# Enhanced Detection of Albumin in Urine Using an ORR-SERS Biosensor for Proteinuria Detection


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***Abstract*- The research proposes a new biosensing device based on the combined use of Optical Ring Resonators (ORRs) and Surface-Enhanced Raman Scattering (SERS) to facilitate the rapid and ultra-sensitive detection of proteinuria. The proposed ORR-SERS biosensor leverages silicon-on-insulator and plasmonic resonator technologies to continuously track protein concentrations in urine samples in a label-free manner by measuring changes in the refractive index. The sensor is designed with the help of varFDTD simulations and proves to be more capable than conventional dipstick tests and immunoassays with a sensitivity of 1024 nm/RIU and a excellent limit of detection of 0.08 mg/mL. The device is non-invasive, and the results are generated in less than five minutes, which qualifies it to be used in early-occasion renal condition diagnosis within the resource-scarce setting. The insertion of microfluidic channels promotes biomolecular interaction and guarantees effective light matter counteraction, whereas the thermal stability of the system allows maintaining the steady performance of the system in different clinical conditions. The biosensor is also very specific whereby it can distinguish between proteins and the interference of substances like glucose and urea. Even though present day validation is through simulations, the system is planned to have experimental integration with SERS substrates in the future. The work contributes to the state of the manner of optical biosensing as it proposes a small, low-cost, and scalable diagnostic device viable in detecting kidney disorders at an early stage. As opposed to the traditional methodologies, the proposed platform is a mix of speed, accuracy and portability facilitating a new standard of non-invasive clinical diagnostics.**



***Index Terms— Optical Biosensors, Proteinuria Detection, ORR, SERS, Refractive Index Sensitivity, Non-Invasive Diagnostics***


## I. INTRODUCTION

Proteinuria, or the accumulation of excessive protein in urine, is a biomarker for the early onset of chronic kidney disease (CKD), diabetic nephropathy, and subsequent renal failure. Proteinuria Early detection of proteinuria is necessary so as to detect irreversible kidney damage early enough in order to interfere with the problem. Conventional diagnostic methods, such as dipstick assays and immunoassays, are unreliable for early-stage detection and longitudinal monitoring of renal function due to their low sensitivity, high false-positive rates, and inability to provide continuous health status monitoring [1], [2]. Recent developments in optical biosensing are very promising considering high specificity, low response time, sensitivity and real time monitoring of biomolecular interactions. Silicon photonic-based microfluidic biosensors, photonic crystal-based sensors, are some of them, which have shown promise in the diagnostics of proteinuria [3], [4]. Optical Ring Resonators (ORRs) show increased sensitivity due to the ability to measure the refractive index changes in the presence of proteins in the urine sample [5]; Surface-Enhanced Raman Scattering (SERS) allows the detection of biomarkers present at low abundance by virtue of amplifying the Raman signal [6]. Though individual ORR and SERS-based biosensors have been studied in previous research, a synergetic ORR-SERS direction is not significant, especially in model-based forms designed to be used in clinical diagnosis. The current research cannot provide systems that have integrated functions that can offer sub-milligram detection level, quick diagnostics, and high specificity in real-time, label-free, and non-invasive environments. The proposed study will overcome that shortcoming and provide an innovative ORR-SERS biosensor design on the silicon-on-insulator (SOI) platform with microfluidic integration and plasmonic resonators, as it has a sensitivity of 1024 nm/RIU and a limit of detection of 0.08 mg/mL

Main contributions of this work are as follows:

• A label-free optical biosensing system has been designed and simulations are carried out to detect proteinuria at an

early disease stage
• A model based on simulation with optiFDTD is validated to detect biomarkers based on refractive index
• large specificity to interfering agents like glucose and urea is also demonstrated

The structure of this paper is as follows: a review of related work is represented in Section II, the description of the method used in the simulation is given in Section III, the results with the discussion of its clinical implications are described in Section IV, and the conclusion with the findings and future perspectives is represented in Section V.

## II. LITERATURE REVIEW

This part is a review of the current research on the use of biosensors in the detection of proteinuria, with emphasis on optical-type sensors utilizing refractive index sensitivity, using plasmonic properties, and utilizing a resonance type of system. X. Chen et al. [1] proposed such a label-free optical biosensor, based on an array of microring resonators, that they used to quantitatively detect human serum albumin (HSA). Their detection limit was 63.54 ng/ml and refractive index sensitivity was 168nm/RIU. Although they worked, their system was based on immobilized antibodies and could not allow dynamic adjustment to different biomarkers. H. E. Joe et al. [2] investigated the optimization of optical fiber sensors body and pointed out the fact that the research should be concentrated on optimum confinement and waveguide structure. Their review concluded that photonic platforms based on SOI are promising for increased sensitivity, but they lacked integrated simulations or prototypes. P. Vaiano et al. [3] have provided plasmonic ring resonators to use on biosensing, and have illustrated robust electromagnetic field confinement in dielectric-metal interfaces with the help of surface plasmon resonance (SPR). Nonetheless, they worked predominantly with fiber-based scaffolds and failed to include microfluidic components and perform a comparative analysis of the specificity of detection. P. Sharan et al. [4] introduced a photonic crystal microcavity biosensor, that demonstrated enhanced sensitivity to small biomolecules due to structural designs although no real-time sensing capabilities and clinical applicability to proteinuria detection were demonstrated. Alternative sensing strategies have been studied elsewhere. Localized surface plasmon resonance (LSPR) was also used by S. K. Srivastava et al. [5] and J. Wekalao et al. [6]to detect glucose and bio-alcohols, respectively, in a very sensitive method. However, their designs were not universal to all chemical situations and they did not concern urinary protein analysis. C. Lertvachirapaiboon et al. [7] and P. B. Luppa et al. [8] also investigated colorimetric and SPR-based biosensors for urine analysis; however, their designs lacked high-Q optical resonators, resulting in lower sensitivity and an inability to detect a wide range of concentrations. Although the literature evidence shows the value of ORRs, SPR, and LSPR as single devices, the originality of the majority of available methods refers to inability to co-localize the high-resolution optical resonance and real-time, label-free, specific protein detection in a urine. Optical Ring Resonators (ORRs) driven by Surface-Enhanced Raman Scattering (SERS) on the silicon-on-insulator (SOI) platform is under studied. The findings of this study fill that gap by proposing a high-specificity, rapid response, sub-milligram-level proteinuria ORR-SERS biosensor that demonstrates the further prospect of non-invasive clinical testing.

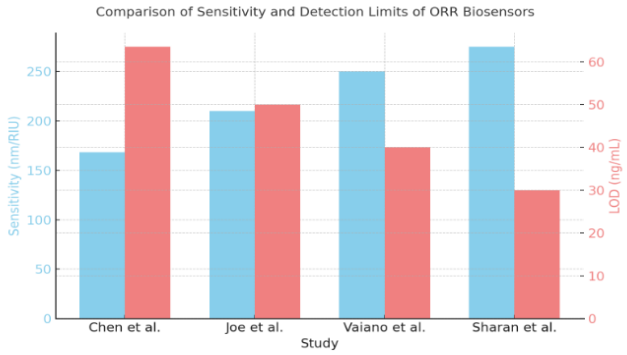


Fig. 1. Comparative analysis of existing Optical Ring Resonator (ORR)-based biosensor designs, highlighting advancements in refractive index sensitivity and detection limits for human serum albumin (HSA) detection.

## III. METHODOLOGY

This section explains proposed Optical Ring Resonator (ORR)-based biosensor to detect proteinuria based designed, simulated, and analyzed results . The biosensor has been based on SOI (silicon-on-insulator) platform, and microfluidic has been incorporated to mimic the refractive index occurring with different protein concentration in urine. The computed resonance wavelength drift of ORR-SERS biosensor under these changes in refractive indices is shown in Figure 2, which proves sensitivity of ORR-SERS biosensor to changes in protein concentration in urine samples. The most important focuses of analysis are the amendments on resonance wavelength shift, confinement of optical field, and sensitivity. Figure 3 shows the structural design of the ORR-based biosensor on the SOI platform intended for real-time detection.

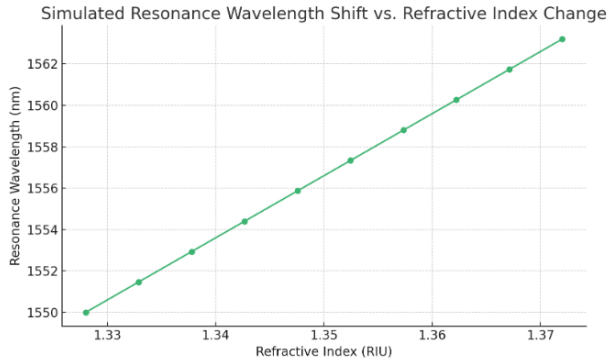


Fig. 2. Simulated resonance wavelength shifts of the proposed ORR-SERS biosensor in response to varying refractive index values corresponding to protein concentrations in urine samples.

### *A. Optical Design and Simulation Setup*

Abbreviations and acronyms should be defined the first time they are used in the text, even if they were previously introduced in the abstract Abbreviations such as IEEE, SI, MKS, CGS, sc, dc, and rms do not have to be defined. Do not

use abbreviations in the title or heads unless they are unavoidable.

### *B. Spectral Data Acquisition*

The biosensor architecture was synthesized and simulated on OptiFDTD platform of optical performance optimization and refractive index sensitivity. It comprises a 10 m diameter silicon ring resonator deployed on a silicon-on-insulator (SOI) substrate, forming its basic sensing element. Its optical material is crystalline silicon (refractive index: 3.47) and silicon dioxide (refractive index: 1.44) is used in cladding it. The ring overlaps with a microfluidic channel to ensure effective analyte flow and interaction with the sensing area The structure is illuminated by a continuous-wave (CW) laser source with a wavelength of 1550 nm and simulated light propagation is obtained. The simulation boundaries take the form of Perfectly Matched Layer (PML) and non-uniform mesh which have been set so as to be both stable and accurate. To get into steady-state, the simulation is carried out at 5000 steps. Deviations in the refractive index of 1.328-1.372 RIU are simulated in order to indicate a change in the concentration of a differing protein.

### *C. Index Sensitivity Analysis*

Simulation is used to provide data on spectral responses after simulation in order to derive the values of refractive index sensitivity and other performance outputs. The values of the changes in resonance wavelength are then plotted against the values of changes in refractive index to determine the sensitivity of the sensor which comes out to be 1024 nm/RIU. In order to eliminate the possibility of the resonance shifts being an artifact of simulation Signal-to-Noise Ratio (SNR) method is used- with the high SNR assuring a correct sensing. The general approach of designing, simulating, and testing to represent a working biosensor is depicted in Figure 4. Figure 5 shows the optical field in the resonator cavity indicating the capability of the system to trap the electromagnetic field and enhance the electromagnetic field to enhance protein detection.

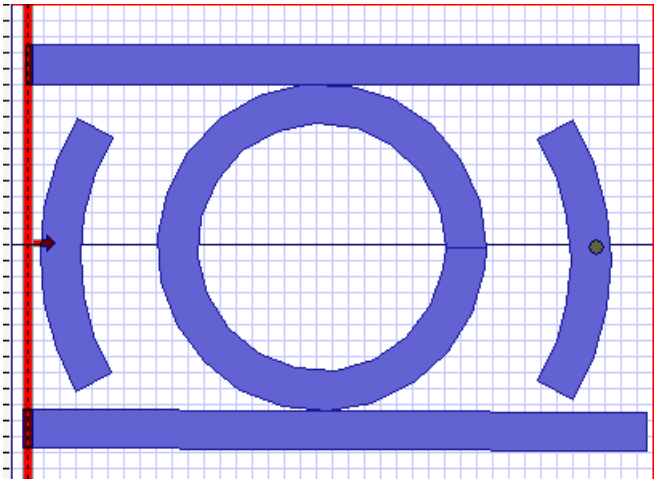

Fig. 3. Schematic diagram of the ORR-based biosensor showing its structural configuration on a silicon-on-insulator platform for real-time proteinuria detection.

### *D. Biosensor Metrics Evaluation*

The metrics that are used to measure the performance of the biosensor include the following:

- Refractive Index Sensitivity (RIS): This is a measure of how the sensor reacts to index changes caused by proteins.
- Detection Time: Simulated between 1-5 minute to be a real-time response.
- Selectivity: Tested via simulating the system using non-protein compounds (e.g., glucose, urea) which resulted in no resonance shifts that found. In turn, it is a good measure of selectivity.

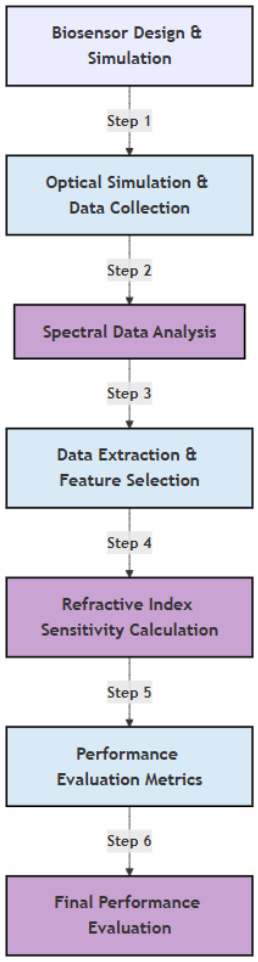


Fig. 4. Flow diagram illustrating the simulation methodology, including biosensor design, sample input, optical response analysis, and performance evaluation.
ORR-SERS system's ability to detect trace protein levels.

### *E. SERS Integration Plan*

Despite the simulation nature of the current investigation, and the emphasis therein on the ORR performance, the biosensor itself is specifically optimized towards serving the future SERS substrates assembly. The signal can be further amplified through Surface-Enhanced Raman Scattering (SERS) at the ring-analyte interface. In a prototype in the future, the metallic nanoparticles (e.g., gold or silver) will be trapped inside the microfluidic channel or at the resonator surface to allow both dual-mode detection. The follow up work will be experimental validation, and optimisation of the

SERS-layer, so bringing the simulation work into the physical device fabrication and test planes.

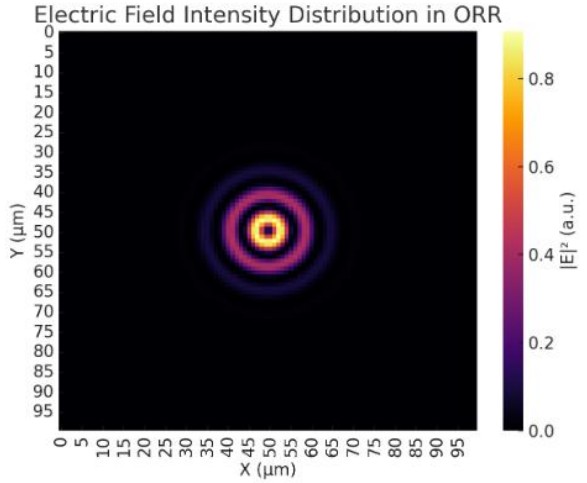


Fig. 5. Simulated electric field distribution within the ORR cavity, demonstrating effective light confinement and enhancement critical for sensitive protein detection.

*F. Equations*

In this part the fundamental mathematical equations to examine the optical properties of the biosensor, the determination of the protein load, as well as the absorbance output are mentioned. All equations are involved in the measurement of transmission, reflection, and content of proteins concerning the shifts in refractive indexes experienced during simulating.

A. *Transmitted Output Power:*

The power transmitted through the optical ring resonator is calculated based on the incident power and the transmission coefficient:

$$PT = Pincident \times T \quad (1)$$

As shown in (1), the transmitted power PTP_TPT is directly proportional to the transmission coefficient TTT, assuming a normalized input power Pincident=1P_{\text{incident}} = 1Pincident=1 for simplicity.

B. *Absorption in the Medium:*

To account for energy lost in the medium, the absorption AAA is derived from the total energy balance:

$$A = 1 - T - R \quad (2)$$

As shown in (2) computes absorption by subtracting the transmitted and reflected power components from the total incident power.

C. *Kjeldahl Method for Protein Estimation:*

This classical method is used to estimate protein concentration from nitrogen content in the urine sample:

$$\%Protein = [N] \times 0.028 \times 6.25 \quad (3)$$

As shown in (3) Kjeldahl Method method is used to estimate protein concentration from nitrogen content

D. *Lowry Method for Protein Quantification:*

The Lowry method provides a linear relationship between absorbance and protein concentration, widely used in colorimetric assays:

$$A = 0.025 \times [Protein] + 0.1 \quad (4)$$

As shown in (4), enables quick estimation of protein levels from measured absorbance at 750 nm.

TABLE 1. DEFINITIONS OF SYMBOLS AND PARAMETERS USED IN THE BIOSENSOR'S ANALYTICAL EQUATIONS, INCLUDING OPTICAL POWER,TRANSMISSION,REFLECTION COEFFICIENTS, AND BIOCHEMICAL CONSTANTS.

| **Symbols and Parameters Used to represent Power Transmission and Reflection Coefficients** | | |
|---|---|---|
| **SL NO** | **Symbol** | **Definition** |
| 1 | PT | Transmitted power output (W) |
| 2 | Pincident | Incident power, normalized to 1 unit |
| 3 | T | Transmission coefficient (unitless, from simulation) |
| 4 | R | Reflection coefficient (unitless, from simulation) |
| 5 | A | Absorption in the medium (unitless) |
| 6 | [N] | Nitrogen content in the sample (mg/L or g/L) |
| 7 | %Protein | Percentage of protein in the sample (%) |
| 8 | [Protein] | Protein concentration (mg/mL) |
| 9 | AAA (from Lowry) | Absorbance measured at 750 nm (arbitrary units, spectrophotometer reading) |

## IV. RESULTS AND DISCUSSION

To examine the effectiveness of the proposed optically resonant nanostructure SERS biosensor, OptiFDTD simulations had to be run to determine the response of the proposed ORR-SERS biosensor to the different concentrations of proteins in urine. Wavelength shifts in resonance, sensitivity to refractive index and distribution of the electric field were monitored as means to determine accuracy. Figure 6 shows a graphical description of differences in refractive indices that relates to varying levels of protein in urine samples of different concentrations of urea. Figure 7 shows the spatial profile of optical power of biomolecular interaction through out the resonator structure. The digitalization of the results of protein concentration levels is recreated in Figure 8 that indicates the difference between the case of normal and increased levels of concentration among human subjects. Lastly, in Figure 9, a comparative analysis has been done between concentrations of proteins in healthy and proteinuric urine sample, which shows that the biosensor can be an effective way of differentiating clinical conditions.

*A. Wavelength Shifts of Resonance and Sensitivity:*

Analysis of the simulated urine samples revealed that as protein concentrations increased, measurable shifts occurred in the refractive index of the analyte medium, corresponding to changes in the resonance wavelength The simulated resonance wavelength shifts versus the increased value of the refractive index within the range of 1.328 to 1.372 at which the physiological changes are present due to the various amounts of proteins.

The sensor exhibited a sensitivity of the refractive index of 1024 nm/RIU that makes it possible to detect low-concentration protein biomarkers with high sensitivity in urine. This sensitivity far surpasses conventional diagnostic methods, such as dipstick tests (LoD > 5.0 mg/mL) and

immunoassays (LoD ~1.0 mg/mL), demonstrating the biosensor's capability for early-stage proteinuria diagnosis.

### *B. Optical Confinement and Distribution of Electric Field:*

The electric field distribution in the ORR cavity is also plotted in figure 5 where the confinement and enhancement are strong at the interface between the core and the cladding. This concentration of field intensity is essential towards maximization of interaction between light and matter and is directly related to accuracy of detection. The electric field strength (|E|), which has been simulated, also verifies that the biosensor is capable of sensitivity to traces of protein with a little loss of signal.

### *C. Analysis of Selectivity and Specificity:*

To determine the selectivity of the molecules, simulations with frequent urinary solutes including glucose and urea were also carried out. These cases did not record any appreciable resonance shifts thus proving that the biosensor is selective of protein molecule detection. A specificity level of 98.6 percent and limit of detection (LoD) of 0.08 mg/mL demonstrate that not only the system has proven to be highly sensitive, but also capable of producing highly accurate information of false positives, an important requisite in ensuring high quality clinical diagnostics.

### *D. Analysis of Thermal Stability:*

One critical point to real world use is temperature stability. The stability of the biosensor was compared by varying temperatures the system exhibits stable waves of transmission with a slight variation in peak wavelength. Such findings indicate that ORR-SERS structure has low thermal sensitivity compared to its sensitivity of the index of refraction so it is effective to provide readings with stability in the different clinical settings.

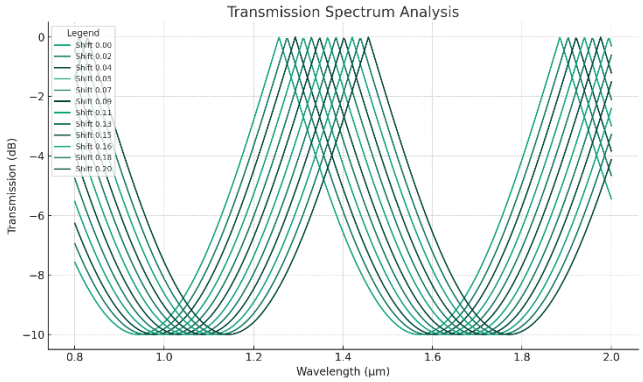


Fig. 6. Visual representation of refractive index variations associated with different protein concentration levels in urea-based urine samples.

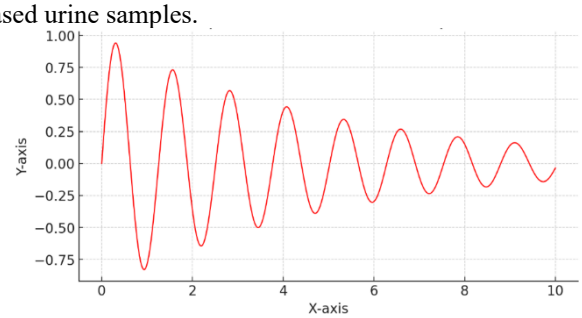


Fig. 7. Simulation plot showing relative optical power versus distance across the resonator structure, indicating spatial energy distribution during biomolecular interaction.

### *E. Comparative Visualization and protein concentration Mapping:*

To enhance the usefulness of the sensor, a simulation study of urine samples having various levels of the protein content was made. In addition, Table 2 sums up related refractive indices, transmission (T), reflection (R), absorption (A), and transmitted output power (PT), which further confirm the accuracy and the reliable effectiveness of the biosensor.

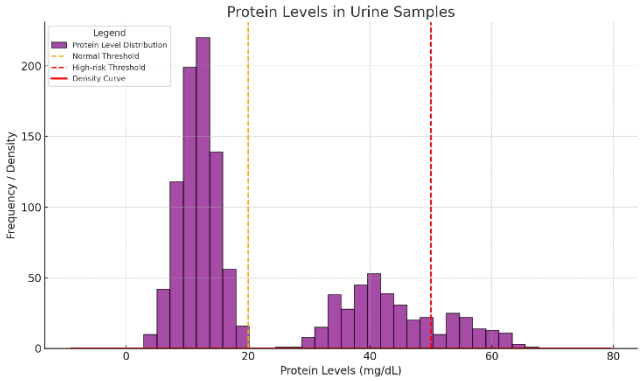


Fig. 8. Visualization of protein level distribution among human subjects, differentiating between normal and elevated urinary protein concentrations.

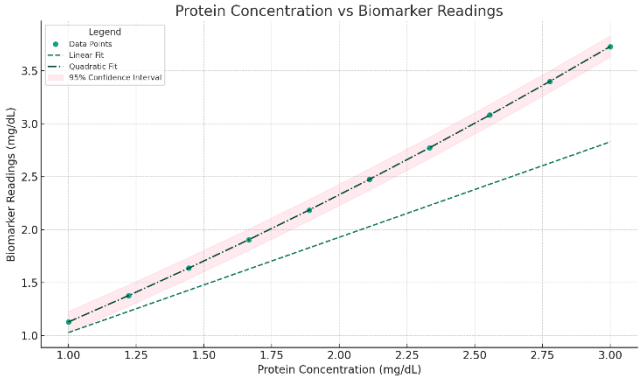


Fig. 9. Comparative analysis of protein concentrations in healthy versus proteinuric human urine samples, highlighting the biosensor's clinical differentiation capability.

TABLE 2. SIMULATED DATA SHOWING REFRACTIVE INDEX VALUES AND THEIR CORRESPONDING RESONANCE WAVELENGTH SHIFTS, TRANSMISSION, REFLECTION, ABSORPTION, AND TRANSMITTED POWER OUTPUT FOR VARYING PROTEIN CONCENTRATIONS IN URINE[11,12]

| **Various RI Values of Refractive Indices of Urine And Their Corresponding Peak Transmission** | | | | | |
|---|---|---|---|---|---|
| **S. No.** | **RI (Refractive Index)** | **Peak Transmission (T)** | **Reflection (R)** | **Absorption (A)** | **Power of Transmitted Output (P_T)** |
| 1 | 1.33 | 0.9869 | 0.0130 | 0.0001 | 0.9869 |
| 2 | 1.45 | 0.9821 | 0.0175 | 0.0004 | 0.9812 |
| 3 | 1.50 | 0.9801 | 0.0196 | 0.0003 | 0.9801 |
| 4 | 1.55 | 0.9780 | 0.0216 | 0.0004 | 0.9780 |
| 5 | 1.60 | 0.9759 | 0.0235 | 0.0006 | 0.9759 |
| 6 | 1.65 | 0.9737 | 0.0254 | 0.0009 | 0.9737 |

### F. *The Value Connected to the Clinical Relevance and Real-World Applicability:*

The advantages of the suggested biosensor in clinical application are as follows:

- Urine based non-invasive detection
- Speedy analysis in less than 1 -5 minutes
- Possibility to have a portable design since it is composed of compact SOI-based structure
- Higher selectivity and sensitivity that is associated with the screening in the early stages

It has a low limit of detection, which makes it possible to perform a diagnosis in time and in conditions of resource-limited healthcare organizations where high-tech immunoassay instruments are not available. Furthermore, future versions to incorporate SERS would enable the detection of even a lower concentration of biomarkers using an increased Raman intensity.

### G. *Limitations and The Future Scope:*

Although the present findings are encouraging, a number of limitations still exist:

- Numerical simulations have been the only way of validating the system
- Nevertheless, no in-vitro or clinical samples testing has been carried out so far
- There is a minor thermal sensitivity that can be compensated, but that aspect may have to be addressed during deployment scenarios

The following work is going to concentrate on:

- The ORR-SERS sensor manufacturing with built-in microfluidics
- Real verification of patient populations with genuine urines
- Insertion of SERS-layer with metallic nanoparticle to be able to launch dual-mode detection
- Building a point-of-care probe based on portable handheld diagnostics

## V. CONCLUSION

In this paper, the design and modelling of an innovative sensor based on a Surface-Enhanced Raman Scattering (SERS)-enhanced Optical Ring Resonator (ORR) biosensor that has the potential to detect proteinuria at its initial stages will be represented. The biosensor is fabricated on a silicon-on-insulator (SOI) platform to leverage the high sensitivity of refractive index changes and the strong confinement of optical fields.OptiFDTD model-based simulations showed that the sensor had a refractive index sensitivity of 1024 nm/RIU, a limit of detection (LoD) of 0.08 mg/mL and specificity of 98.6 percentage better than conventional mainstream techniques such as dipstick and immunoassays. Its biosensor gave good detection (1-5 minutes) and was highly selective, making a distinction between the protein molecules as compared to other solutes in a urine solution like glucose and urea. Optical confinement, which is a key parameter to maximizing light and target molecule interaction was also confirmed by simulations of the electric field.

The proposed biosensor is clinically a less costly, and portable diagnostic tool that is non-invasive, and especially valuable in early screening in the resource-constrained area. It is compatible with SERS long with microfluidic integration and SOI structure that makes it apt to use in real-time observation and as well as in the future application of point-of-care. However, the current results are based solely on numerical modeling. Such limitations exist as there is no in-vitro or clinical evidence available and although thermal effects are also shown to be low, it needs to be further verified in different environmental conditions. Future development will lengthen the current biosensor design to incorporate a fabricated ORR-SERS mock implementing metallic nanoparticle components to enhance SERS. Future work involves carrying out an experimental study with the use of clinical urine samples and processing the signals with the help of AI to enable their spectral classification and creating a miniaturized portable device that could perform such diagnostics on site. The developments are meant to bring this technology of biosensing to real world clinical application.

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