Rapid Detection of COVID-19 Using Transistor-based Biosensors

ECE 730 (Biosensing: Fundamentals and Applications) Final Project

Jessica Chong
20715446
Winter 2023

1.0 Introduction

COVID-19 is a fast-spreading airborne virus that has triggered a global pandemic. To curb the spread of the virus, a low-cost and rapid ultraprecise detection method for on-site and point-of-care molecular testing has become an increasing need. WHO issued a guideline stating the most suitable diagnostic tests must be ASSURED, that is, affordable, sensitive, specific, user-friendly, rapid/robust, equipment-free, and deliverable to end users [1]. Current testing procedures use a quantitative reverse-transcription polymerase chain reaction (qRT-PCR) technique. However, this procedure alone takes over 2 hours to process and requires samples to be tested using complex laboratory equipment and skilled personnel to operate [2]. Because of their potential for label-free, real-time sensing with small sample volume requirements and their flexible integration options and mass producibility, transistor-based biosensors are attractive biochemical sensing platforms [3], [4]. This project report aims to describe a brief literature review of a few different transistor-based biosensors for rapid COVID-19 detection. The report will be organized as follows: the literature review in section 2, the current challenges in the field in section 3, an opinionated future research direction in section 4, and final conclusions in section 5.

2.0 Literature Review

2.1 Transistors

A transistor is a semiconductor device that can be thought of as a switch or a voltage controlled current source [5]. Typical field-effect transistors (FETs) are three-terminal devices where the terminals are conventionally referred to as the source, drain, and gate on top of a substrate [6]. A semiconductor is found between the source and drain terminals, and a dielectric material sits between the gate and semiconductor. An applied gate voltage polarizes the immobile dipoles in the dielectric, inducing an electric field causing holes to accumulate at the interface between the semiconductor and dielectric, a process known as doping in semiconductor physics [6]. By placing a sample under test over the sensing channel and varying the gate voltage, changes in the channel current due to specific targets are monitorable [4]. This change in the channel current with respect to the gate voltage is called transconductance and describes the amplification of the gate voltage signal [6]. Transistors with high transconductance are attractive voltage amplifiers in various applications such as chemical and biological sensors in the medical industry that require low power [7]. The high sensitivity, wide dynamic range, and excellent limit of detection (LoD) make transistors great candidates in biosensing [8].

An important component to a FET is the semiconductor material that the sensing channel is comprised of [4]. Some examples of popular nanomaterials used in designing FET-based biosensors for rapid COVID-19 detection are graphene [9], [10], [11]; silicon nanowire (SiNW) [3]; and carbon-nanotubes (CNT) [12] – each material with its own advantages and disadvantages. A lesser-known nanomaterial that has been studied in COVID-19 detection is tungsten diselenide (WSe_2) [13]. Organic electrochemical transistors (OECTs) were developed in the early 80s but have become more popular in recent years [14] and applied to COVID-19 detection [7]. Instead of using a dielectric, transistor-based biosensors usually use an electrolyte solution since biosensors mainly operate in liquid environments [9]. Since the transistor only provides the sensing platform, the device requires receptors or linkers to be immobilized to the surface of the semiconductor material to bind to target analytes or viral proteins [4]. This is achieved through using aptamer probes and antibodies selected to detect the target analyte or spike protein in the sample under test [4]. It is possible to detect other diseases by functionalizing the device to target those specific viral proteins, an example demonstrating the flexibility of transistor-based biosensors.

2.2 Graphene Field Effect Transistors

Graphene is a popular nanomaterial first introduced in 2004 by Geim and Novoselov, nearly 20 years ago. It exhibits extraordinary physiochemical properties including a high electronic conductivity, high carrier mobility, and a large 2D planar surface [9], [3], [10]. Due to their ultra-fast charge transport, GFET response times are nearly instantaneous, making them highly attractive nanomaterials for real-time monitoring and detection applications [1], [4]. The limit of detection of GFET biosensors typically fall between pico-molar to femto-molar, but it may be possible to even detect atto-molar concentrations [9]. Thus, GFET biosensors are capable of ultraprecise detection while operating with ultra-low noise [10], [15]. However, GFETs suffer from a lack of band gap [4] attributed to its massless electrons, a trait that increases power consumption because a zero-band gap makes the devices difficult to turn off [15]. False signals could also arise from current leakage while the device is off [13]. There is a tremendous effort in the scientific community in studying graphene and GFETs. Using them in biosensing and disease detection applications has been an increasing trend.

GFETs (graphene FETs) integrated with molecular electromechanical systems (MolEMS) for the direct testing of COVID-19 samples were studied in [9] by Wang et al. The MolEMS were comprised of a self-assembled double-stranded DNA tetrahedral base immobilized to the surface of the graphene and a single-stranded DNA acting as a cantilever link to the aptamer probe. The goal of the MolEMS was the bio-recognition process – detecting target analytes and linking to them [9]. Upon the application of a negative gate voltage, they would bend downwards, bringing the target analytes closer to the sensing channel of the GFET, which converts the chemical or biological sensing responses into electrical signals [9], [16]. The probes were functionalized to target SARS-CoV-2 RNA or reverse-transcribed complementary DNA for the ORF1ab gene [9]. Without the need for labelling or amplifying a sample, it allows samples to be tested directly using the device in their current medium. Wang et al. demonstrated the simple operation of the device with sample readings in less than 4 minutes. Furthermore, a prototype of the device was made for on-site and point-of-care testing, that would be connected to a smartphone or computer for results using a USB, wifi, or Bluetooth. This prototype was used for clinical sample testing and demonstrated high sensitivity towards diluted samples and was able to differentiate between healthy volunteers and COVID-19 infected volunteers perfectly.

Another study using GFETs was conducted in [10] by Seo et al. using SARS-CoV-2 antibodies to detect SARS-CoV-2 spike proteins. The antibodies were immobilized onto the surface of the graphene using a probe linker, 1-pyrenebutyric acid N-hydroxysuccinimide ester (PBASE). The authors demonstrated the biosensor was capable of detecting SARS-CoV-2 spike proteins at a concentration of 100 gf/mL in a diluted universal transport medium (UTM). It was determined that no sample preparation or preprocessing was required before testing the sample with the device. The authors also demonstrated the potential real-time detection of the virus by testing cultured SARS-CoV-2 cells. When the cultured cells were added to the device, there was a signal response for concentrations at 1.6×10^1 pfu/mL. Clinical samples were tested as well, where the device was able to accurately differentiate between healthy patients and those who were positive with COVID-19.

2.3 Silicon Nanowire Field Effect Transistors

Silicon nanowire is a mature technology in the semiconductor industry with high sensitivity and mass producibility [4], [17]. It is commonly found in modern-day microelectronic devices and is a more mature field of study compared to graphene and tungstein diselenide nanomaterials [17]. Unfortunately, even with its mature fabrication processes, it suffers from device-to-device variation in manufacturing [4]. Silicon nanowire FETS (SiNWFETs) have high surface-volume ratios, large dynamic range [18], but a low electron carrier mobility [4]. These FETs have a limit of detection in the femto-molar concentration range. Additionally, SiNWFETs possess novel electronic and optical properties that depend on that depend on the morphology, wire growth direction, and band gap depending on diameter size [19]. Like other transistor-based biosensors, SiNWFETs are prone to false positive results [17].

Wasfi et al. proposed a SiNWFET for COVID-19 detection in [17] and was the first paper to develop a proof of concept of this device for this application. Unlike the other papers mentioned in this project report, the authors took a slightly different approach to studying the sensor configuration and application. Other papers had a fabricated device and experimental results, either with clinical samples or with purchased spike proteins. However, Wasfi et al. took a semiempirical modelling approach using the Quantumwise Atomistix ToolKit (ATK) with Virtual NanoLab (VNL) for simulations. A model of the SiNWFET was built in the software and was coated with the SARS-CoV-2 antibody to target the SARS-CoV-2 spike proteins. After studying the current variation, conductance, and transmission spectra through simulated results, they concluded that the designed sensor in the software should be capable of detecting the viral proteins belonging to the target virus, if the sensor were to be fabricated.

2.4 Tungstein Diselenide Field Effect Transistors

Tungsten diselenide is a member of the family of semiconducting two-dimensional (2D) transition metal dichalcogenides (TMDCs) are considered "beyond graphene" and exhibits a small, but non-zero band gap [13], [20]. In comparison to graphene, WSe_2 has a 1.67 eV band gap, allowing it to exhibit a smaller off-state current leakage and improved signal-to-noise ratios, while maintaining high sensitivity and high carrier mobility [13]. However, they also exhibit ambipolar transistor behaviour where they can conduct both electrons and holes, which are great for CMOS circuits, but comes with its disadvantages [20]. To address this issue, researchers are studying various dopants that can be used to achieve polarity control [20]. WSe_2 FETs also experience higher off-state current leakage compared to traditional unipolar FETs [20].

Fathi-Hafshejani et al. fabricated a monolayer WSe_2 FET device with interdigitated electrodes to detect SARS-CoV-2 spike proteins in [13]. A chemical linker, 11-mercaptoundecanoic acid (MUA), was added to the surface of the WSe_2 to act as a probe linker and then activated with n-hydroxysuccinimide (NHS) and carbodiimide hydrochloride (EDC) solution. To functionalize the device for SARS-CoV-2 spike proteins, the SARS-CoV-2 antibody was immobilized on the sensing surface through the MUA. Being a not yet well-developed technology, no clinical tests were done, and all the SARS-CoV-2 spike proteins and antibodies were purchased from a biotech company. The authors demonstrated that the device was capable of real-time readings. When performing the experiment, they were able to obtain instantaneous results when adding spike protein droplets to the sensing channel. One challenge of this work was the device-to-device variation, because the fabrication of the WSe_2 nanosheets had a lack of growth monitoring and control. Due to this aspect, the authors were unable to provide the standard deviation or accuracy for each of the measurements.

2.5 Organic Electrochemical Transistors

An organic electrochemical transistor, or OECT, is one of the two types of organic thin-film transistors. The other transistor is an organic field effect transistor, or OFET [7]. In comparison to traditional metal oxide semiconductor FETs (MOSFETs), OECTs contain a conducting polymer instead of a semiconductor one and uses an electrolyte solution instead of a dielectric [21]. Because electrolyte solutions are comprised of mobile ions, applying a gate voltage causes ions to be driven into the conducting polymer channel, which in turn causes holes to accumulate throughout the semiconductor film [6]. This feature gives rise to the high gate-channel capacitance of OECT devices, leading to high transconductance and slow device operation [6]. OECTs also require complex sensor designs and the operation needs to be in a tightly controlled environment [7]. Albeit its disadvantages, they have a promising future in low power medical applications thanks to their low operating voltages [7].

Guo et al. examined the application of OECT devices for rapid COVID-19 detection in [7] and was the first paper to implement the SpyCatcher/SpyTag protein conjugation system in a biosensor. They proposed two OECT devices, one operating in depletion mode with a poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS) channel and the other operating in accumulation mode with a conjugated polymer, p(g0T2-g6T2), channel. This paper was also the first to use an OECT device in accumulation mode. The SpyTag/SpyCatcher protein conjugation system is sometimes termed as "molecular superglue". The nanobody-SpyCatcher protein links to the coat proteins of the spike virus while binding with the SpyTag peptide that is immobilized to the 1,6-hexanedithiol self-assembled monolayer on the surface of the disposable gold gate electrode. The gate electrode was placed over the reusable transistor base consisting of a phosphate-buffered saline (PBS) solution as the electrolyte solution. Between the two devices, it was shown that the accumulation mode using the conjugated polymer had improved sensitivity over the PEDOT:PSS device operating in depletion mode. Guo et al. demonstrated quick device operation of about 10 minutes of sample incubation time and a reading in 15 minutes. The authors believe that real-time measurements may be achieved by integrating the biosensor with microfluidics.

3.0 Current Challenges

There are several current challenges in the general field of transistor-based sensors for biological and chemical sensing applications, not specifically to the detection of COVID-19. WHO has issued a guideline as previously mentioned, but it is difficult to commercialize the transistor-based biosensors due to the miniaturization process and the device-to-device variation [22]. Other issues and challenges have been mentioned throughout the literature review when giving a brief overview some different materials used in the sensing channel of these transistor-based devices. This section will summarize the challenges faced in COVID-19 testing and the challenges of commercializing transistor-based biosensors for the current market.

The main challenge to COVID-19 diagnosis is the slow test time using PCR tests, because it requires a lengthy sample preparation time and complicated testing procedure [2]. Since the start of the pandemic, there has been worldwide effort to determine a testing method that could be used for on-site and point-of-care testing. Detecting targets directly in unaltered and unamplified biofluids are a challenge and most biosensors are unable to detect them with ultraprecise sensitivity. This is because background noise is generated from the crowding of nonspecific proteins, nucleic acids, and background biomolecules over the sensing interfaces [9]. In this aspect, Wang et al. in [9] have demonstrated that their fabricated device had an anti-fouling layer created from their immobilized MolEMS, keeping unwanted molecules away from the sensing surface so that they did not interfere with the FET channel and sensing performance. However, this could remain a challenge for other transistor-based devices as different sizes and concentrations of biomarkers could affect the sensing performance of the device [23]. Other works such as in [13] and [17] did not demonstrate the device for clinical testing and human swab or saliva samples, which could be drastically more challenging to analyze.

As mentioned in the literature review, although silicon-based transistors are a more mature technology, there are newer technologies, such as carbon-based transistors (e.g. GFETs, CNTFETs) and organic devices, that compete with silicon for sensitivity and speed. A summary between SiNWFET and GFET biosensor performance can be found in [23], where GFET biosensors are capable of a wider dynamic range, improved sensitivity, and better limits of detection than SiNWFET biosensors. Although GFETs are promising technologies, they have their own limitations as previously described. Because of their zero-band gap, they are prone to off-state current leakage and increased power consumption [4], which would be the opposite of the cost-effective device sought for. Therefore, the field of TDMCs are being extensively studied to produce materials that provide similar properties as graphene, but with a tunable band gap structure [20]. Unfortunately, being newer and immature technologies, TDMC-based FETs have their own challenges, requiring different dopants and fabrication strategies [20]. All the presented devices are should minimize undesirable current leakage to prevent false positive responses.

One challenge with transistor-based biosensors is the size of the specific surface area, which is required for improving the sensitivity of the device [22]. According to [22], there is work done on using silicon nanoribbon structures instead of nanowire structures to increase the sensing area of the device. The high sensitivity of graphene can be attributed to its large 2D planar surface, again making it a competitive candidate to the mature silicon-based technologies. Another challenge is device-to-device variation and possible defects or damages during the fabrication process [22]. Having as small of a device-to-device variation as possible will ensure proper sensing performance across all the fabricated devices, which requires new innovative fabrication techniques largely guided through simulations [22]. Lastly, the device miniaturization process would also be a challenge because it requires the emerging ultra-large-scale integration (ULSI) technologies compared to the current very large-scale integration (VLSI) ones [22]. Even if the device was miniaturized, thermal stress, power dissipation, and current leakage all degrade the device performance and reliability [22]. Therefore, when designing a device for commercialization, there are many factors to take into consideration. Across all the literatures mentioned in this project report, many share the same perspective that transistor-based biosensors will become the next generation of biosensors due to their promising advantages.

4.0 Future Research Directions

From the presented works in the literature review, some authors mentioned that there would be importance in conducting a quantitative COVID-19 diagnosis, rather than a qualitative one. For example, the work conducted by Guo et al. in [7] mentioned their device could only tell if a sample was positive or negative. Their device was unable to determine the exact concentration of viral proteins in a sample under test, and they determined that there was no extractable correlation between the concentration and the signal responses, besides the evident positive or negative diagnosis. They believe that if they were to optimize the device further, their device would be able to provide quantitative readings. On the other hand, in the work presented by Wang et al. in [9], they determined that there was a correlation between signal response and the cycle threshold of the SARS-CoV-2 swab samples. I think the next step in these works would be a proof-of-concept study showing that the devices are capable of quantifiable readings. In current rapid COVID-19 antigen tests, the readings give us a negative or positive reading. In terms of rapid testing, the qualitative readings of the devices may be enough. For other applications, it may be beneficial to give a numeric value upon testing. This may be achieved through implementing a machine learning algorithm to classify a signal response to a concentration or cycle threshold value if there is a direct correlation.

Although it has not been discussed in this report, aluminum gallium nitride (AlGaN) and gallium nitride (GaN) high electron mobility transistors (HEMTs) provide higher efficiency, better output power, and improved power density compared to conventional silicon technologies [24]. In comparison to graphene and other TMDCs, they have a wideband gap [25] which could possibly account for the disadvantages of graphene. Unfortunately, like other technologies AlGaN/GaN HEMT technologies are prone to self-heating and performance degradation occurs if its internal temperature surpasses 200°C [24]. Majority of AlGaN/GaN research efforts have been in high frequency, high voltage, and high switching applications. Thriveni and Ghosh in [22] also propose AlGaN/GaN HEMTs as a potential future research direction in biosensing. A major disadvantage to AlGaN/GaN HEMT technologies is that they are extremely expensive, and the end device may not be affordable for the average user. If there is a way to cheaply fabricate and lower the costs of material of these devices, applying them for the case of biosensing may be an interesting future research direction.

In the next generation of transistor-based biosensors, there may be an emerging path in integrating them with internet-of-things (IoT) for remote and wireless real-time monitoring applications. Wang et al. [9] have presented a prototype that is capable of wifi or Bluetooth connection, which could be a great initial start to integrating these new emerging technologies together. Through integrating, it may be possible to create a decentralized healthcare and detect the dynamics of disease spread and herd immunity regions [2]. There could also be a smart system, which tells users that there was a COVID-19 infected individual or individuals near them, this way people are more up to date with the virus spread.

5.0 Conclusion

In conclusion, a literature review of different transistor-based biosensors for COVID-19 has been presented, along with the advantages and disadvantages of using different nanomaterials, and the need for new technologies. The fabricated devices presented in the literature survey all demonstrate a high sensitivity and selectivity, a wide dynamic range, and rapid measurements with minimal sample preparation, all in accordance with the guidelines issued by WHO. The reported results in the works suggest that the sensors have a qualitative performance comparable to PCR testing. The devices are highly integrable with other technologies such as microfluidics or other electronic devices and have the flexibility to be functionalized for the ultraprecise detection of other diseases. The challenges of detecting COVID-19 and device miniaturization have been discussed. Machine learning algorithms to quantify signal responses to numeric results, the use of AlGaN/GaN HEMT devices for biosensing, and device integration with IoT technologies have been proposed as possible future research directions.

References

[1] J. Sengupta and C. M. Hussain, "Graphene-based field-effect transistor biosensors for the rapid detection and analysis of viruses: A perspective in view of COVID-19," *Carbon Trends,* vol. 2, January 2021.

[2] E. Morales-Narvaez and C. Dincer, "The impact of biosensing in a pandemic outbreak: COVID-19," *Biosensors and Bioelectronics,* vol. 163, May 2020.

[3] S. Wang, X. Qi, D. Hao, R. Moro, Y. Ma and L. Ma, "Review--Recent Advances in Graphene-Based Field-Effect-Transistor Biosensors: A Review on Biosensor Designing Strategy," *Journal of The Electrochemical Society,* vol. 169, February 2022.

[4] C.-A. Vu and W.-Y. Chen, "Field-Effect Transistor Biosensors for Biomedical Applications: Recent Advances and Future Prospects," *Sensors,* vol. 19, no. 4214, October 2019.

[5] R. Pethig and S. Smith, Introductory Bioelectronics for Engineers and Physical Scientists, John Wiley & Sons, Ltd, 2013.

[6] J. T. Friedlein, R. R. McLeod and J. Rivnay, "Device physics of organic electrochemical transistors," *Organic Electronics,* vol. 63, pp. 398-414, September 2018.

[7] K. Guo, S. Wustoni, A. Koklu, E. Díaz-Galicia, M. Moser, A. Hama, A. A. Alqahtani, A. N. Ahmad, F. S. Alhamlan, M. Shuaib, A. Pain, I. McCulloch, S. T. Arold, R. Grünberg and S. Inal, "Rapid single-molecule detection of COVID-19 and MERS antigens via nanobody-functionalized organic electrochemical transistors," *Nature Biomedical Engineering,* vol. 5, pp. 666-677, July 2021.

[8] A. K. Mia, M. Meyyappan and P. K. Giri, "Two-Dimensional Transition Metal Dichalcogenide Based Biosensors: From Fundamentals to Healthcare Applications".

[9] L. Wang, X. Wang, Y. Wu, M. Guo, C. Gu, C. Dai, D. Kong, Y. Wang, C. Zhang, D. Qu, C. Fan, Y. Xie, Z. Zhu, Y. Liu and D. Wei, "Rapid and ultrasensitive electromechanical detection of ions, biomolecules and SARS-CoV-2 RNA in unamplified samples," *Nature Biomedical Engineering,* vol. 6, pp. 276-285, March 2022.

[10] G. Seo, G. Lee, M. J. Kim, S.-H. Baek, M. Choi, K. B. Ku, C.-S. Lee, S. Jun, D. Park, H. G. Kim, S.-J. Kim, J.-O. Lee, B. T. Kim, E. C. Park and S. I. Kim, "Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor," *ACS Nano,* vol. 14, no. 4, pp. 5135-5142, April 2020.

[11] X. Zhang, Q. Qi, Q. Jing, S. Ao, Z. Zhang, M. Ding, M. Wu, K. Liu, W. Wang, Y. Ling, Z. Zhang and W. Fu, "Electrical probing of COVID-19 spike protein receptor binding domain via a graphene field-effect transistor".

[12] M. Thanihaichelvan, S. N. Surendran, T. Kumanan, U. Sutharsini, P. Ravirajan, R. Valluvan and T. Tharsika, "Selective and electronic detection of COVID-19 (Coronavirus) using carbon nanotube field effect transistor-based biosensor: A proof-of-concept study," *Materials Today: Proceedings,* vol. 49, pp. 2546-2549, 2022.

[13] P. Fathi-Hafshejani, N. Azam, L. Wang, M. A. Kuroda, M. C. Hamilton, S. Hasim and M. Mahjouri-Samani, Two-Dimensional-Material-Based Field-Effect Transistor Biosensor for Detecting COVID-19 Virus (SARS-CoV-2).

[14] L. Kergoat, B. Piro, M. Berggren, G. Horowitz and C. Pham, "Advances in organic transistor-based biosensors: From organic electrochemical transistors to electrolyte-gated organic field-effect transistors," *Analytical and Bioanalytical Chemistry,* vol. 402, pp. 1813-1826, September 2011.

[15] J. B. Chahardeh, "A Review on Graphene Transistors," *International Journal of Advanced Research in Computer and Communication Engineering,* vol. 1, no. 4, June 2012.

[16] C. Chircov and A. M. Grumezescu, "Microelectromechanical Systems (MEMS) for Biomedical Applications," *Micromachines,* vol. 13, no. 164, January 2022.

[17] A. Wasfi, F. Awwad, J. G. Gelovani, N. Qamhieh and A. I. Ayesh, "COVID-19 Detection via Silicon Nanowire Field-Effect Transistor: Setup and Modeling of Its Function," *Nanomaterials,* vol. 12, no. 2638, July 2022.

[18] A. Battacharjee, T. C. Nguyen, V. Pachauri, S. Ingebrandt and X. T. Vu, "Comprehensive Understanding of Silicon-Nanowire Field-Effect Transistor Impedimetric Readout for Biomolecular Sensing," *Micromachines,* vol. 12, no. 39, December 2020.

[19] P. Namdari, H. Daraee and A. Eatemadi, "Recent Advances in Silicon Nanowire Biosensors: Synthesis Methods, Properties, and Applications," *Nanoscale Research Letters,* vol. 11, no. 406, 2016.

[20] Ansh, J. Kumar, G. Sheoran, R. Mishra, S. Raghavan and M. Shrivastava, "Selectrive Electron of Hole Conduction in Tungstein Diselenide (WSe2) Field-Effect Transistors by Sulfur-Assisted Metal-Induced Gap State Engineering," *IEEE Transactions on Electron Devices,* vol. 67, no. 1, pp. 383-388, January 2020.

[21] I. B. Dimov, M. Moser, G. G. Malliaras and I. McCulloch, "Semiconducting Polymers for Neural Applications," *Chemical Reviews,* vol. 122, no. 4, pp. 4356-4396, 2022.

[22] G. Thriveni and K. Ghosh, "Advancement and Challenges of Biosensing Using Field Effect Transistors," *Biosensors,* vol. 12, no. 647, August 2022.

[23] Y.-C. Syu, W.-E. Hsu and C.-T. Lin, "Review--Field-Effect Transistor Biosensing: Devices and Clinical Applications," *ECS Journal of Solid State Science and Technology,* vol. 7, no. 7, June 2018.

[24] S. Azam, "Microwave Power Devices and Amplifiers for Radars and Communication Systems," Liutryck, Linköping University, Linköping, Sweden, 2009.

[25] X. Chen, S. Boumaiza and L. Wei, "Modeling Bias Dependence of Self-Heating in GaN HEMTs Using Two Heat Sources," *IEEE Transactions on Electron Devices,* vol. 67, no. 8, August 2020.