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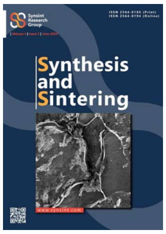

Research article

A surface plasmon resonance biosensor for bacteria and virus detection: A Comsol Multiphysics simulation

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ABSTRACT

This study provides a comprehensive simulation-based investigation into the design and performance optimization of a surface plasmon resonance (SPR) biosensor. The main goal of this study is to improve sensitivity and accuracy by combining optical and colorimetric biosensing techniques. The biosensor is studied, examined, and simulated using Comsol Multiphysics. Sensing medium, black phosphorus, tungsten diselenide (WSe_2), gold (Au), magnetite (Fe_3O_4), and N-BK7 glass as prism are the layers that make up the structure of the proposed sensor. The study evaluates various parameters such as electric potential distribution, surface temperatures, conductive heat flux, eigenfrequency, electric field norm, and temperature gradients. The use of WSe_2 aims for a higher sensitivity for detecting biomolecules. This paper proves the effect of using Fe_3O_4 and WSe_2 among the six layers of the sensor in increasing the selectivity and sensitivity of the SPR biosensor. The findings reveal intricate interactions between the biosensor layers, which influence its thermal and electromagnetic behavior. The findings of this study contribute to the advancement of SPR biosensor technology, which has the potential for a variety of applications in the biomedical field.

KEYWORDS

Tungsten diselenide
Sensitivity
Black phosphorus
SPR
Biomolecule detection

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1. Introduction

Surface plasmon resonance (SPR) interferometry represents a pivotal transduction mechanism utilized for inducing optical alterations. This method capitalizes on the collective electron oscillations within the interface of a metal and dielectric material to engender a charge density wave. Its application in elucidating nucleic acid hybridization dynamics stems from its capability to delineate the binding kinetics between biomolecules and receptor ligands [1]. An SPR immunosensor configuration typically encompasses a light source, prism, and transduction surface predominantly comprising gold films, biomolecular entities, a flow system, and a detector. Operationally, incident light impinges upon the metal-layered surface and the sample, giving rise to a transverse wave manifesting as a surface plasmon wave (SPW), eliciting changes in reflected light intensity at the SPR angle. The excitation of SPR necessitates the utilization of p-polarized light, aligned parallel to the incident plane [2]. Conversely, s-polarized light assumes significance for illuminating the surface perpendicularly to the incident light. The interaction between the input light and SPW culminates in a discernible dip in reflected light intensity, indicative of the SPR angle [2].

The extension of the evanescent electric field beyond the metal layer permits interaction with surface compounds, effectuating alterations in the SPR angle conducive to sensing. Gold is typically favored for enhancing the evanescent wave in SPR setups [3]. The immobilization of biomolecules on the transduction surface facilitates the recognition of target analytes, thereby modulating the SPR angle in a concentration-dependent manner as shown in Fig. 1.

Notable advantages of SPR biosensors include their capability for rapid, real-time measurements, affording insights into the dynamic

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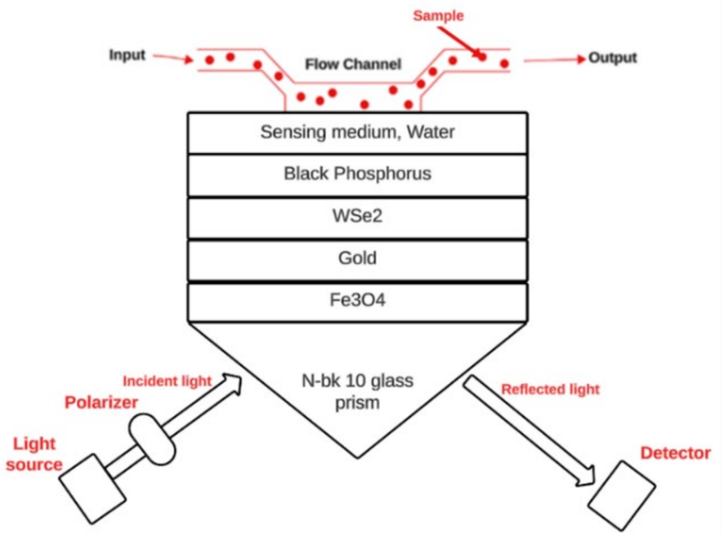

Fig. 1. Schematic representation of sensor layers of SPR.

binding kinetics and layer formation processes [1]. Furthermore, the label-free approach obviates the need for extensive reagent purification, thereby conferring exceptional sensitivity with minimal resource consumption. However, challenges such as the requirement for expensive instrumentation, the potential for contamination due to biomolecule leakage, and sterilization issues associated with non-sterilized probes leading to denaturation, impinge on the method's widespread adoption and applicability [1].

This project is about a surface plasmon resonance-based biosensor that can detect biomolecules. The project aims to provide an optical biosensor model that uses Fe_3O_4, a type of magnetic-based nanoparticle, as a signal transducer. Knowing that the main characteristics of biosensors are selectivity, stability, sensitivity, reproducibility, linearity, and biocompatibility, the project also proposes a model that can provide better characteristics based on physics and the type of study chosen for this project, primarily focusing on better selectivity and sensitivity. Additionally, the study suggests the use of a new layer in the biosensor design, which is WSe_2, acting as a biospecific bilayer following the same working principle as a sandwich assay immunosensor. The study is targeted toward biomedical engineers, molecular biologists, and chemists to help in investigating and developing biosensors with higher sensitivity and specificity to detect biomolecules in the human body, aiding in the early detection of infectious diseases to prevent treatment failure and the development of pandemics.

The paper started by explaining what Surface SPR interferometry is, its main advantages and drawbacks in the field of biosensors, and how these can be improved. It will also discuss how SPR optical-based biosensors can aid in the detection of infectious or bacterial diseases, followed by objectives and a literature review. The second part of the report explains what Comsol Multiphysics is and the benefits and advantages it offers to simulate a biosensor model. The report will continue by explaining the different layers used for various parts of this study, including water, black phosphorus (BP) as the sensing layer of biomolecules, WSe_2 as a bilayer between Gold and BP to enhance light absorption, Gold (Au) as the transduction surface, Fe_3O_4 as the magnetic-based nanoparticle for coating the sensor, and water. The report mentions the characteristics of each material and the reasons behind choosing them. Additionally, the report will continue by explaining the effects of physics and the type of study used in the provided model. Finally, the results that was obtained from the proposed model simulated using Comsol Multiphysics by comparing them with previously published studies about biomolecules detection will be discussed.

Biosensors can be considered as an application of system medicine by using a holistic approach to system biology [1]. The system approach consists of 3 steps, starting with identifying system variables of the case of study as the first step, detecting and characterizing the interactions going on between the variables selecting the key ones, and finally investigating the consequence of these interactions [4]. To detect bacteria and/or Plasmodium parasites, cell-based biosensors can be used. Cell base means detecting the cells involved in the disease by using an enzyme-based recognition element. To make the biosensor to be cell-based, the sensor needs some main properties and characteristics including high sensitivity, and cost efficiency to detect the enzyme that is secreted in malaria and also, waterborne viruses [5]. Water can act as a reagent to detect the presence or concentration of the analyte of our interest, which in the case of the study are bacteria [6]. As water is added to the biosensor, it will result in color change in case of the presence of harmful contaminates, and as water has a covalent bond, it can produce a dipole moment between the atoms of hydrogen and oxygen, so it is considered as a weak acid, therefore, it can be used for multiple test or bioassays that conduct at the same time [7].

2. Methodology

2.1. Comsol Multyphysics

Comsol Multiphysics is an extensive simulation program used by engineers from various fields, including biomedical, electrical, mechanical, and materials science. It provides a full set of tools, allowing users to specify geometry, assign materials, simulate physical phenomena, mesh, and evaluate simulations [8]. Utilizing Comsol Multiphysics effectively necessitates proficiency in mathematical problem-solving, analytical skills encompassing statistical methods, and a robust understanding of engineering and scientific principles [8]. To gain insight into the behavior of the system being studied, the software's process usually entails defining and assigning geometric parameters, defining material characteristics, meshing layers for simulation, and assessing the findings [9]. Comsol Multiphysics is an essential instrument in scientific research and engineering because of its systematic approach, which not only helps with design optimization but also allows engineers to obtain precise and dependable findings [9].

2.2. Mathematical model

In charge particle tracing, plasmas are events resulting from a collisionless state in space in the way that particle collisions are rare to happen. As a result of this collision, there will be a distribution of charged particles in which they do not follow a typical pattern in a denser system. Turbulent plasmas are a process that considers events including interactions between particles and waves and the interaction between the waves, where such events are known as complex nonlinear kinetic processes. Generally, plasmas-related events are used to explain concepts such as energy or momentum exchanges in the environment that the event is happening (heat transfer) [8], such process can be explained by the expression:

$$\frac{d}{dt}\left(m_p \frac{dq}{dt}\right) = F_t \tag{1}$$

The equation is a type of differential expression of Newton's second low of motion. This equation was used to derive the force carried by the charged particle where m_p stands for the particle mass, F_t is the total mass acting on the particle, and dq/dt is the rate of change of the particle's generalized coordinate. In the mentioned equation, $m_p dq/dt$ is known as momentum derivative of the generalized coordinate [11].

$$\nabla.D=\rho\_v \tag{2}$$

$$E = -\nabla V \tag{3}$$

In the Eq. 2, D stands for electric flux, ρ_v is the volume charge density, and ∇ is the divergence operator. Eq. 3 explains the relationship between E and V in an electric field as E is a representation of electric field vector, ∇V is the gradient of the electric potential V, and finally, V represents electric potential.

Heat transfer is the process that involves 3 mechanisms to transfer energy in the form of heat from one matter to other using thermodynamic phenomena. These three mechanisms are conduction, convection, and thermal radiation. Conduction is a slow process as it requires a direct transformation of the heat between adjacent molecules. Convection is a faster process in comparison with conduction as it refers to the movement of heat by a fluid. Thermal radiation transfers heat by employing electromagnetic waves [14].

The process of heat transfer can be described by the following formula:

$$d_z \rho C_p \vec{u}.\nabla T + \nabla.q = d_z Q + q_0 + d_z Q_{ted} \tag{4}$$

$$q = -d_z k \nabla T \tag{5}$$

Eq. 4 consists of seven main parameters including ρ representing the material density, C_p as specific heat capacity at constant pressure, u as the velocity of the fluid flow, ∇T as the gradient of the temperature field T, q as the heat flux vector, q_0 as volumetric heat generation term, and Q_{ted} as the specific type of heat source. In Eq. 5, the same parameters are repeated to describe Fourier's law of heat conduction.

2.3. Design of SPR biosensor

The proposed SPR model of the study uses rectangular geometry with dimensions of 1.2 × 0.25 mm in 2D space for all five layers using the Kretschmann configuration. Based on the Kretschmann configuration, the reflection of the light or electrical particles is subsequently measured after light passes through the thin layer of a metal or magnetic-based nanoparticle (Fe_3O_4) and strikes the glass prism [13]. Plasmon resonant occurs because of the absorption of light or electrical particles at a certain incident angle of the light in which this angle has the same frequency as the incident angle and is called resonance angle [15]. Following the principles of Kretschmann, in the proposed model of the study, there are no gaps between the layers, so the output of each layer is the input of the next layer [16]. If the angle that the particles hit is greater than the critical angle, the light will reflect internally towards the material causing an event known as evanescent waves [17]. As a result of evanescence, the wave particles will travel inside the thin metal layer rather than moving to the next layer so that they will not propagate along the surface of the layer [17]. A part of this study focuses on the detection of virus and bacteria infection in the detection of malaria that is caused by Plasmodium parasites. Detecting such kinds of infections requires the use of highly sensitive biosensors to trace the amount of specific enzymes secreted by the malignant-malaria-causing parasite [18]. In recent years, BP has shown a great capability to be used as a perfect substituent instead of other 2D materials including molybdenum disulfide (MoS_2), hexagonal boron nitride (h-BN), and graphene. Excellent electrical, mechanical, and electrochemical properties make them more applicable in the field of biosensors. In this study, BP was used due to its ability to provide sensitive detection of target analytes [19]. Despite all the advantages that BP is offering, this material is suffering to provide particle absorption. To overcome this issue, the simulated SPR model is using WSe_2 by using the sandwich assay method as one of the direct immunosensor techniques to provide better absorption of electric particles by considering WSe_2 as a bilayer between BP and Au layer.

Au was used as a coating layer or recognition element of the sensor. Knowing that in all biosensors, the transducer will detect the electrochemical changes caused by interactions between immobilized recognition element and analyte, characteristics including effective catalysis, good biocompatibility and excellent conductivity, high density, and surface-to-volume ratio, made Au to be the best candidate as coating layer in the purposed biosensor to provide a better surface reaction [20]. Using the Kretschmann configuration is highly dependent on the thickness of the layers especially the thickness of the metal/magnetic nanoparticle. Table 1 represents the thickness and respective thermal conductivity used for each of the layers. As for the thickness of BP and tungsten diselenide layers, their thickness was

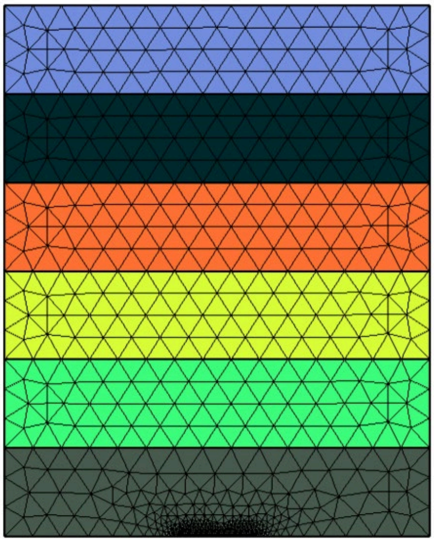

Fig. 2. The resultant mesh of the proposed model.

determined by their scaling factor, which for BP is G × 0.53 nm and for WSe_2 is L × 0.7 nm. Respectively, thicknesses of 42 nm, 40 nm, and 0.589 nm were used for Au, Fe_3O_4, and N-BK7 glass (prism). Due to the small thickness of the magnetic nanoparticle (40 nm), the generated evanescent wave at the prism exists as the surface plasmon (SP) at the metal layer [16]. Where the higher thickness of the Fe_3O_4 layer could result in a damping effect and a lower thickness will result in complete absorption of the particles at the indicated layer [16].

The thickness of each material in the biosensor influences the propagation of surface plasmon waves and the penetration depth of electromagnetic fields, affecting the sensor's sensitivity to biomolecular interactions.

2.4. Particle propagation and detection

To describe the physic phenomena used in the model, ensure the accuracy of the detected analyte because of the interaction of analyte and recognition element, and also for computational efficiency, a finer mesh shown in Fig. 2 was used to break the geometry model into smaller parts to facilitate numerical expression of partial differential equations (PDEs) to describe physical phenomena [21].

Colorimetric is a type of biosensor based on thermodynamic rules in which the output is in the form of heat as the result of interactions within the sample recognition element and analyte. In this method, the output can be represented in either an exothermic or endothermic shape. In the exothermic process, heat or energy is generated, and the energy of electrical particles is lower in the product or output in comparison with the input. In contrast, in the endothermic process, the energy of heat is consumed; and the energy of output is higher than the energy of the input for electrical particles [22]. Compared to optical-based biosensors, colorimetric-based biosensors have lower sensitivity but higher accuracy. The proposed model combines optical and colorimetric biosensors to cover both characteristics.

Table 1. Thickness and thermal conductivity of the used materials in the proposed structure.

Material	Thickness of layers (nm)	Thermal conductivity (W/(m.K))
BP	G × 0.53	60
WSe_2	L × 0.7	1.1
Au	42	317
Fe_3O_4	40	5
N-BK7	0.589	-

3. Results and discussion

The simulation results provide profound insights into the behavior and performance of the biosensor, which incorporates a variety of materials. The counterclockwise rotation of the electric potential distribution (-4.7596E-17 rad/s) shown in Fig. 3a emphasizes the intricate interactions between the biosensor layers. This phenomenon may be caused by the unique electrical properties of materials such as black phosphorus and WSe_2, which influence the overall electric potential distribution across the biosensor surface.

Surface temperature variations, as demonstrated by the simulation (max/min surface temperature), are critical for optimizing the biosensor's thermal management. Temperature differences between layers, possibly caused by thermal conductivity variations, highlight the importance of precise temperature control in improving biomolecular interactions and detection sensitivity.

Heterogeneous conductive heat flux across the biosensor surface (min/max scatter surface conductive heat flux = 1.41421) indicates non-uniform heat dissipation properties, which may affect thermal stability and biomolecular binding kinetics [23]. Understanding these variations in heat flux is critical for reducing thermal gradients and maintaining consistent biosensor performance.

The eigenfrequency of the biosensor system (-7.5579E-18 Hz), shown in Fig. 3b which represents its natural oscillatory response, indicates complex dynamics influenced by material properties and layer configurations. Damped oscillations, as indicated by the imaginary component, reflect dissipative effects within the biosensor, which may influence its dynamic response to external stimuli and biomolecular interactions [24].

The distribution of the electric field norm across the biosensor layers provides information about the electromagnetic behavior required for biomolecular sensing. Variations in electric field strength can affect the efficiency of biomolecular binding and detection processes, emphasizing the importance of optimizing the electric field distribution for better sensing performance [25].

Localized temperature gradients within biosensor layers (max/min point temperature normal, x-component (K)) may have a significant impact on biomolecular interactions and detection sensitivity. Understanding these gradients is critical for optimizing biosensor design and operation, resulting in accurate and reliable detection of target analytes.

By thoroughly analyzing these simulation results, valuable insights into the complex interplay of material properties, thermal dynamics, and electromagnetic behavior within the biosensor are obtained.

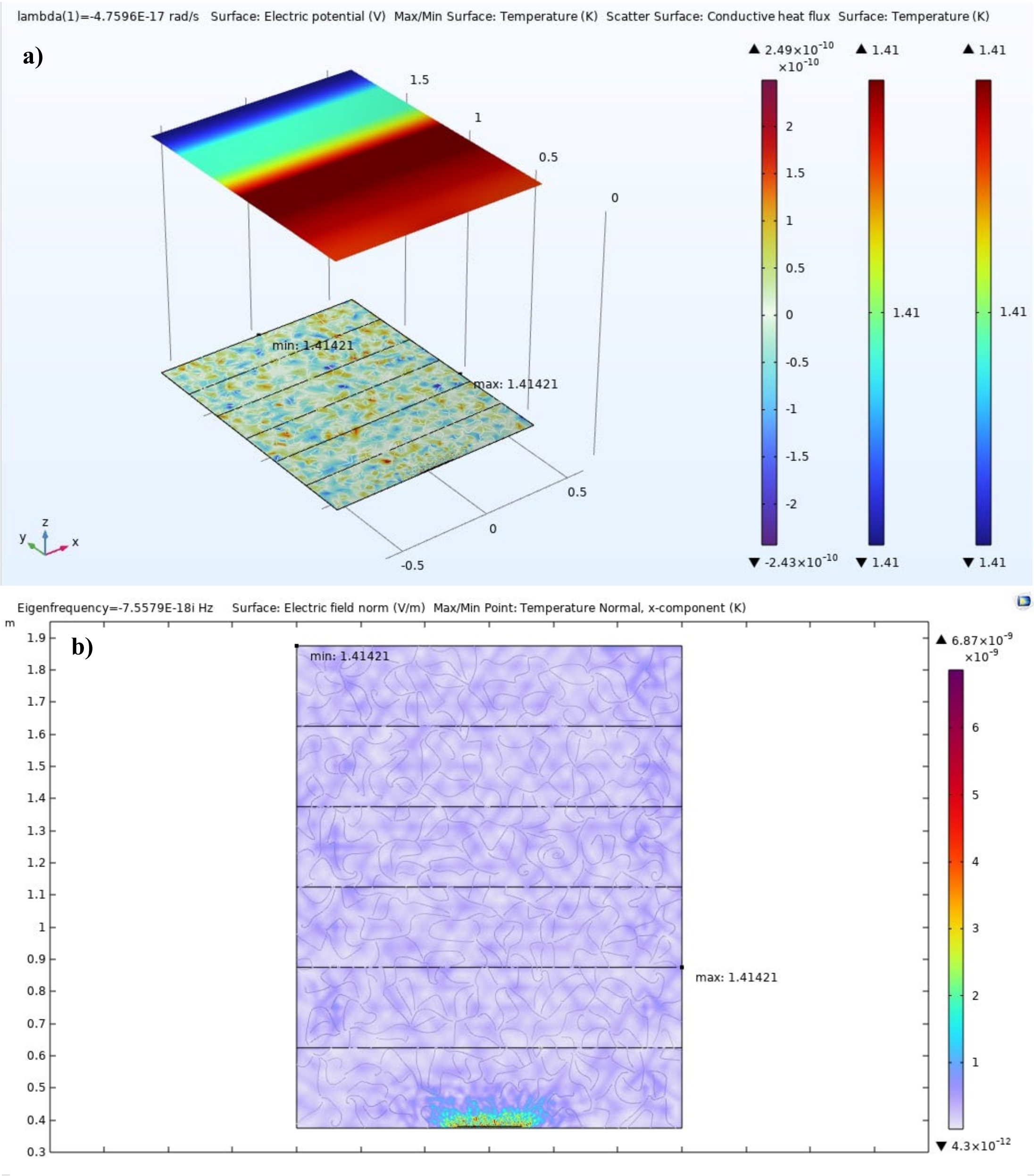

Fig. 3. a) Result of electric potential and b) result of electric field norm. Both figures include min/max temperature.

4. Conclusions

This study describes the successful simulation of an advanced SPR biosensor with Comsol Multiphysics, resulting in significant sensitivity and accuracy improvements. By combining optical and colorimetric biosensing techniques, the model takes advantage of their synergistic effects to achieve superior performance. Key materials used in the design include black phosphorus, which improves sensor sensitivity due to its exceptional optical properties; WSe_2, which contributes to increased sensitivity and responsiveness; Au, which ensures robust plasmonic activity; Fe_3O_4, which adds a magnetic dimension to sensing capabilities; and N-BK7 glass as the prism, which provides a stable and reliable substrate for the sensor.

The novel combination of these materials and sensing approaches overcomes the limitations of traditional single-method sensors, providing a more comprehensive detection mechanism that improves biomolecular interaction measurement accuracy. This multi-material and multi-modal biosensing strategy demonstrates the potential for developing next-generation SPR biosensors with improved performance, with significant implications for biomedical and environmental monitoring applications.

CRediT authorship contribution statement

Loujayn Ayache: Validation, Data Curation, Visualization, Writing-original draft.

Kiana Mahtabi Nourani: Conceptualization, Methodology, Investigation, Writing-review & editing.

Shahla Azizi: Project administration, Supervision, Writing-review & editing.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Declaration of competing interest

The authors declare no competing interests.

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References

[1] S.A. Ozkan, B. Uslu, M. Kemal Sezgintürk, Biosensors. CRC Press, Boca Raton. (2022). https://doi.org/10.1201/9781003189435.

[2] H.H. Nguyen, J. Park, S. Kang, M. Kim, Surface plasmon resonance: a versatile technique for biosensor applications, Sensors (Basel). 15 (2015) 10481–510. https://doi.org/10.3390/s150510481.

[3] F. Fathi, R. Jalili, M. Amjadi, M.R. Rashidi, SPR signals enhancement by gold nanorods for cell surface marker detection, Bioimpacts. 9 (2019) 71–78. https://doi.org/10.15171/bi.2019.10.

[4] J. Loscalzo, A.-L. Barabasi, Systems biology and the future of medicine, WIREs Syst. Biol. Med. 3 (2011) 619–627. https://doi.org/10.1002/wsbm.144.

[5] R. Apweiler, T. Beissbarth, M.R. Berthold, N. Blüthgen, Y. Burmeister, et al., Whither systems medicine?, Exp. Mol. Med. 50 (2018) e453–e453. https://doi.org/10.1038/emm.2017.290.

[6] X. Song, Z. Fredj, Y. Zheng, H. Zhang, G. Rong, et al., Biosensors for waterborne virus detection: Challenges and Analysis, J. Pharm. Anal. 13 (2023) 1252–1268. https://doi.org/10.1016/j.jpha.2023.08.020.

[7] S.M.Z. Hossain, N. Mansour, Biosensors for on-line water quality monitoring – a review, Arab J. Basic Appl. Sci. 26 (2019) 502–518. https://doi.org/10.1080/25765299.2019.1691434.

[8] T.W. Graham Solomons, C.B. Fryhle, S.A. Snyder, Organic Chemistry, John Wiley & Sons. (2016).

[9] X. Wang, H. Yue, G. Liu, Z. Zhao, The Application of COMSOL Multiphysics in Direct Current Method Forward Modeling, Procedia Earth Planet. Sci. 3 (2011) 266–272. https://doi.org/10.1016/j.proeps.2011.09.093.

[10] W.B.J. Zimmerman, Multiphysics modeling with finite element methods: Vol. 18, World Scientific Publishing Company. (2006).

[11] A. Osmane, A.M. Hamza, Relativistic acceleration of Landau resonant particles as a consequence of Hopf bifurcations, Phys. Plasmas. 19 (2012) 030702. https://doi.org/10.1063/1.3692234.

[12] W. Hayt, J. Buck, Engineering electromagnetics, McGraw Hill. (2019).

[13] J.S. Murray, P. Politzer, The electrostatic potential: an overview, WIREs Comput. Mol. Sci. 1 (2011) 153–163. https://doi.org/10.1002/wcms.19.

[14] M.N.O. Sadiku, S. Nelatury, Elements of electromagnetics, Oxford University Press. (2020).

[15] G. Nellis, S. Klein, Heat transfer, Cambridge University Press. (2008).

[16] A. Camarca, A. Varriale, A. Capo, A. Pennacchio, A. Calabrese, et al., Emergent Biosensing Technologies Based on Fluorescence Spectroscopy and Surface Plasmon Resonance, Sensors. 21 (2021) 906. https://doi.org/10.3390/s21030906.

[17] A.S. Kushwaha, A. Kumar, R. Kumar, S.K. Srivastava, A study of surface plasmon resonance (SPR) based biosensor with improved sensitivity, Photonics Nanostruct- Fundam. Appl. 31 (2018) 99–106. https://doi.org/10.1016/j.photonics.2018.06.003.

[18] L.B. Felsen, Evanescent waves, J. Opt. Soc. Am. 66 (1976) 751–760. https://doi.org/10.1364/JOSA.66.000751.

[19] N.K.Singh, P.D. Thungon, P. Estrela, P. Goswami, Development of an aptamer-based field effect transistor biosensor for quantitative detection of Plasmodium falciparum glutamate dehydrogenase in serum samples, Biosens. Bioelectron. 123 (2019) 30–35. https://doi.org/10.1016/j.bios.2018.09.085.

[20] J.R. Choi, K.W. Yong, J.Y. Choi, A. Nilghaz, Y. Lin, et al., Black Phosphorus and its Biomedical Applications, Theranostics. 8 (2018) 1005–1026. https://doi.org/10.7150/thno.22573.

[21] P. Jiang, Y. Wang, L. Zhao, C. Ji, D. Chen, L. Nie, Applications of gold nanoparticles in non-optical biosensors, Nanomaterials. 8 (2018) 977. https://doi.org/10.3390/nano8120977.

[22] C. Fairclough, Efficiently Mesh Your Model Geometry with Meshing Sequences, COMSOL Multiphysics. (2016).

[23] S. Kaziz, Y. Saad, M.H. Gazzah, H. Belmabrouk, 3D simulation of microfluidic biosensor for SARS-CoV-2 S protein binding kinetics using new reaction surface design, Europ. Phys. J. Plus. 137 (2022) 241. https://doi.org/10.1140/epjp/s13360-022-02470-8.

[24] N. Varnakavi., N. Lee, A Review on Biosensors and Recent Development of Nanostructured Materials-Enabled Biosensors, Sensors. 21 (2021) 1109. https://doi.org/10.3390/s21041109.

[25] N. Bibhu Prasad, P. Rani, P. Paul, N. Aman, S. Ganti Subrahmanya, R. Bhatia, Recent Trends and Impact of Localized Surface Plasmon Resonance (LSPR) and Surface-Enhanced Raman Spectroscopy (SERS) in Modern Analysis, J. Pharm. Anal. (2024). https://doi.org/10.1016/j.jpha.2024.02.