensing, Nanomaterial, CNTFET, Covid-19, Hearing aid, Cholesterol, and Cancer

I. INTRODUCTION

Nanotechnology is the latest technology that is gaining as much attention as it can be used to make advanced technology. It includes a variety of materials that are produced on a nano-meter scale using a variety of chemical and physical methods. This wide range of building materials makes it accessible to a wide variety of new magnetic, electrical, mechanical, or visual structures. Nanotubes are part of a promising group of nanomaterials.

We know that MOSFET is an integrated circuit that can benefit both electrical power and signal strength when the MOS capacitor plays an important role. It is a device that is controlled by the voltage of the gate, and its operation is based on the voltage used. In addition, its functions are based on the reduction mode and the device upgrade mode. But the biggest limit is process variability, short channel effect, hot carrier effect, and the high leakage current issues. CNTFET is a four-terminal device with each terminal, namely, source, suction, gate, and body. CNTFET is a transistor that operates in an environment that uses one or more carbon nanotubes as channels and replaces the bulk silicon as a standard MOSFET.

Biomedical sensors have attracted a lot of attention lately, and have a wide variety of applications in health care, environmental monitoring, food quality, and protection in [1]. This is because they react to certain chemicals or biological compounds and convert this information into electrical signals. Typically, a substance with high chemical reactions is used in chemical and biological sensors in [4]. Carbon nanotubes (CNTs) can be single or multiple layers of graphene sheets rolled to form tubes and combine lightweight benefits and have a complete hexagonal connection structure. The distinct electrical conductivity of CNT makes them useful for nanodevices. The CNTs are small at the atomic level to provide good electrostatic control over the channel so that there is no problem in reducing the size of the device. This small CNTs structure adds many benefits when used as a sensitive sensor in [14]. Compared to other technologies, CNTFET-based sensors have the advantages of high sensitivity, high selectivity, easy operation, low operating temperature, fast response speed, short recovery time, and good stability in [3]. With reference to their distinct visual capacity and function, CNTFETs are expected to play a key role in the nervous system.

II. CARBON NANOTUBE FIELD-EFFECT TRANSISTOR (CNFET)

CMOS has its own limitations such as leakage current, extreme short channel effects, high field effects and process variation. Some of the device parameters like bandgap (Eg) and built-in junction potential are material parameters and cannot be varied according to our needs. Also, the parameter like threshold voltage cannot be scaled due to considerations of leakage. Hence it makes the scaling of CMOS difficult and Moore's law cannot be accomplished.

CNTFET is a three terminal device similar to MOSFET as shown in Fig.1. It consists of substrate made of Si. It also consists of a layer of Silicon dioxide. The semiconducting channel between the two terminals drain and source consists of carbon nanotubes. The channel is turned ON/OFF electrostatically via gate.

A portion of CNT in the channel region is intrinsic. The source and drain terminal are doped heavily with n+ or p+ dopants depending on the type of device structure. The threshold voltage (Vth) of the CNFET is a function of the bandgap of the nanotubes, which in turn can be adjusted by proper selection of the orientation of the CNT graphene sheet.

CNTFETs can be classified according to current injection methods: Schottky barrier CNTFETs (SB-CNTFETs) are made of metal electrodes to form Schottky contacts, and CNTFETs used with doped CNT electrodes to form Ohmic contacts (similar to the MOSFET design). The type of contact determines the current transport mechanism and CNTFET output characteristics. In SB-CNTFETs, the current means tunnelling of electrons and holes from the potential barriers at the source and drain junctions. The barrier width is controlled by the gate voltage, which thus controls the current. The Ohmic contact CNTFET type uses the n-doped CNT as the contact. The doped source and drain regions behave just like MOSFETs. A potential barrier is formed in the centre of the channel, and the current is controlled by a variable height barrier (control voltage of the gate).

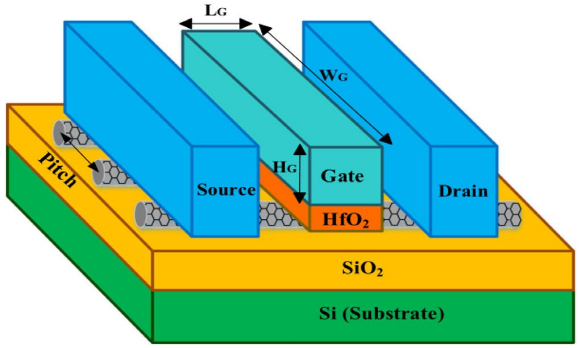


Fig.1 Structure of a CNFET using multiple CNT in the channel region

III.APPLICATIONS

A. Carbon nanotube field-effect transistor (CNTFET)-based Bio-sensor for Covid-19 detection

1) *Rapid Detection of SARS-CoV-2 Antigens Using High-Purity Semiconducting Single-Walled CNTFET*: Early detection of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is essential to facilitate appropriate containment and treatment procedures in [5]. By using high-purity semiconducting single-walled carbon nanotube (SWCNT) -based field-effect transistors (FET) with certain binding chemicals we can detect the presence of SARS-CoV-2 antigens in nasopharyngeal clinical samples. These SWCNT FET sensors, which activate the anti-SARS-CoV-2 spike protein antibody (SAb) and anti-nucleocapsid protein antibody, detected S antigen (SAg) and N antigen (NAg), reached the detection limit 0.55 fg / mL of SAg and 0.016 fg / mL of NAg in measurement samples. SAb's efficient FET sensors also demonstrated sensory efficacy in discriminating positive or negative clinical samples, indicating evidence of a system that could be used as a diagnostic tool for COVID-19 antigen because of its high sensitivity for analysis and low cost. This is a SARS-CoV-2 antigen (Ag) FET nano biosensor with high-purity semiconducting single-walled carbon nanotube (SWCNT) that works with a specific antibody to achieve the existence of two SARS-CoV-2 structural proteins: spike (S antigen, SAg) and nucleocapsid protein (N antigen, NAg) (Fig. 2). In addition, SWCNT is much cheaper and more widely available than chemical vapor deposition graphene films, thus reducing SWCNT FET sensor costs. Proper comparisons of Nucleic Acid Amplification Test with SARS-CoV-2 Ag FET machine have shown effective differentiation between positive and negative samples, which enhances their potential for COVID-19 diagnosis in [13].

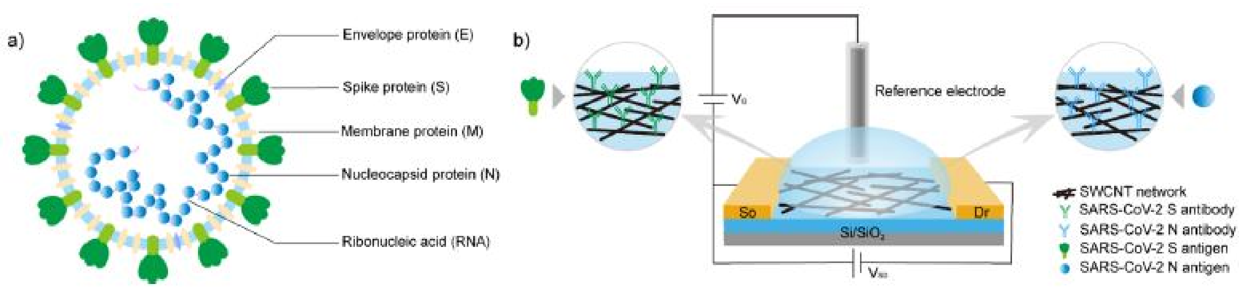
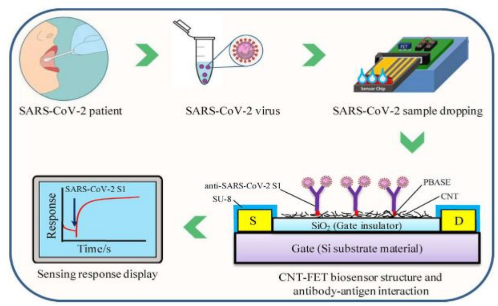


Fig.2 Detection of SARS-CoV-2 Ag using SWCNT-based FET biosensors. (a) Schematic structure of SARS-CoV-2 to demonstrate targeting proteins. (b) Schematic illustration of a liquid-gated SWCNT FET for detection of SARS-CoV-2 SAg and NAg.

2) *Rapid Detection of SARS-CoV-2 surface Spike Protein S1 using CN FET Based Biosensor:* Here we discuss a biosensor, easy to use, low cost, and electrochemical value based on carbon nanotube field-effect transistors (CNT-FET) that allows digital SARS-CoV-2 S1 detection quickly (that takes 2-3 minutes) and accurately in [15]. This is enhanced in the Si/SiO2 field by CNT printing with the inclusion of anti-SARS-CoV-2 S1 in [12]. The SARS-CoV-2 S1 antibody does not move in the CNT area within the S-D channel area using the 1-pyrenebutanoic acid succinimidyl ester (PBASE) link by non-covalent interaction. So, the SARS-CoV-2 S1 commercial antigen can be used to demonstrate the electrical output of the CNT-FET biosensor. SARS-CoV-2 S1 antigen at 10 mM AA buffer pH 6.0 was successfully detected by CNT-FET biosensor at concentrations from 0.1 fg / ml to 5.0 pg / ml. The limit of detection (LOD) of the developed CNT-FET biosensor was 4.12 fg/ml. The biosensor showed high selectivity (no response to SARS-CoV-1 S1 or MERS-CoV S1 antigen) with SARS-CoV-2 S1 antigen detection in the 10 mM AA buffer pH 6.0. The biosensor is very sensitive, time-saving, and can be a useful platform for quickly detecting the SARS-CoV-2 S1 antigen in a patient's saliva. The Fig.3 displays the steps involved in the process. SWCNT as a sensing nanomaterial and anti-SARS-CoV-2 S1 immobilized on the CNT via PBASE (linker). The CNI-FET biosensor senses the SARS-CoV-2 spike protein based on the corresponding effects on the electrical signal properties. It starts from device fabrication then the fabricated FET is soaked in PBASE and washed in the sensing area to remove unbound excess PBASE. In the next step, the antigen sample is prepared and tested. Also, CNFET biosensor selectivity is measured and then SARS-CoV-2 S1 fortified saliva is prepared and electrical response is measured.



Scheme 1. Schematic diagram of CNT-FET biosensor and SARS-CoV-2 S1 testing steps. SWCNT as a sensing nanomaterial and anti-SARS-CoV-2 S1 immobilized on the CNT via PBASE (linker). The CNT-FET biosensor sense the SARS-CoV-2 spike protein based on the corresponding effects on the electrical signal properties.

Fig.3 Schematic diagram of CNTFET biosensor and SARS-CoV-2 S1 testing steps.

B. *Hearing Aid*

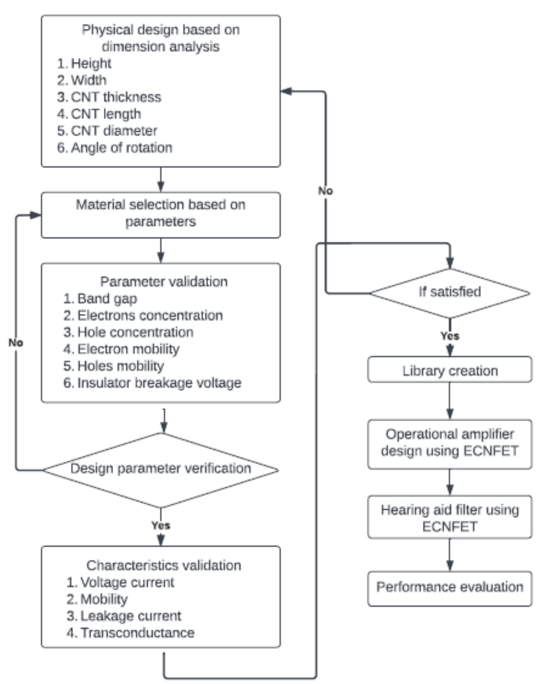


Fig. 4 Flowchart of CNFET based hearing and filtering application

Initially, the structure was designed in 10 layers based on a certain size, and different materials were placed in each layer. It includes gold, silicon, silicon dioxide, bismuth telluride, and carbon tube. Then, parameters such as bandgap, concentration of electron, concentration of hole, electron mobility, hole mobility, and insulator breakage voltage are verified to determine the efficiency of the structure in [2]. When all the parameters are satisfied, the characteristics such as voltage current, leakage current, mobility, and transconductance are verified. Once all the steps are satisfied, the library is created for ECNFET design. In addition, the operational amplifier is designed based on the function of the library function. After amplification, the hearing aid filter is designed using the proposed ECNFET structure.

Here, five different materials such as gold, silicon, silicon dioxide, bismuth telluride, and single walled carbon nanotube are placed in the layers. After selecting these materials, the parameters are verified. As shown in Fig. 4, once all the parameters are satisfied, the characteristics of the layout are validated for proving the performance of the proposed design. It includes voltage current, transconductance, mobility, and leakage current, which are all satisfied; the library is created for the ECNFET layout. Thereafter, the operational amplifier is designed based on the generated library function, which is used to improve the level of frequency. Finally, the hearing aid filter is implemented with the use of ECNFET layout that improves the accuracy by efficiently reducing the noise. The experimental results test the performance of this application based on various performance parameters such as area consumption, power consumption, frequency range, and speed. The proposed ECNFET-hearing aid filter provides better performance in drain voltage, current, threshold voltage, and mobility compared to the existing layout designs.

C. Diagnosis of Prostate Cancer Based on CNTFET

Cancer can be detected by biosensors based on carbon nanotube field effect transistors (CNT-FET). CNTFETs can be used to diagnose cancers in [9]. CNTFET can be used as a biosensor to diagnose cervical cancer in [10], to increase the sensitivity of the response. A system containing the CNTFET in series can be used, by comparing the response obtained from a standard analyte with cancer analyte, intensity of the cancer-causing agent can be analysed and the current flow variation is consistent with the severity of the cancer cell in the analyte.

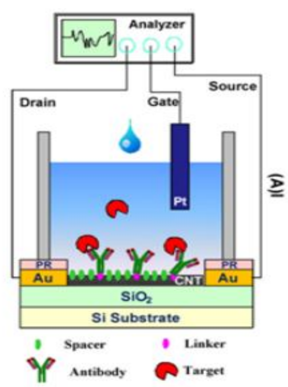


Fig. 5 Cross-section schematic diagram of the experimental setup for real-time PSA-ACT complex sensing.

Prostate-specific antigen (PSA), a glycoprotein comprising 93% peptide and 7% glucose, which is specially produced by prostatic tissue, is the best serum maker currently available for the detection and treatment of prostate cancer. PSA-ACT as shown in Fig. 5 is the predominant form of PSA complex in [8]. PSA-ACT and f-PSA (free form) two molecules, by comparison, can be used to treat prostate cancer. In normal cases, the concentration of PSA in human serum will be less than 4.0 ng/ml, while cancer should be present if it is more than 20 ng/ml. A range of 4.0 to 20 ng/ml is considered a “gray dose” in which additional medical examinations should be performed before the disease can be detected. Therefore, PSA dosage tests are highly recommended by doctors to diagnose, or monitor prostate cancer in [11]. CNT-FETs are modified under various molar concentrations of linkers to spacers so that the charged proteins can be easily approached. CNT-FET modified with a linker to spacer can effectively suppress unintentional proteins and obtain by selecting a targeted protein in a mixed environment that contains a high concentration of human serum. This strategy has enabled the development of CNT-FET biosensor systems based on a well-established antibody response antibody. Modification of CNT location by spacers has few advantages for CNT-FET-based biosensors. First, all antibodies designed for the diagnosis can be used to construct CNT-FET biosensors.

D. CNTFET for Cholesterol Detection

The importance of cholesterol in human metabolism is well known that high cholesterol levels lead to heart problems that can lead to high blood pressure and hypotension. Therefore, there is always a growing need for the development of new ways to measure simple, fast, and reliable quantification of cholesterol. Determination of the level of cholesterol in the blood serums helps in the diagnosis and treatment of various heart diseases, liver diseases and type 2 diabetes. The normal level of cholesterol in a person's serum should be between 130-260 mg/dL.

To measure cholesterol, ChOx has been immobilized covalently on the sensing layer PPy / K / CNT nanocomposite. Carbon nanotube-based nanocomposite has been used due to its unique and attractive properties. Due to its excellent electronic features and structure in addition to its excellent compatibility with high k dielectrics, CNT could soon replace silicon. Carbon nanotubes provide high surface area and loading capacity of enzymes while at the same time maintaining enzyme activity in [6]. It also has an amazing ability to mediate rapid charge transfer between biomolecules and transferable elements. Alkali metal potassium (K) and conducting polymer of pyrrole are added to improve the conduction and dispersion of nanocomposite properties for better reaction time and extraction time. ChOx promotes the conversion of cholesterol into Cholest-4-en-3-one and H_2O_2 Eq. 1 and 2 show the reaction of the enzyme and the sensitive layer of cholesterol ENFET.

$$\mathrm{Cholesterol} + \mathrm{O_2} \xrightarrow{\mathrm{ChOx}} \mathrm{Cholest} - 4 - \mathrm{en} - 3 - \mathrm{one} + \mathrm{H_2O_2} \ldots (1)$$

$$H_2O_2 \xrightarrow{Electrode} O_2 + 2H^+ + 2e^- \ldots (2)$$

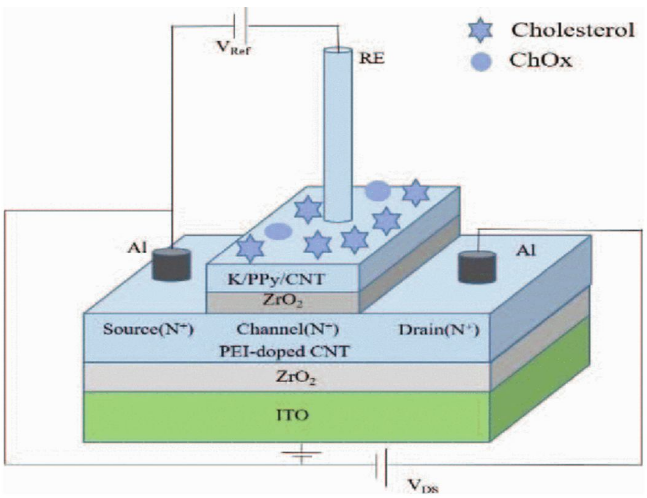


Fig. 6 CNT-based FET for detection of cholesterol.

It consists of a 3-electrode system with a reference electrode Ag / AgCl, a platinum electrode and an active electrode (ITO substrate). The thickness of the covered layer is measured using a gravimetric analysis method. CNT is made in the form of n by infusing it with ~30-40% PEI (polyethyleneimine). PEI doped CNT prepared by mixing CNT and PEI / methanol in equal doses and stored in a sonicator for about 20 minutes for the distribution of CNT particles. The sonicated CNT hybrid layer is applied to the ZrO2 protective layer through a spin coating process using a flexible spin coupling system (spinNXG-P2H). The ZrO2 layer is fitted with ECD to the channel position that acts as the top gate protector in [7]. A high K / PPy / CNT / ChOx sensor layer is inserted into insulating ZrO2 with spin coating. The formation of ENFET cholesterol is shown in the Fig. 6.

IV. CONCLUSIONS

Strong advances in interfacing novel nanomaterials, CNTs, and biological materials can enable significant advances in biomedical applications such as the diagnosis and treatment of diseases. Key elements in the development of active biosensors are high sensitivity and simplification of the treatment process in advance. CNT FET-based biosensors can be developed as a reliable, fast and inexpensive method of existing diagnostic techniques. Technological advancement has led to much more scientific research, it can be found that CNTFETs could be a better alternative to conventional CMOS in terms of its high performance and small size. Structures such as excellent network company flow, high dielectric position, ballistic conduction, channel length, transconductance, heat dissipation and threshold voltage play an important role.

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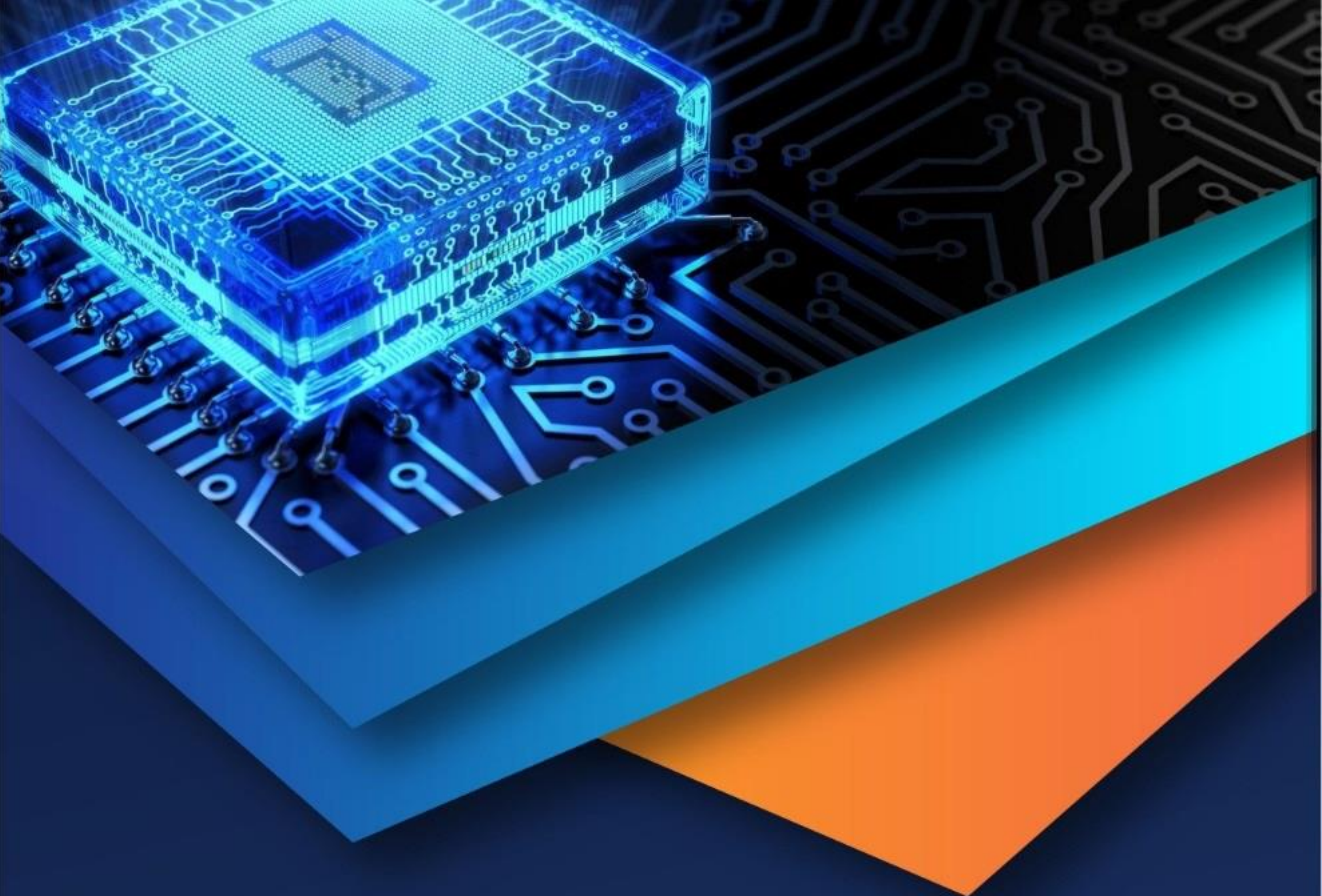

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