# Impedimetric Sensor Aided by Polydopamine Nanoparticles for Label-Free Detection of Breast Cancer Cells – A Review



Bhuneshwari Dewangan 1 0, Naina Bhoyar 1 0

#### **Abstract**

Integrating an impedimetric sensor with polydopamine nanoparticles presents a novel approach for detecting breast cancer cells without labels. This innovative technique is significant for painless and sensitive early identification of cancerous cells. However, challenges, such as precise characterization and functionalization of polydopamine nanoparticles, may impact the sensor's sensitivity. This review paper suggests Real-Time Enhanced Surface Functionalization (R-TESF), utilizing polydopamine nanoparticles to enhance the sensor's specificity. Impedance data is processed with machine learning and analytical models to accurately distinguish cancer cell signatures from background noise. The method leverages polydopamine's specificity to proteins associated with breast cancer, making it a powerful tool for early detection. Simulation analysis validates and refines the proposed method, providing insights into its performance across various variables and scenarios. Beyond breast cancer diagnostics, the integration of experimental and computational methods showcased in this study has the potential to transform cancer research.

**Keywords:** Impedimetric Sensor, Polydopamine, Nanoparticles, Label-Free Detection Breast Cancer Cells

**Significance** | Evolutionary Computation Network for Drug Repositioning reveals oral cancer stem cells, informing targeted therapies for treatment.

\*Correspondence:

Bhuneshwari Dewangan, Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.

Email:

ku.bhuneshwaidewangan@kalingauniversity.ac.in

Editor Mohamed Khadeer Ahamed Basheer And accepted by the Editorial Board Dec 7, 2023 (received for review Nov 7, 2023)

## 1. Introduction

Utilizing an innovative impedimetric sensor supported by polydopamine nanoparticles, the label-free identification of breast cancer cells stands as a significant advancement in cancer diagnostics and personalized therapy (Suthar, J., 2022). Early diagnosis is paramount in the successful treatment of breast cancer, a prevalent and lethal global malignancy. Traditional diagnostic methods often involve invasive procedures or the use of contrast chemicals, both of which can be uncomfortable and risky (Li, Y., 2020). Therefore, the development of non-invasive, highly sensitive, and targeted detection approaches is crucial (Abedi, R., 2023). The impedimetric sensor strategy aims to overcome these challenges by leveraging the specific binding capability of polydopamine nanoparticles to breast cancer cells (Won, H. J., 2020). Immobilizing these nanoparticles on the sensor surface facilitates the collection of cancer cells from a patient's blood or other body fluids without the need for labels or extensive sample preparation (Rahmati, Z., 2021). However, realizing the full potential of this technology faces several hurdles (Sanko, V., 2023). Differentiating between cancer cells and normal cells or contaminants in the sample is crucial for the sensor's efficacy, necessitating improvements in sensitivity and specificity (Fan, T., 2019). Engineering challenges include maintaining the binding affinity of polydopamine nanoparticles for cancer cells while enhancing their immobilization on the sensor surface (Yadav, A. K., 2023). Integrating the impedimetric sensor into clinical practice and validating it with diverse patient samples present additional challenges. Overcoming these obstacles could lead to the development of a highly sensitive, non-invasive, and label-free technology for early-stage breast cancer detection, significantly improving patient outcomes through timely intervention and

## Author Affiliation:

<sup>1</sup> Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.

## Please cite this article:

Bhuneshwari Dewangan, Naina Bhoyar. (2023). Discovering Novel and Old Drug Targets in Oral Cancer Stem Cells Using bio-inspired methods — A Review, Journal of Angiotherapy, 7(2), 1-12, 9400

2207-8843/© 2019 ANGIOTHERAPY, a publication of Eman Research Ltd, Australia.

This is an open access article under the CC BY-NC-ND license.

(http://creativecommons.org/licenses/by-nc-nd/4.0/).

(https://publishing.eman

personalized treatment plans (Zhang, F., 2022).

A promising strategy for early cancer diagnosis involves employing an impedimetric sensor supported by polydopamine nanoparticles for label-free detection of breast cancer cells (Gajdosova, 2020). Polydopamine nanoparticles, known for their strong affinity to breast cancer cell markers, are utilized to functionalize sensor surfaces in existing methods (Feng, Y. G., 2019). Alterations in electrical impedance, caused by the presence of breast cancer cells in a sample, can be measured and evaluated (Chen, F., 2019). This label-free technology offers advantages in cancer cell detection by eliminating the need for elaborate sample preparation, expensive labels, or antibodies (Yaman, Y. T., 2023). However, various obstacles impede progress in this technology. Maximizing sensitivity and specificity is crucial (Sahraei, N., 2022), ensuring consistent discrimination between breast cancer cells and non-cancerous cells or other contaminants in complex clinical samples. Another critical consideration is maintaining the consistency and reliability of polydopamine nanoparticle coatings on sensor surfaces (Hassanpour, S., 2021). Inconsistencies in nanoparticle attachment and sensor performance compromise the reliability of findings. Standardization, scalability, must be addressed before automation implementation in clinical practice (Malla, P., 2021). For widespread application, intuitive devices and protocols need to be designed for use in clinical laboratories or at the point of care. Validation with a diverse range of patient samples is essential to prove its clinical utility and reliability across different breast cancer subtypes and stages (Linh, N. D., 2023). While the impedimetric sensor aided by polydopamine nanoparticles shows promise for label-free breast cancer cell detection, its full potential for early cancer diagnosis and individualized treatment cannot be realized until its limitations are overcome (Chen, L., 2017).

The primary objective is to establish a label-free method for detecting breast cancer cells using polydopamine nanoparticles within an innovative impedimetric sensor technique. This novel strategy aims to develop a painless and highly sensitive method for detecting breast cancer at an early stage.

Enhancing sensor specificity, sensitivity, and signal-to-noise ratio is the primary focus of this study, addressing challenges associated with characterizing and functionalizing polydopamine nanoparticles. A Real-Time Enhanced Surface Functionalization (R-TESF) approach is proposed to improve the sensor's real-time functionality.

The research aims to accurately distinguish breast cancer cell signatures from background noise by integrating machine learning approaches and analytical models for analyzing impedance data. This objective underscores the potential use of the sensor in clinical settings for early-stage breast cancer detection.

The subsequent sections of the paper delve into existing treatment options following the label-free detection of breast cancer cells in Section 2. A new technique, Real-Time Enhanced Surface Functionalization (R-TESF), is introduced and mathematically explored in Section 3. Section 4 discusses the findings, while Section 5 offers a comprehensive synopsis and analysis of the data (Won, H. J., 2020).

## 2. Literature Survey

Researchers significantly contributes to the continually expanding field of biomedical materials, whether it involves the synthesis of polydopamine nanoparticles, the advancement of non-invasive tracking techniques for cancer treatment, or the design of multifunctional bio-capture Nano platforms.

Polydopamine nanoparticles (PDA NPs) developed by Bolat, G. et al. (2021) showcase unique properties for biomedical systems, and the exploration of PDA-derived nanostructures for future innovations is a rapidly growing area. The current work utilizes the self-polymerization of dopamine in an alkaline environment to produce PDA NPs, presenting a moderate and cost-effective synthesis method.

Non-invasive techniques (N-IA) proposed by Linh, N. D. et al. (2023) offer a method for tracking the progress of treatment in terminal cancer patients. The enhanced mechanical stability of this electrochemical interface is achieved through the coordination between gold and carbonaceous material. The introduction of polydopamine onto modified electrodes, through the self-polymerization of dopamine in an alkaline solution, further enhances the efficacy of this approach.

Multi-walled carbon nanotubes (MWCNTs) proposed by Mujica, M. L. et al. (2022), non-covalently functionalized with avidin (Av) as support to immobilize a biorecognition element, emerge as a versatile and multifunctional biocapture nanoplatform. The biosensor, tested with a variety of DNA sequences, demonstrated admirable performance.

Tungsten disulfide (WS2) presented by Esfandiari, M. et al. (2023) is an excellent candidate for enhancing cytosensor performance due to its high binding affinity toward cancer cells. Laser photons create electron-hole pairs, increasing interfacial electron transport and enhancing electrochemical performance. Biosensors made with whole blood samples exhibited a high recovery rate.

Zirconium-based metal-organic frameworks (Zr-MOFs) invented by Li, Y. et al. (2020) exhibit a remarkable capacity to stabilize the aptamer-cells combination in aqueous solution. The connection between PO4-Apt and Zr-atom centers improves aptamer immobilization and sensing performance, overcoming limitations associated with label-free immobilized aptamers.

Amidst these various methods, the proposed Real-Time Enhanced Surface Functionalization (R-TESF) technology stands out as a

novel strategy with the potential to revolutionize surface functionalization for biological applications. Its efficiency enhancement across a broad spectrum of materials and methods brings hope for its application in biomedical research and practical use (Suthar, J., 2022).

## 3. Breast Cancer Detection through Polydopamine-enhanced Impedimetric Sensors and predictive model

The study introduces an innovative approach that integrates impedimetric sensor technology with the adaptability of polydopamine particles to achieve rapid and precise breast cancer detection. Traditional tagging techniques for identifying cancerous breast cells are both expensive and time-consuming. ( Siegel et al,2019). This novel approach proposes the application of polydopamine nanoparticles to enhance the sensor's sensitivity and accuracy, thus overcoming these limitations ( Rahman et al,2019). In the context of tumor identification, this label-free monitoring approach holds the potential to significantly advance the field.

Transporting living cells poses challenges that are difficult, if not impossible, to address solely through chemical or physical changes to the surface. The study introduces a cell-membrane-camouflaged nano system with significant advantages, demonstrating active inhibition of pulmonary dissemination from breast cancer (Khorrami et al,2019). The synergy qualities of the cell membrane are speculated to enhance blood preservation, immune defense, and targeting precision. A veiled flavonoid version was created to inhibit and treat breast cancer or its metastasis in the lungs, showcasing improved immune responses and reduced metastasis (Figure 1) (Sadighbayan et al,2019).

The research incorporates nanoparticles, with sizes ranging from 1 to 100 nm, which have become integral to innovative clinical studies. Nanomaterials, distinguished by outstanding thermal rigidity, ease of derivatization, and substantial area-to-volume ratios, have opened new frontiers in medical sciences (Sharifi et al,2020). Carbon materials, evolving from traditional charcoal extraction, have now narrowed down to nanotechnology, with various allotropes such as nanodiamonds, carbon fiber nanobuds, graphene oxide, and carbon nanotubes (Campuzano et al,2017). These materials, particularly carbon-based ones, have been extensively explored for their ability to enhance biosensor selectivity and functionality.

The study introduces the Real-Time Enhanced Surface Functionalization (R-TESF) method, a groundbreaking strategy for label-free identification of cancerous breast cells. Integrating an impedimetric sensor with polydopamine nanoparticles forms the core of this approach, offering a potent strategy for early cancer detection (Sierra et al,2020). The sensor's ability to detect

changes in resistance upon contact with different chemicals, combined with the attachment of polydopamine nanoparticles, enhances its performance.

Equations and mathematical models are employed to quantify and analyze various aspects of the research, including nanoparticle concentration, signal threshold factors, and probability of delivery ( Jeong et al,2020). The research also emphasizes the importance of analytical modeling and simulation to understand the behavior of the detection device and the interaction between polydopamine nanoparticles and cancer cells ( Alarfaj et al,2018).

$$BL_{i}(C) = \frac{BS_{ij}(1-[C-C_{j}]^{2/2}}{QE(1-[C-C_{j}]^{2/(2})}$$
(1)

Equation (1)  $BL_i(C)$  denotes the breast lung cancer cells , BS is the membrane of breast surface, QE is the tumour constant, and C is the cancer cell annotation.

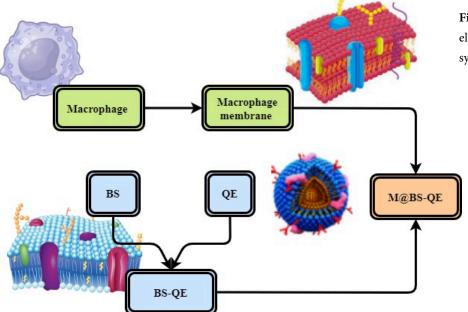
The measurement of nanoparticles is on a scale of 1 to 100 nm. Given their distinctive attributes, nanoparticles are currently employed in innovative clinical studies, ushering in an era of innovation in the medical sciences (An et al,2020). Nanomaterials may be distinguished from different materials for their outstanding thermal rigidity, ease of derivatization, and considerable area-to-volume ratios. Since the beginning, people relied on modern equipment to extract charcoal from the earth to harness its special attributes for health and conservation purposes (Moura et al,2020). As nanoscience progressed, carbon materials narrowed from minuscule to nanotechnology (Figure 2).

$$C_{NS} = \frac{(N_{min} - N)}{\log(N_{max} - N_{min})} / \frac{[BS_{max} - N]}{BS_{min}}$$
(2)

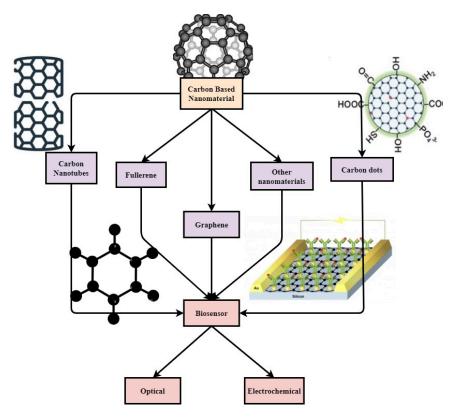
As per equation (2)  $C_{NS}$  be the carbon materials taken from nanomaterials,  $N_{min}$  be the nanomaterial component in minimal quantity,  $N_{max}$  be the nanomaterial component in max quantity,  $BS_{max}$  be the breast surface of affected area. N be the number of infected part of lungs.

$$THF = \emptyset - \log(\partial \sqrt{2\log C}) - \partial )$$
 (3)

Principal component analysis is used to remove extraneous data from equation (3), where THF is the signal threshold factor, Øthe specific input's wavelength, the deviation angle, and C is the length of the sample.



**Figure 1.** Biomimetic transmission electron microscopy (TEM) image synthesis.



**Figure 2.** A classification flowchart for carbon nanomaterial-based biosensors.

## **Box 1.** Predictive algorithm model.

Input: Xi = (yi,y2.....yn), N no. of. Cancer Cells

Output: Micro-cancer = (Ci,C2.....Cn)

Step 1: N = cancer-tumour Step 2: Tumor detection

Step 3: C <- N

Step 4: In final C micro cancer formed

Step 5: Micro-cancer < - Micro-cancer  $\cap$  C Step 6: return Micro-cancer detection

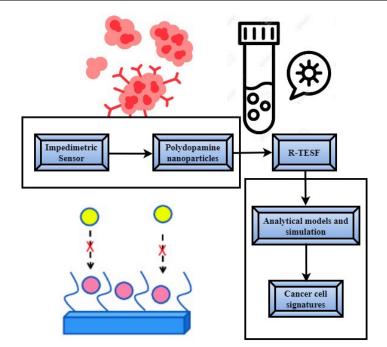


Figure 3. R-TESF (Real-Time Enhanced Surface Functionalization).

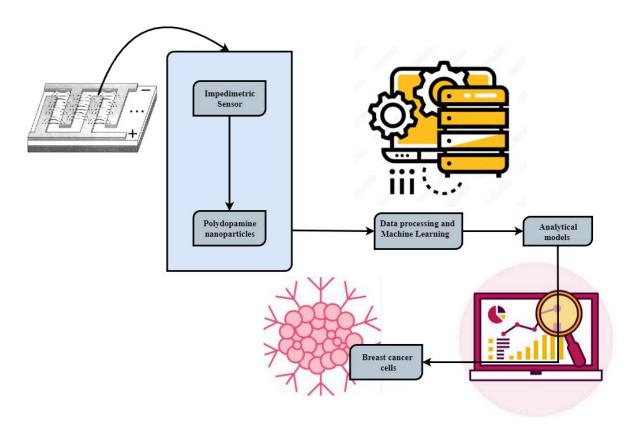


Figure 4. Methods Combining Experiment and Computer Simulation.

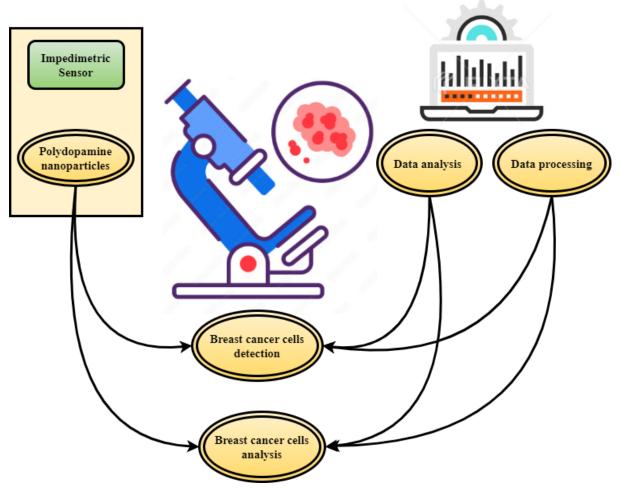


Figure 5. Using a Polydopamine Nanoparticle-Aided Impedimetric Sensor for Label-Free Breast Cancer Cell Detection.

Carbon nanomaterials, a key component of nanotechnology, have garnered global scientific interest due to their diverse properties. Carbon exists in various allotropes, including nanodiamonds, carbon fiber nanobuds, graphite, graphene oxide, carbon nanocones, carbon nanotubes (CNTs), and quantum dots, each finding applications in fields such as magnetic field displays, nanoelectronics, high-energy electronics, and power storage (.Luo et al,2020). Over the years, carbon-based materials have been extensively explored for enhancing biosensor selectivity.

Figure 3 introduces a groundbreaking approach called Real-Time Enhanced Surface Functionalization (R-TESF), which has the potential to revolutionize cancer diagnosis. This method integrates an impedimetric sensor with polyacrylamide nanoparticles, providing a powerful strategy for label-free identification of cancerous breast cells (Akhtartavan et al,2020). The impedimetric sensor, capable of detecting resistance changes upon interacting with different chemicals, forms the core of this approach, with polydopamine nanoparticles playing a crucial role in the sensor's surface functionality (Kilic et al,2018). This innovative method holds promise for advancing cancer diagnosis and improving the selectivity of biosensors.

$$P(x, y) = RC * log ((x, y) + log(RC) - THF)$$
(4)

probability of delivery can be calculated as P(x,y) where RC is the radiation constant from the function above equation (4) and the MRI properties of a signal at those coordinates be x and y.

$$P(x,y) = RC * log ((x,y) + log(RC) - \emptyset - log(\partial \sqrt{2 log C}) - \partial)$$
(5)

polydopamine nanoparticles.

above equation. The above technique's exterior functioning process takes place in real time, a feature crucial to its efficiency. The Real-Time Enhanced Surface Functioning (R-TESF) method represents a novel approach to breast cancer detection (Zhu et al,2021). By integrating impedimetric sensors with polydopamine

Equation (5) is obtained from equation (4) by solving THF in the

nanoparticles, this method allows the sensor's outermost portion to dynamically change, enhancing responsiveness and specificity in real-time (Pourmadadi et al,2022). The key objective is to achieve better signal-to-noise ratios by addressing the fundamental relationship between impedimetric sensors and

Analytical Modeling and Simulation are crucial components of R-TESF, enabling scientists to understand the sensor's behavior and refine its operation ( Quan et al,2021). The resistive data collected from sensor-nanoparticle interactions undergoes a comprehensive data processing process, resulting in the creation of Cancer Cell

Signatures. These signatures, with specific structures, confirm the presence of tumor cells in breast tissue (Rahimzadeh et al,2021).

The multimodal strategy aims to facilitate the early detection of cancerous breast cells. The selective nature of polydopamine nanoparticles towards target proteins associated with breast malignancies enables the detection of cancer at an incipient stage. R-TESF has shown promising results in identifying cancer early, contributing to improved patient prognoses and outcomes ( Torre et al,2017).

The method effectively combines empirical and analytical approaches, bridging the gap between theory and practice. R-TESF's success lies in its innovative fusion of experimental and quantitative methodologies, emphasizing specificity in targeting cancer cell antigens (Akgönüllü et al,2021). As a beacon of hope, R-TESF holds the potential to enhance cancer identification and, consequently, elevate the standard of patient care in this evolving field of study.

$$C_p = \frac{\sum A_{xy}^2}{\beta_{xy}} - \int (x+y)dz - Z, (z=1,2,3....n)$$
(6)

Data is stored in mathematical representations that can be communicated to higher layers of AI logic. In equation (6)  $C_p$  describes the signals seen by a cancer patient throughout treatment. Each layer's input z is weighted differently by the angle applied to the data input xy (Zare et al, 2022).

$$C(P) = P + \sum_{z=0}^{N-1} C_p + (T(xy) - x))^2$$
(7)

It is evident from equation (4) that  $\mathcal{C}(P)$  represents the fullness of the patient's knowledge required for cancer detection and diagnosis. Let's say there are N total patients. Let's call the scenario E the examination, the preparation P, and the patient's treatment T(xy) (Mohammadpour-Haratbar et al,2022).

However, the research signifies a significant advancement in breast cancer detection, proposing a novel and highly sensitive approach that combines experimental and computational methodologies. The integration of an impedimetric sensor with polydopamine nanoparticles, along with real-time surface characterization and quantitative models, holds promise for revolutionizing cancer diagnosis (Ramon-Marquez et al,2018). The study's holistic approach, combining physical and computational methods, exemplifies the evolving nature of scientific research and opens new avenues for breakthroughs in various disciplines. The R-TESF method emerges as a beacon of hope for enhanced cancer identification and improved patient care as scientific exploration continues to progress.

Figure 4 illustrates a groundbreaking approach that merges hands-on experimentation with computer methods, marking a

significant shift in scientific investigation. The method combines an Impedimetric Sensor and Polydopamine Nanoparticles, exemplifying a hybridization of laboratory-based techniques (Volder et al,2013). The sensor collects data through its physical interaction with polydopamine nanostructures, initiating a scholarly expedition. Analytical Modeling and Simulation play a crucial role in understanding the sensor's behavior and its interaction with breast cancer cells. This integration of empirical and computational approaches accelerates discoveries in various scientific disciplines (Erdely et al,2013).

The schematic outlines an advanced breast cancer detection technique, combining an impedimetric sensor with polydopamine nanoparticles for label-free recognition. The sensor, measuring impedance changes, improves its performance with the incorporation of polydopamine nanoparticles, which selectively engage with molecular targets on breast cancer cells (Shrivastav et al,2021). The label-free approach offers accurate detection without the need for costly and intrusive labeling procedures.

The algorithm demonstrates real-time detection and evaluation of breast cancer cells by coupling impedimetric sensors with polydopamine nanoparticles. The electrostatic changes caused by the interaction are picked up in real-time, allowing for the identification of breast cancer cells without the use of labels (Ausó et al,2020). The label-free, highly accurate method minimizes the likelihood of mistaken results and interference with cell integrity. The breakthrough in detecting breast malignancies with this approach relies on its label-free nature, real-time identification, and excellent sensitivity. The specificity and effectiveness of the determination method are enhanced through advanced computational methods and algorithms (Reddy et al,2020). This promising advancement in medical diagnosis has the potential to fundamentally alter the sector, offering improved outcomes for patients and increased success in the fight against breast cancer.

## 4. Discussion

Innovative sensors for label-free cancer cell detection, employing Real-Time Enhanced Surface Functionalization (R-TESF) with polydopamine nanoparticles, offer a significant advancement in early diagnosis and treatment. Analyzing the temporal behavior of the sensor's impedimetric properties is crucial. Incubation time, the duration polydopamine spends on the sensor, impacts functionality. Longer durations may enhance binding but slow detection (Naresh et al,2021). Understanding the rate of surface functionalization and optimizing detection time is essential for real-time label-free breast cancer cell identification, ensuring the sensor's efficiency.

The advancement of novel sensors designed for the label-free detection of cancer cells significantly enhances the potential for early diagnosis and successful treatment options. A cutting-edge technique, Real-Time Enhanced Surface Functionalization (R-TESF), has emerged to enhance the functionality of impedimetric sensors utilizing polydopamine nanoparticles ( Chen et al,2021).

To comprehend the temporal behavior of the impedimetric sensor improved by polydopamine nanoparticles for label-free breast cancer cell detection, an analysis of time is essential in the context of Real-Time Enhanced Surface Functionalization (R-TESF). In the realm of functionalization, the duration of incubation plays a pivotal role. It signifies the time during which polydopamine nanoparticles interact with the sensor ( Chowdhury et al,2021). Achieving uniform and efficient functionalization of the sensor's surface is crucial, making optimization of this incubation time paramount. While longer incubation periods may enhance nanoparticle binding, they may potentially slow down the detection process.

Additionally, the duration required to identify a phenomenon is crucial, representing how long the sensor remains vigilant for variations in impedance induced by the presence of breast cancer cells. The responsiveness of a sensor is, in part, determined by its ability to swiftly detect environmental changes (Teymourian et al,2020). Understanding the rate of surface functionalization is equally important. In Figure 6(a) & (b), the process involves measuring the speed at which polydopamine nanoparticles adhere to the sensor. A comprehensive temporal analysis of these characteristics is indispensable to maximize the sensor's performance and ensure its suitability for real-time label-free identification of breast cancer cells (Chia et al,2021).

Within the framework of the impedimetric sensor, supported by polydopamine nanoparticles for the label-free detection of breast cancer cells, frequency analysis stands out as a pivotal element in Real-Time Enhanced Surface Functionalization (R-TESF) (Lenters et al,2012). An illustrative instance of frequency analysis in this context is the adjustment of the cycle rate of the alternating current employed for impedance assessment. By examining impedance responses at various frequencies, the sensor can glean crucial insights into the interactions among polydopamine nanoparticles, cancer cells, and the sensor surface (Wang et al,2019).

Measurements of impedance that are frequency-dependent enable the understanding of the electrical properties of the functionalized surface and the kinetics of interactions. Different frequencies unveil alterations in the dielectric characteristics of the sensor's interface, the distribution of charges, and the nature of binding interactions ( Gitler et al,2017). The strategic selection of the most informative frequencies and optimization of the frequency range can significantly enhance the sensor's sensitivity and specificity, transforming it into a potent tool for label-free, real-time detection of breast cancer cells.

Figure 7(a) highlights the contrast between Frequency Analysis and Real-Time Enhanced Surface Functionalization (R-TESF), showcasing the potential advantages of the latter in evaluating surfaces across diverse frequencies. The temporal considerations and real-time capabilities of these methods are elucidated in Figure 7(b), where a comparison is drawn between Frequency Analysis and Real-Time (RT) methodologies (Qin et al,2020).

In the context of the impedimetric sensor, augmented by polydopamine nanoparticles for the label-free detection of breast cancer cells, specificity analysis emerges as a critical aspect of the Real-Time Enhanced Surface Functionalization (R-TESF) technique. The assessment focuses on the sensor's ability to discern and selectively respond to breast cancer cells, while concurrently suppressing reactions to irrelevant chemicals or potential confounding variables. The accuracy and reliability of the sensor in clinical applications hinge significantly on its specificity (Verwilst et al, 2018).

Typically, sensors undergo testing with a diverse array of samples, including breast cancer cells, healthy cells, and suspected interfering chemicals, to determine their specificity. The sensor's proficiency in distinguishing between breast cancer cells and non-target elements is gauged by detecting impedance changes and analyzing the sensor's response pattern. Achieving high specificity, characterized by low cross-reactivity with unrelated compounds, is imperative for accurately identifying breast cancer cells within complex biological samples (Kim et al, 2020).

Validating the sensor's suitability for clinical use necessitates a thorough specificity analysis, confirming its capacity to deliver precise and dependable label-free detection of breast cancer cells with minimal false-positive or false-negative outcomes. Figure 8(a) underscores the contribution of R-TESF to enhancing surface modification specificity by comparing Specificity Analysis with R-TESF. Meanwhile, Figure 8(b) delves into the roles of Specificity Analysis and the Real-Time (RT) approach in achieving specificity within surface functionalization processes (Zhang et al, 2020).

The assessment of the Real-Time Enhanced Surface Functionalization (R-TESF) technique, particularly in the context of an impedimetric sensor supported by polydopamine nanoparticles for label-free breast cancer cell detection, heavily relies on accuracy analysis. The primary objective is to quantitatively measure the reliability and precision of the sensor's detection output. Accuracy is paramount as it directly influences the sensor's dependability in medical settings (Ganesh et al,2016). The investigation into accuracy entails a thorough examination of the sensor's responses to both breast cancer cells and non-target chemicals, comparing the obtained readings with reference values or ground truth. The closer the sensor's readings align with the actual values, the higher the reliability (Chang et al,2021).

Ensuring accurate detection of breast cancer cells and the ability to differentiate them from background noise is critical for the sensor to be trustworthy in providing precise results. To validate the sensor's performance and guarantee its suitability for real-world clinical applications, an assessment of its accuracy is imperative for early diagnosis and effective therapy (Aziz et al,2019). Figure 9(a) compares accuracy analysis with real-time enhanced surface functionalization (R-TESF), illustrating how the latter contributes to increased precision during surface modification. Figure 9(b) further explains the roles each plays in achieving the ultimate goal of precise surface functionalization processes (Dong et al,2020). In the same vein, the evaluation of Real-Time Enhanced Surface Functionalization (R-TESF) includes a focus on resource efficiency when applied to an impedimetric sensor supported by polydopamine nanoparticles for label-free breast cancer cell detection. Resource efficiency, in this context, emphasizes the effective utilization of inputs such as polydopamine nanoparticles and reagents to accomplish detection tasks ( Derkus et al,2013). R-TESF's reliance on resource efficiency ensures cost-effective installation with minimal environmental impact, enhancing the sensor's economic viability. By reducing resource waste and maximizing usage, the sensor becomes more widely applicable in clinical and research settings, aligning with sustainability goals in the medical and scientific community (Sung et al, 2020). Figure 10(a) offers a detailed comparison of Efficiency Analysis and R-TESF, highlighting the potential gains in efficiency provided by R-TESF in surface modification. Figure 10(b) further contrasts Efficiency Analysis with Real-Time (RT) approaches, exploring how both contribute to maximizing productivity while minimizing waste in surface functionalization procedures (Rauf et al, 2021).

## 5. Conclusion

The utilization of polydopamine nanoparticles to augment the functionality of an impedimetric sensor introduces a groundbreaking technique for label-free breast cancer cell detection, holding considerable promise in advancing early-stage cancer identification. This innovative approach addresses the imperative need for painless and sensitive cancer cell detection methods during their earliest and most treatable phases. However, it is essential to acknowledge the challenges inherent in this state-of-the-art technology.

The precise characterization and functionalization of polydopamine nanoparticles pose potential challenges that could impact the sensor's sensitivity, specificity, and signal-to-noise ratio. Nevertheless, the Real-Time Enhanced Surface Functionalization (R-TESF) approach emerges as a viable solution to enhance sensor functionality in real-time. The integration of machine learning methods and analytical models for processing impedance data becomes crucial in addressing these challenges.

The inherent selectivity of polydopamine nanoparticles allows them to target proteins associated with breast cancer, thereby improving the sensor's capacity to identify the disease in its early stages. This strategic approach successfully heightens the sensor's specificity, enabling it to differentiate cancer cell signatures from background noise. The incorporation of simulation analysis plays a vital role in validating and refining the method by elucidating its behavior under diverse conditions and parameters.

The convergence of experimental and computational approaches showcased in this study holds transformative potential not only for breast cancer diagnostics but also for the broader field of cancer research and diagnosis. The advent of non-invasive, highly sensitive tools for early-stage cancer detection could significantly enhance patient outcomes through timely intervention and targeted treatment regimens. This breakthrough device offers a glimpse into a future where such advancements become a reality.

## **Author Contributions**

B.D. and N.B. conceptualized, wrote, and reviewed the article.

## Acknowledgment

None declared.

## Competing financial interests

The authors have no conflict of interest.

## References

- Abedi, R., Raoof, J. B., Mohseni, M., & Hashkavayi, A. B. (2023). Development of a label-free impedimetric aptasensor for the detection of Acinetobacter baumannii bacteria. Analytical Biochemistry, 679, 115288.
- Alarfaj, N. A., El-Tohamy, M. F., & Oraby, H. (2018). New label-free ultrasensitive electrochemical immunosensor-based Au/MoS 2/rGO nanocomposites for CA 27-29 breast cancer antigen detection. New Journal of Chemistry, 42(13), 11046-11053.
- An, Y., Li, R., Zhang, F., & He, P. (2020). Magneto-mediated electrochemical sensor for simultaneous analysis of breast cancer exosomal proteins. Analytical chemistry, 92(7), 5404-5410.
- Ausó, E., Gómez-Vicente, V., & Esquiva, G. (2020). Biomarkers for Alzheimer's disease early diagnosis. Journal of Personalized Medicine, 10(3), 114.
- Aziz, A., Asif, M., Azeem, M., Ashraf, G., Wang, Z., Xiao, F., & Liu, H. (2019). Self-stacking of exfoliated charged nanosheets of LDHs and graphene as biosensor with real-time tracking of dopamine from live cells. Analytica chimica acta, 1047, 197-207.
- Bolat, G., Vural, O. A., Yaman, Y. T., & Abaci, S. (2021). Polydopamine nanoparticlesassisted impedimetric sensor towards label-free lung cancer cell detection. Materials Science and Engineering: C, 119, 111549.
- Campuzano, S.; Pedrero, M.; Pingarron (2017), J.M. Non-invasive breast cancer diagnosis through electrochemical biosensing at different molecular levels. Sensors, 17, 1993.

Chang, Y., Chen, Y., Shao, Y., Li, B., Wu, Y., Zhang, W., ... & Guo, G. (2021). Solid-phase microextraction integrated nanobiosensors for the serial detection of cytoplasmic dopamine in a single living cell. Biosensors and Bioelectronics, 175, 112915.

- Chen, F., Wu, Q., Song, D., Wang, X., Ma, P., & Sun, Y. (2019). Fe3O4@ PDA immune probe-based signal amplification in surface plasmon resonance (SPR) biosensing of human cardiac troponin I. Colloids and Surfaces B: Biointerfaces, 177, 105-111.
- Chen, L., Liu, X., & Chen, C. (2017). Impedimetric biosensor modified with hydrophilic material of tannic acid/polyethylene glycol and dopamine-assisted deposition for detection of breast cancer-related BRCA1 gene. Journal of Electroanalytical Chemistry, 791, 204-210.
- Chia, H. L., Sturala, J., Webster, R. D., & Pumera, M. (2021). Functionalized 2D germanene and silicene enzymatic system. Advanced Functional Materials, 31(16), 2011125.
- Derkus, B., Emregul, E., Yucesan, C., & Emregul, K. C. (2013). Myelin basic protein immunosensor for multiple sclerosis detection based upon label-free electrochemical impedance spectroscopy. Biosensors and Bioelectronics, 46. 53-60.
- Dong, H., Zhou, Y., Hao, Y., Zhao, L., Sun, S., Zhang, Y., ... & Xu, M. (2020). "Turn-on" ratiometric electrochemical detection of H2O2 in one drop of whole blood sample via a novel microelectrode sensor. Biosensors and Bioelectronics, 165, 112402.
- Esfandiari, M., Khodayari, M., Shojaee, M., Kamankesh, M., Esfandiari, B., & Mohajerzadeh, S. (2023). A laser-assisted electrochemical biosensor based on folic acid-functionalized tungsten disulfide nanosheets for label-free cancer cell detection. Sensors and Actuators B: Chemical, 381, 133443.
- Fan, T., Mao, Y., Liu, F., Zhang, W., Lin, J. S., Yin, J., ... & Jiang, Y. (2019). Label-free fluorescence detection of circulating microRNAs based on duplex-specific nuclease-assisted target recycling coupled with rolling circle amplification. Talanta, 200, 480-486.
- Feng, Y. G., Wang, X. Y., Wang, Z. W., Wang, A. J., Mei, L. P., Luo, X., & Feng, J. J. (2021). A label-free electrochemical immunosensor based on encapsulated signal molecules in mesoporous silica-coated gold nanorods for ultrasensitive assay of procalcitonin. Bioelectrochemistry, 140, 107753.
- Gajdosova, V., Lorencova, L., Kasak, P., & Tkac, J. (2020). Electrochemical nanobiosensors for detection of breast cancer biomarkers. Sensors, 20(14), 4022.
- Ganesh, H. V., Chow, A. M., & Kerman, K. (2016). Recent advances in biosensors for neurodegenerative disease detection. TrAC Trends in Analytical Chemistry, 79, 363-370.
- Gitler, A. D., Dhillon, P., & Shorter, J. (2017). Neurodegenerative disease: models, mechanisms, and a new hope. Disease models & mechanisms, 10(5), 499-502.
- Hassanpour, S., & Hasanzadeh, M. (2021). Label-free electrochemical-immunoassay of cancer biomarkers: Recent progress and challenges in the efficient diagnosis of cancer employing electroanalysis and based on point of care (POC). Microchemical Journal, 168, 106424.

Jeong, S., Park, M. J., Song, W., & Kim, H. S. (2020). Current immunoassay methods and their applications to clinically used biomarkers of breast cancer. Clinical biochemistry, 78, 43-57.

- Khorrami, S., Tavakoli, M., & Safari, E. (2019). Clinical value of serum S100A8/A9 and CA15-3 in the diagnosis of breast cancer. Iranian Journal of Pathology, 14(2), 104.
- Kilic, T., Valinhas, A. T. D. S., Wall, I., Renaud, P., & Carrara, S. (2018). Label-free detection of hypoxia-induced extracellular vesicle secretion from MCF-7 cells. Scientific reports, 8(1), 9402.
- Kim, K., & Park, C. B. (2020). Femtomolar sensing of Alzheimer's tau proteins by water oxidation-coupled photoelectrochemical platform. Biosensors and Bioelectronics, 154, 112075.
- Li, J., Sapkota, A., Kikuchi, D., Sakota, D., Maruyama, O., & Takei, M. (2018). Biosens. Bioelectron. 2009, 25(2), 306-312.
- Li, Y., Hu, M., Huang, X., Wang, M., He, L., Song, Y., ... & Du, M. (2020).
  Multicomponent zirconium-based metal-organic frameworks for impedimetric aptasensing of living cancer cells. Sensors and Actuators B:
  Chemical, 306, 127608.
- Li, Y., Wang, C., Li, Z., Wang, M., He, L., & Zhang, Z. (2020). Zirconium-porphyrin complex as novel nanocarrier for label-free impedimetric biosensing neuron-specific enolase. Sensors and Actuators B: Chemical, 314, 128090.
- Linh, N. D., Huyen, N. T. T., Dang, N. H., Piro, B., & Thu, V. T. (2023). Electrochemical interface based on polydopamine and gold nanoparticles/reduced graphene oxide for impedimetric detection of lung cancer cells. RSC advances, 13(15), 10082-10089.
- Linh, N. D., Huyen, N. T. T., Dang, N. H., Piro, B., & Thu, V. T. (2023). Electrochemical interface based on polydopamine and gold nanoparticles/reduced graphene oxide for impedimetric detection of lung cancer cells. RSC advances, 13(15), 10082-10089.
- Luo, L., Wang, L., Zeng, L., Wang, Y., Weng, Y., Liao, Y., ... & Chen, J. (2020). A ratiometric electrochemical DNA biosensor for detection of exosomal MicroRNA. Talanta, 207, 120298.
- Malla, P., Chen, G. C., Liao, H. P., Liu, C. H., & Wu, W. C. (2021). Label-free parathyroid hormone immunosensor using nanocomposite modified carbon electrode. Journal of Electroanalytical Chemistry, 880, 114917.
- Mohammadpour-Haratbar, A.; Mazinani, S.; Sharif, F.; Bazargan, A.M. ( 2022)

  Improving Nonenzymatic Biosensing Performance of Electrospun Carbon

  Nanofibers decorated with Ni/Co Particles via Oxidation. Appl. Biochem.

  Biotechnol.,194, 6, 2542
- Moura, S. L., Martín, C. G., Martí, M., & Pividori, M. I. (2020). Electrochemical immunosensing of nanovesicles as biomarkers for breast cancer. Biosensors and Bioelectronics, 150, 111882.
- Mujica, M. L., Rubianes, M. D., & Rivas, G. (2022). A multipurpose biocapture nanoplatform based on multiwalled-carbon nanotubes non-covalently functionalized with avidin: Analytical applications for the non-amplified and label-free impedimetric quantification of BRCA1. Sensors and Actuators B: Chemical, 357, 131304.
- Naresh, V., & Lee, N. (2021). A review on biosensors and recent development of nanostructured materials-enabled biosensors. Sensors, 21(4), 1109.

Pourmadadi, M.; Yazdian, F.; Ghorbanian, S.; Shamsabadipour, A.; Khandel, E.;

Rashedi, H.; Rahdar, A.; Díez-Pascual ( 2022), A.M.Construction of

Aptamer-Based Nanobiosensor for Breast Cancer Biomarkers Detection

Utilizing g-C3N4/Magnetic Nano-Structure. Biosensors, 12, 921.

- Qin, J., Kim, S., Cho, M., & Lee, Y. (2020). Hierarchical and ultra-sensitive amyloid beta oligomer sensor for practical applications. Chemical Engineering Journal, 401. 126055.
- Quan, J.; Wang, Y.; Zhang, J.; Huang, K.; Wang, X.; Jiang, H. Aptamer ( 2021)
  Embedded Arch-Cruciform DNA Assemblies on 2-D VS2Scaffolds for
  Sensitive Detection of Breast Cancer Cells. Biosensors,11, 378
- Rahimzadeh, Z.; Naghib, S.M.; Askari, E.; Molaabasi, F.; Sadr, A.; Zare, Y.; Afsharpad, M.; Rhee, K.Y. (2021) A rapid nanobiosensingplatform based on herceptin-conjugated graphene for ultrasensitive detection of circulating tumor cells in early breast cancer. Nanotechnol. Rev., 10, 744–753.
- Rahman, S. A., Al–Marzouki, A., Otim, M., Khayat, N. E. H. K., Yousef, R., & Rahman, P. (2019). Awareness about breast cancer and breast self-examination among female students at the University of Sharjah: a cross-sectional study. Asian Pacific journal of cancer prevention: APJCP, 20(6), 1901.
- Rahmati, Z., Roushani, M., & Hosseini, H. (2021). Thionine functionalized hollow N-doped carbon nanoboxes: as a high-performance substrate for fabrication of label-free electrochemical aptasensor toward ultrasensitive detection of carcinoembryonic antigen. Journal of Electroanalytical Chemistry, 903, 115858.
- Rauf, S., Lahcen, A. A., Aljedaibi, A., Beduk, T., de Oliveira Filho, J. I., & Salama, K. N. (2021). Gold nanostructured laser-scribed graphene: A new electrochemical biosensing platform for potential point-of-care testing of disease biomarkers. Biosensors and Bioelectronics. 180. 113116.
- Reddy, K. K., Bandal, H., Satyanarayana, M., Goud, K. Y., Gobi, K. V., Jayaramudu, T., ... & Kim, H. (2020). Recent trends in electrochemical sensors for vital biomedical markers using hybrid nanostructured materials. Advanced Science, 7(13), 1902980.
- Reindl, M., Linington, C., Brehm, U., Egg, R., Dilitz, E., Deisenhammer, F., ... & Berger, T. (1999). Antibodies against the myelin oligodendrocyte glycoprotein and the myelin basic protein in multiple sclerosis and other neurological diseases: a comparative study. Brain, 122(11), 2047-2056.
- Sadighbayan, D., Sadighbayan, K., Khosroushahi, A. Y., & Hasanzadeh, M. (2019).
  Recent advances on the DNA-based electrochemical biosensing of cancer biomarkers: Analytical approach. TrAC Trends in Analytical Chemistry, 119, 115609.
- Sahraei, N., Mazloum-Ardakani, M., Khoshroo, A., Hoseynidokht, F., Mohiti, J., & Moradi, A. (2022). Electrochemical system designed on a paper platform as a label-free immunosensor for cancer derived exosomes based on a mesoporous carbon foam-ternary nanocomposite. Journal of Electroanalytical Chemistry, 920, 116590.
- Sanko, V., & Kuralay, F. (2023). Label-Free Electrochemical Biosensor Platforms for Cancer Diagnosis: Recent Achievements and Challenges. Biosensors, 13(3), 333.

Sharifi, M.; Hasan, A.; Attar, F.; Taghizadeh, A.; Falahati, M. (2020) Development of point-of-care nanobiosensors for breast cancers diagnosis. Talanta, 217, 121091

- Siegel, R. L., Miller, K. D., & Jemal, A. (2019). Cancer statistics, 2019. CA: a cancer journal for clinicians, 69(1), 7-34.
- Sierra, J., Marrugo-Ramirez, J., Rodriguez-Trujillo, R., Mir, M., & Samitier, J. (2020).
  Sensor-integrated microfluidic approaches for liquid biopsies applications in early detection of cancer. Sensors, 20(5), 1317.
- Song, Z., Zhou, Y., Han, X., Qin, J., & Tang, X. (2021). Recent advances in enzymelessbased electrochemical sensors to diagnose neurodegenerative diseases. Journal of Materials Chemistry B, 9(5), 1175-1188.
- Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 71(3), 209-249.
- Suthar, J., Prieto-Simon, B., Williams, G. R., & Guldin, S. (2022). Dual-mode and label-free detection of exosomes from plasma using an electrochemical quartz crystal microbalance with dissipation monitoring. Analytical Chemistry, 94(5), 2465-2475.
- Suthar, J., Prieto-Simon, B., Williams, G. R., & Guldin, S. (2022). Dual-mode and labelfree detection of exosomes from plasma using an electrochemical quartz crystal microbalance with dissipation monitoring. Analytical Chemistry, 94(5), 2465-2475.
- Teymourian, H., Barfidokht, A., & Wang, J. (2020). Electrochemical glucose sensors in diabetes management: An updated review (2010–2020). Chemical Society Reviews, 49(21), 7671-7709.
- Torre, L.A.; Islami, F.; Siegel, R.L.; Ward, E.M.; Jemal ( 2017), A. Global Cancer in Women: Burden and TrendsGlobal Cancer in Women:Burden and Trends.

  Cancer Epidemiol. Biomark. Prev., 26, 444–457
- Verwilst, P., Kim, H. S., Kim, S., Kang, C., & Kim, J. S. (2018). Shedding light on tau protein aggregation: the progress in developing highly selective fluorophores. Chemical Society Reviews, 47(7), 2249-2265.
- Wang, L., Zhang, Y., Cheng, C., Liu, X., Jiang, H., & Wang, X. (2015). Highly sensitive electrochemical biosensor for evaluation of oxidative stress based on the nanointerface of graphene nanocomposites blended with gold, Fe3O4, and platinum nanoparticles. ACS applied materials & interfaces, 7(33), 18441-18449.
- Won, H. J., Robby, A. I., Jhon, H. S., In, I., Ryu, J. H., & Park, S. Y. (2020). Wireless label-free electrochemical detection of cancer cells by MnO2-Decorated polymer dots. Sensors and Actuators B: Chemical, 320, 128391.
- Won, H. J., Robby, A. I., Jhon, H. S., In, I., Ryu, J. H., & Park, S. Y. (2020). Wireless label-free electrochemical detection of cancer cells by MnO2-Decorated polymer dots. Sensors and Actuators B: Chemical, 320, 128391.
- Yadav, A. K., Verma, D., Kumar, A., Bhatt, A. N., & Solanki, P. R. (2023). Biocompatible epoxysilane substituted polymer-based nano biosensing platform for label-free detection of cancer biomarker SP17 in patient serum samples.

  International Journal of Biological Macromolecules, 239, 124325.

Yaman, Y. T., Vural, O. A., Bolat, G., & Abaci, S. (2023). Fabrication of trastuzumab conjugated curcumin nanoparticles based impedimetric cytosensor for the cancer cell detection. Microchemical Journal, 191, 108773.

- Zare, Y.; Rhee, K.Y. (2022) Effect of contact resistance on the electrical conductivity of polymer graphene nanocomposites to optimize the biosensors detecting breast cancer cells. Sci. Rep., 12, 1–10.
- Zhang, C., Liu, Z., Zhang, L., Zhu, A., Liao, F., Wan, J., ... & Tian, Y. (2020). A Robust

  Au– C≡ C Functionalized Surface: Toward Real-Time Mapping and Accurate

  Quantification of Fe2+ in the Brains of Live AD Mouse Models. Angewandte

  Chemie International Edition, 59(46), 20499-20507.
- Zhang, F., Fan, L., Liu, Z., Han, Y., & Guo, Y. (2022). A label-free electrochemical aptasensor for the detection of cancer antigen 125 based on nickel hexacyanoferrate nanocubes/polydopamine functionalized graphene.

  Journal of Electroanalytical Chemistry, 918, 116424.
- Zhu, L.; Zhao, J.; Guo, Z.; Liu, Y.; Chen, H.; Chen, Z.; He, N. (2021) Applications of Aptamer-Bound Nanomaterials in Cancer Therapy.Biosensors ,11, 344.