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Self-Assembled Nanostructured Substrates for ATR-SEIRA Applications

by

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SCUOLA POLITECNICA E DELLE SCIENZE DI BASE

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Dedication

I humbly dedicate my Ph. D. thesis to my beloved Father Abdul Manaf, and my beloved mother Shamskhat Bibi, and beloved Piana Ghulam Murtaza whose unwavering support and encouragement made this academic journey possible. Their guidance and sacrifices have been my pillars of strength, and without their selfless contributions, this achievement would not have been possible.

SELF-ASSEMBLED NANOSTRUCTURED SUBSTRATES FOR ATR-SEIRA APPLICATIONS

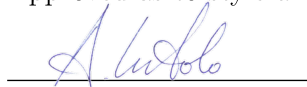
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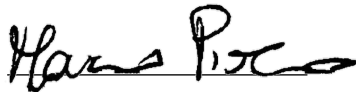
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Candidate's declaration

I hereby declare that this thesis submitted to obtain the academic degree of Philosophiæ Doctor (Ph.D.) in Information Technology and Electrical Engineering is my own unaided work, that I have not used other than the sources indicated, and that all direct and indirect sources are acknowledged as references.

Napoli, March 11, 2024

A handwritten signature in dark ink, reading "Babar Ali", enclosed within a thin black rectangular border. Below the signature, there is a horizontal line.

Babar ALi

Abstract

Infrared (IR) spectroscopy is a versatile tool for point-of-care systems such as biological sensors. Due to small the intrinsic cross-section of a molecular vibration which limits the sensitivity of detection, but it can be addressed in several ways, including improving the IR light source, forming extremely sensitive IR detection devices, by taking advantage of the SEIRA (Surface Enhanced Infrared Absorption) phenomenon. The first two solutions are costlier in comparison to the SERIA phenomenon because its inexpensive and efficient way to improve the interaction of light with matter. The key objective of this study was to develop, fabricate, and analyze a low-cost plasmonic substrate for attenuated total reflectance SEIRA (ATR-SEIRA). This is a highly effective method for detecting even the smallest quantities, including conformational flexibility, and improving the vibrational modes of compounds. We have used a FEM (finite element method) based wave optics module in the frequency domain (COMSOL Multiphysics) to numerically analyze plasmonic nanostructure based on a periodic gold Nano disk array to determine its sensitivity and tunability. We developed a numerical model using the Otto configuration to simulate the effect of a SEIRA substrate in ATR-SEIRA instrumentation's (by including the "prism-effect" in the model). To validate the numerical method, self-assembled Nano-spheres lithography fabrication based SEIRA substrates are characterized using the scanning electron microscope (SEM) and ATR-FTIR (ATR-Fourier Transform IR) spectrometer. Furthermore, we have demonstrated the ATR-SEIRA phenomenon by fictionalizing the SEIRA substrate with a self-assembled bio-absorbed analyte 4-aminothiophenol (4-ATP) as monolayer. The outcomes obtained are in good agreement with the numerical analysis. As a standard benchmark, we have evaluated the performance of our realized SEIRA substrate by calculating the amplification factor, which amounts to 10^5 . These results confirm the accuracy of numerical modelling and show that the proposed low-cost ATR-SEIRA substrates are repeatable, homogeneous, and can increase sensitivity. Overall, the proposed SEIRA substrate can be available tool for performing IR absorption spectral analyses, offering better performance compared to standard FTIR approaches.

Key Words: IR, ATR-SEIRA, ATR-FTIR, self-assembled substrates, SEM, biological sensing.

Sintesi in lingua italiana

La spettroscopia a infrarossi (IR) è uno strumento versatile per i sistemi point-of-care come i sensori biologici. A causa della piccola sezione trasversale intrinseca di una vibrazione molecolare che limita la sensibilità di rilevamento, ma può essere affrontata in diversi modi, incluso il miglioramento della sorgente luminosa IR, formando dispositivi di rilevamento IR estremamente sensibili, sfruttando il SEIRA (Surface fenomeno dell'assorbimento infrarosso migliorato). Le prime due soluzioni sono più costose rispetto al fenomeno SERIA perché rappresentano un modo economico ed efficiente per migliorare l'interazione della luce con la materia. L'obiettivo chiave di questo studio era sviluppare, fabbricare e analizzare un substrato plasmonico a basso costo per la riflettanza totale attenuata SEIRA (ATR-SEIRA). Questo è un metodo altamente efficace per rilevare anche le quantità più piccole, inclusa la flessibilità conformazionale, e migliorare le modalità vibrazionali dei composti. Abbiamo utilizzato un modulo di ottica d'onda basato su FEM (metodo degli elementi finiti) nel dominio della frequenza (COMSOL Multifisica) per analizzare numericamente la nanostruttura plasmonica basata su un Nano disk array periodico d'oro per determinarne la sensibilità e la sintonizzabilità. Abbiamo sviluppato un modello numerico utilizzando la configurazione Otto per simulare l'effetto di un substrato SEIRA nella strumentazione ATR-SEIRA (inclusendo l'effetto prisma nel modello). Per convalidare il metodo numerico, i substrati SEIRA basati sulla fabbricazione di litografia di nanosfere autoassemblate sono caratterizzati utilizzando il microscopio elettronico a scansione (SEM) e lo spettrometro ATR-FTIR (ATR-Trasformata di Fourier IR). Inoltre, abbiamo dimostrato il fenomeno ATR-SEIRA romanzando il substrato SEIRA con un analita bioassorbito autoassemblato 4-amminotiofenolo (4-ATP) come monostrato. I risultati ottenuti sono in buon accordo con l'analisi numerica. Come punto di riferimento standard, abbiamo valutato le prestazioni del nostro substrato SEIRA realizzato calcolando il fattore di amplificazione, che ammonta a 10^5 . Questi risultati confermano l'accuratezza della modellazione numerica e mostrano che i substrati ATR-SEIRA a basso costo proposti sono ripetibili, omogenei e possono aumentare la sensibilità. Nel complesso, il substrato SEIRA proposto può essere uno strumento disponibile per eseguire analisi spettrali di assorbimento IR, offrendo prestazioni migliori rispetto agli approcci FTIR.

standard.

Parole Chiave: IR, ATR-SEIRA, ATR-FTIR, substrati auto-assemblati, rilevamento biologico.

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List of Acronyms

IR	Infrared
SEIRA	Surface-Enhanced IR Absorption
FTIR	Fourier Transform IR
ATR	Attenuated Total Reflectance
FEM	Finite Element Method
SEIRA	Surface-Enhanced IR Absorption
4-ATP	4-AminothiophenoL
SPPs	Surface Plasmon Polaritons
LSPR	Localized Surface Plasmon Resonance
SEM	Scanning Electron Microscopy
GND	Gold Nano Disks
EF	Enhancement Factor
EM	Electromagnetic
PC	Personal Computer
UATR	Universal ATR
HATR	Horizontal ATR
OPD	Optical Path Difference

ZPD	Zero Path Difference
CsI	Cesium Iodide
KBr	Potassium Bromide
Ge	Germanium
DTGS	Deuterated TriGlycine Sulfate
PE	Polyethylene
MCT	Mercury Cadmium Telluride
IRE	Internal Reflection Element
SP	Surface Plasmons
SER	Surface Enhanced Raman
PoC	Point of Care
SL	Surface Lattice
PE	Plasmon Enhanced
FWHM	Full Width at Half Maximum
PMMA	Polymethyl Methacrylate
EBL	Electron Beam Lithography
ML	Machine Learning
AI	Artificial Intelligence
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
PDEs	Partial Differential Equations
WOM	Wave Optics Module
THD	Time-Harmonic Domain
E	Electric-Field
PML	Perfect Matching Layers

BC	Boundary Condition
ewfd	Electromagnetic Waves, Frequency Domain
S11	Scattering Parameters (Reflection Coefficient at the Input Port)
abs	Absolute
E_0	Electric Mode Field Amplitude
NSL	Nano-Sphere Lithography
BSE	Back-Scattered Electrons
SE	Secondary Electrons
EDS	Energy Dispersive X-ray Spectroscopy
TD	Top-Down
BU	Bottom-Up
NA	Nanoantenna

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Introduction

Biosensors have attracted significant interest and investment over the last decade in numerous applications, including medical analysis, healthcare, pharmaceutical control and development, food safety, environmental monitoring, agriculture, defense, and security. They are compatible with a variety of point-of-care systems, including those for water quality, forensics, and medicine delivery. They are useful for ensuring the accurate identification of analytes, even in small sample quantities, due to their ability to interact with high-affinity biomolecules. Biosensors have recently been included in quick detection kits in response to the COVID-19 pandemic. By employing optical read-out approaches, plasmonic-based biological sensors have the ability to achieve excellent sensitivity as well as specificity in the identification of chemicals. In actuality, surface plasmon-polaritons (SPPs) provide substantial field confinement as well as enhancement as a result of the communal oscillations of an electron cloud associated with an incident electromagnetic field at the metal/dielectric interaction. Additionally, a dielectric material's reflection index affects the SP frequency. Therefore, SP can be a valuable tool for improving the absorption characteristics of an analyte as well as monitoring the alteration of the refraction index caused by its presence. The key objective of a biological biosensor is to improve an optical transducer's effectiveness in terms of sensitivity, fast reaction time, repeatability, and minimal identification constraints, even down to specific molecule identification. Hence, the surface is designed to simply couple the light coming in with any wave orientation in order to improve the interaction between the electromagnetic evanescent field and the implanted molecule. This leads to the near-field being spatially limited at the metal nanostructures' extremities due to the lightning-rod impact. Based on this, a method called localized surface plasmon resonance (LSPR) biological sensing may be a real-time, label-free, and extremely sensitive technique in comparison to other traditional biochemical tests. As an alternative to conventional SPPs sensors, it is appropriate for sensing the minor deviation

from the surrounding medium refraction index caused by the adsorbed molecules near the nanostructures. Apart from LSPR sensing, this work adds to a novel method of improving the interaction between a cross-section of biomolecules in the promising infrared range, which is home to the functional categories and chemical fingerprints of any living cell. Moreover, surface nanostructures show significant promise in overcoming the weak association cross-sections that traditional Raman, as well as IR spectroscopies, suffer from, which usually occur between the nanometer biomolecules and the micro-metric dimension of the incoming light. Surface engineering is crucial in augmenting the near electromagnetic field for surface-enhanced spectroscopic approaches, particularly when the nanostructures are positioned closely, resulting in the gap effect. In addition, enhanced near-electromagnetic field constraints can be supported by the substrate through creative design. More precisely, gap plasmon interactions in a metal-insulator configuration can be enhanced to reinforce the local confinement. The near-field enhancement of plasmonic nanoantennas is achieved through the combination of lightning and nanodisks, as well as gap interactions at the antenna hotspots. The interaction between molecules positioned at the hotspots as well as the amplified near-electromagnetic fields is advantageous for SEIRA spectroscopy. The resonant SEIRA is represented by the asymmetric patterns that are produced when the antenna design parameters (diameter, gap, and thickness) are adjusted to produce plasmonic resonances.

This Ph.D. thesis focuses on developing, fabricating, and optically characterizing a gold Nano disk-based structure to improve the near electromagnetic fields locally at the disk gap. This thesis explores the development of a self-assembling SEIRA-active substrate using a closed-packed array structure based on Nano disks. This study's objective is to enhance the interaction between evanescent waves and molecular vibrations by using SEIRA nanostructures. To characterize the spectral properties of the SEIRA substrate, a Nano disks array-based structure is patterned onto a glass substrate and analyzed using an FTIR-ATR system. As a numerical analysis tool, COMSOL is used to evaluate various characteristics of the SEIRA substrate, including model stability, geometrical parameter effects, plasmonic tunability, and performance. Moreover, the numerical analysis provides a physical understanding of the factors affecting the self-assembled substrate's SEIRA response. In order to adjust the spectral overlap between the antenna's plasmonic resonance, the geometric parameters are changed. These include the diameter (D), thickness (t_m), and gaps (G) between gold nanodisks. The outcomes of this study present an innovative approach for enhanced detection of trace chemicals and demonstrate the potential of the SEIRA substrate to boost the sensitivity of FTIR spectroscopy as ATR-coupled FTIR measurements. Subsequently, an analysis of the morphology and performance of the SEIRA substrate was conducted using SEM. The findings revealed the formation of a uni-

form, well-ordered nanostructure featuring nanometric gaps, which, according to the numerical simulation, host strong electromagnetic field enhancements. ATR and FTIR spectral characterizations are used in order to assess the performance of the fabricated substrates and compare the results with the numerical predictions. These results confirm the correctness of the numerical modeling and reveal that the proposed cost-effective ATR-SEIRA substrates were repeatable, homogeneous, and suitable to provide a boost of sensitivity up to 10^5 . There are five chapters in the thesis manuscript organization. This thesis follows the four main skills that were learned in order to implement SEIRA detection using advanced plasmonic nanostructures to address the IR absorption features of liquid and gas analytes: numerical simulation, spectral and morphological characterization, and data analysis.

Chapter 1 introduces spectroscopy using an IR spectrometer. This chapter provides a thorough explanation of an IR spectrometer. An apparatus used to measure a substance's IR spectrum is an IR spectrometer. The primary topics covered in this chapter include measurement optimization, IR spectroscopy, the electromagnetic spectrum, and the IR spectrometer. It is an intricate apparatus that analyses the structure and characteristics of molecules using the concepts of the electromagnetic spectrum. The three primary parts of an infrared spectrometer are a monochromator, a detector, and a source. IR light is emitted by the light source, usually a tungsten lamp, and is subsequently filtered by the monochromator. The monochromator functions as a selective wavelength filter, allowing only certain wavelengths of light to pass through. It is extensively employed in materials research, biology, chemistry, the pharmaceutical business, and environmental monitoring. In a variety of scientific domains, IR spectrometers have become essential instruments due to their capacity to furnish comprehensive details regarding the chemical composition of a material. The light is directed toward the sample after it has been filtered. The molecules in the sample absorb light at distinct wavelengths based on their molecular composition. The detector generates a spectrum that depicts the absorption properties of the sample by measuring the intensity of light at each wavelength. The final section provides an explanation of ATR-FTIR integrated spectroscopy.

Chapter 2 gives a general review of plasmon theory and introduces a global theoretical foundation for localized surface plasmons—polaritons in particular. The features of the most common materials utilized in plasmonic applications, such as noble metals, will be discussed. A few plasmonic biosensor generalizations will be discussed. Surface-enhanced sensing concepts and materials are presented. IR spectroscopy methods, such as surface-enhanced IR spectroscopies, are described in depth. Particular focus will be placed on the structure and com-

position of the substrates that serve SEIRA. The final portion of Chapter 2 will be devoted to providing an overview of the most recent discoveries in SEIRA sensing, due to the breadth of plasmonic-based applications.

Chapter 3 will focus on the design and optimization of plasmonic SEIRA substrates, and it will primarily deal with the design of the structure using COMSOL Multiphysics (finite element technique) simulations, which will also describe the periodic arrays of gold Nano disks (GND).

Chapter 4 explains the SEIRA substrate fabrication method, procedure, and morphological analysis (metrology such as SEM). In last, the deposition of the absorbed analyte on the SEIRA active substrate.

Chapter 5 describes the ATR-FTIR characterization of the proposed GND-based SEIRA substrate (as fabrication procedures explained in Chapter 4) in terms of ATR measurement in the existence and absence of an absorbed analyte (4-ATP). An optical characterization of the constructed antennas will next be performed using an FTIR spectrometer. To determine the sensitivity capability of our proposed GND-based SEIRA substrate, we calculated the SEIRA gain and SEIRA EF at different sample positions on the fabricated sample for repeatability and uniformity confirmation of the results. While in next we carried out a numerical fitting analysis of the experimental results in the last section. Based on the experiment and the simulated SEIRA EF, we have achieved 2.83×10^5 and 4.25×10^5 , respectively. It deals with the proof-of-concept of a SEIRA demonstration to detect analytes such as biomolecules in solution. Based on the acquired understanding from numerical approaches and the optical characterizations, the surface-enhanced sensing with Au-based plasmonic nanostructures is successfully proven and is showing some promising results that match the SEIRA state-of-art. The fabricated antennas will be then optically characterized via a FTIR spectrometer.

Experimental analysis of the SEIRA response demonstrates that a hierarchical approach can provide cost-effective SEIRA substrates with superior performances with respect to the simpler single-layer configurations. The experimental and numerical research that has been provided may offer a general strategy for improving the biosensing applications' use of ATR FTIR when combined with SEIRA. Using the powerful SEIRA activity in conjunction with any standard FTIR spectrometer allows for exceptional performance in sensor applications.

The conclusions are described in Chapter 6.

Chapter 1

Infrared Spectroscopy: Principle, Instruments, and Applications

Infrared (IR) radiation is a type of electromagnetic (EM) radiation that has longer wavelengths than visible light. Due to its special qualities, it is useful in many areas, such as heat treatment, medical imaging, security, thermography, and remote sensing. With the increasing comprehension of IR radiation, novel and inventive uses of this fascinating type of light are anticipated. The analytical spectrometers receive a wealth of molecular data from the IR spectral range. By measuring IR radiation's interaction with matter, vibrational spectroscopy (or IR) identifies how it absorbs, emits, or reflects. IR spectroscopy has been acknowledged as a non-destructive, label-free, extremely sensitive, and specific analytical technique since the middle of the 20th century. A strong method that offers important information about the chemical composition and arrangement of molecules is IR spectroscopy. It is used for complicated mixture and material analysis in the chemical, physical, biological, and industrial domains as well as in bio-medicine, materials science, and biotechnology. Scientists can learn important details about the composition and chemical characteristics of molecules by comprehending the fundamentals and uses of IR spectroscopy. In recent decades, tremendous technological advances in novel photo-detectors and optical components have helped IR spectroscopy become one of the most popular experimental tools, which provide a wide range of structural information about a compound. Compared to other spectroscopic instruments, IR spectroscopy is inexpensive, robust, and less costly to use [1].

1.1 Infrared Spectroscopy

William Weber Coblentz [47] realized the potential of IR light in chemical research in the early 1900s after learning that IR light interacts with matter. The first IR spectra were made by Coblentz, who also obtained the information required to characterize a variety of substances. A commercially feasible IR spectrometer was first difficult to develop, but one was eventually released in the 1940s. Throughout the 1900s, IR spectroscopy was constantly improved; Fourier Transform IR (FTIR) spectroscopy revolutionized the field around 1970, and ATR further enhanced it in the late 1980s¹. In the recent years, an ever-increasing demand to develop novel, low-cost, and rapid detection and identification biosensors platforms based on spectroscopic techniques has prompted significant pioneer research work on IR spectroscopic technique [48]. Among them is IR spectroscopy, which is used in a variety of fields including environmental monitoring, biomedical, pharmaceutical, food, and forensics analysis. It does this by detecting vibrations in molecules at particular frequencies. The fundamental equipment for IR spectroscopic instruments is now being continually enhanced and has been improved as a result of advancements in multiple technical sectors (see Figure 1.1).

Future applications of IR spectroscopy techniques may completely reshape several phases of clinical care, from screening to therapy monitoring [49]. Due to its capacity to distinguish between distinct IR active molecular entities, which enables both unanalytical and multianalyte observation, it is highly adaptable in oncological applications. To examine samples, an IR beam is used to induce inter-molecular bond vibrations. These vibrations, according to Beer-Lambert's law [50], will selectively absorb particular IR wavelengths based on the molecular bonding environment [51]. This makes it possible to swiftly and precisely identify and quantify a wide range of fingerprints that are relevant bio-molecules for illness detection. Moreover, advanced multivariate analysis methods can be used to distinguish between different disease states in patients and generate detailed bio-molecule "fingerprint" profiles from different patient sample kinds [52, 53].

1.2 Electromagnetic Spectrum

EM spectrum (as seen in Figure 1.2 is a comprehensive range of EM radiation, encompassing all frequencies of EM waves. Each of these waves has a different wavelength and frequency, and they all interact differently with matter. There

¹<https://www.bruker.com/it/products-and-solutions/infrared-and-raman/ft-ir-routine-spectrometer/what-is-ft-ir-spectroscopy.html>



Figure 1.1. Certain application scenarios that offer expanding market shares for IR spectroscopic instruments and in which IR spectroscopy is frequently used[1].

is no doubt that EM research plays a leading role in medical research and that the interaction between EM fields and biological systems has proven to be an effective method of research[54, 48, 55].

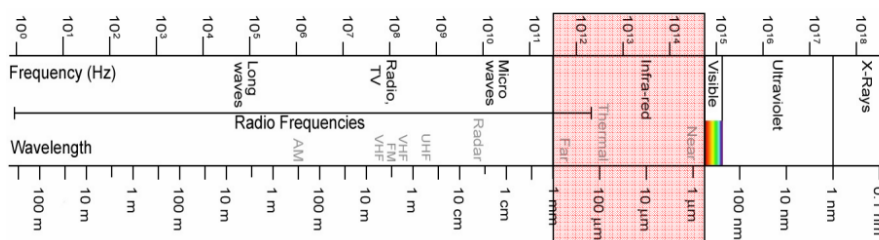


Figure 1.2. The EM spectrum showing the IR region [2]

The wavelength range from $0.78 \mu\text{m}$ to 1 mm is covered by the IR portion of the EM spectrum. A spectrum can be categorized into three types: near, mid, and far. On one side, it borders the visible zone, and on the other, the microwave region. Energy E and its relationship with frequency ν , which is the number of

waves per second and is measured in hertz (Hz), as in the Eq.(1.1) should be used to characterize all regions in the EM spectrum.

$$E = h\nu \quad (1.1)$$

where the Planck's constant ($6.63 \times 10^{-34} Js$) is represented by h . The units used in IR spectroscopy are wavenumber and frequency, respectively. By converting frequency (ν) to wavenumber ($\bar{\nu}$), we can change Eq.(1.1) in to Eq.(1.2).

$$E = hc\bar{\nu} \quad (1.2)$$

where c is ($3 \times 10^8 m/s$) the speed of light in a vacuum and $\bar{\nu}$ is measured in cm^{-1} . These equations teach us that a rise in energy corresponds to a rise in wavenumber. The advancement of biomedical technology has been greatly aided by the application of EM theory. The medical field benefits greatly from the usage of the EM spectrum and related light kinds. Over the ages, the application of the EM spectrum to bio-medicine has completely changed the way that medicine is practiced. There has been significant therapeutic and diagnostic benefit from the interaction of EM fields with biological systems. The interaction between EM fields and biological systems has been of great diagnostic and therapeutic value[56].

1.3 The IR Spectrometer

An IR spectrometer uses absorption, emission, or reflection to quantify the interaction of IR radiation with matter; IR spectra are used to identify chemical compounds or functional groups in solids, liquids, or gases. Spectrometers enable researchers and developers of innovative products in academia, chemicals, polymers, and pharmaceuticals to achieve superior performance and sample flexibility across the mid, near, and far IR ranges with a single device. This study employs the PerkinElmer spectrum 3 FTIR spectrometer as its instrument (see in Figure 1.3). The platform known as FTIR Spectrum 3 is small, highly flexible, and offers dependable, consistent, and problem-free operation.

The PerkinElmer spectrum 3-bench top FTIR instrument has been designed to provide high ordinate accuracy for measurements on optical components. The device can be linked to a personal computer (PC), a network, or other point-to-point connections. With the integrated spectrum IR software suite, you may adjust the obtained spectra and operate the device. The optical system is housed behind the instrument's main cover. The instrument's main cover is typically closed, however most maintenance procedures require that the cover be opened. The device can be used in single-beam, interferogram, or ratio mode. With an

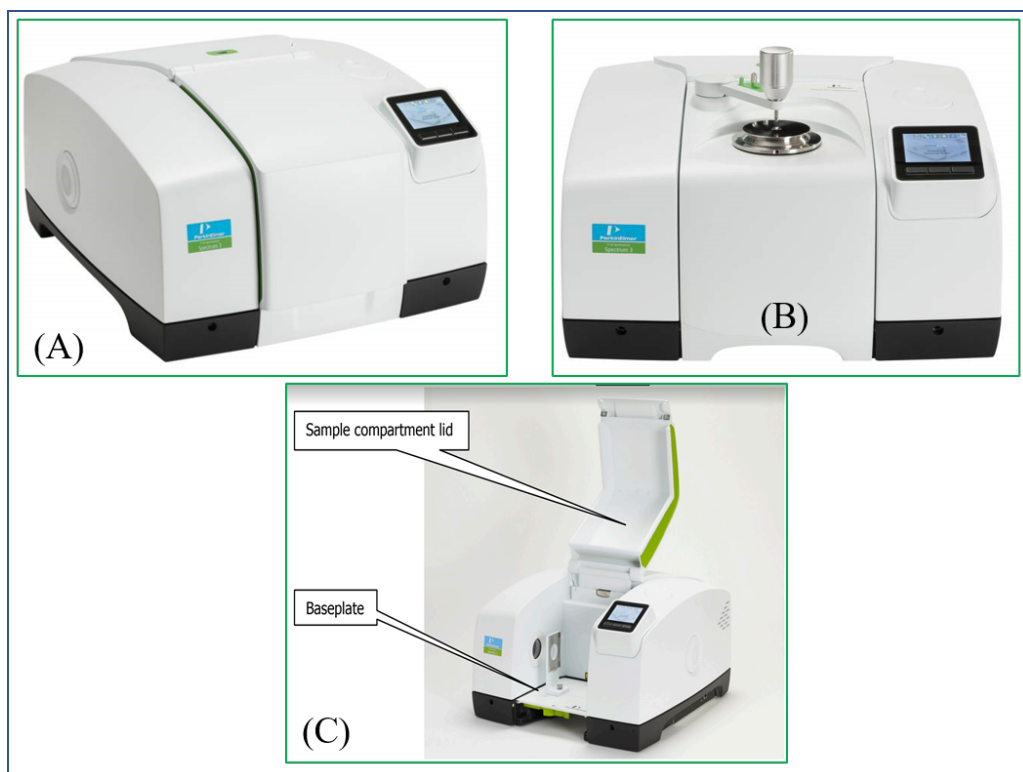


Figure 1.3. (A)Spectrum 3 FT-IR Spectrometer,(B)Spectrum 3 With UATR (C)Spectrum 3 sample compartment[3].

optimal resolution of 0.4, the optical system allows you to gather data over a whole range of 7800 to 350 cm^{-1} (1.28 to $28\text{ }\mu\text{m}$). A beam splitter stop (B-stop) and Jacquinot stop, also known as aperture stop are two variable, software-controlled apertures in the optical system (J-stop). As a baseline, a (lithium tantalate) IR detector. For the spectrum 3 Optical, a variety of specialized sampling tools are available, including the sample shuttle, the Universal ATR (UATR), and the Horizontal ATR (HATR). Moreover, the spectrometer can be modified for quick scanning. Figure 1.4 shows the PerkinElmer Spectrum 3 FT-IR spectrometer schematic.

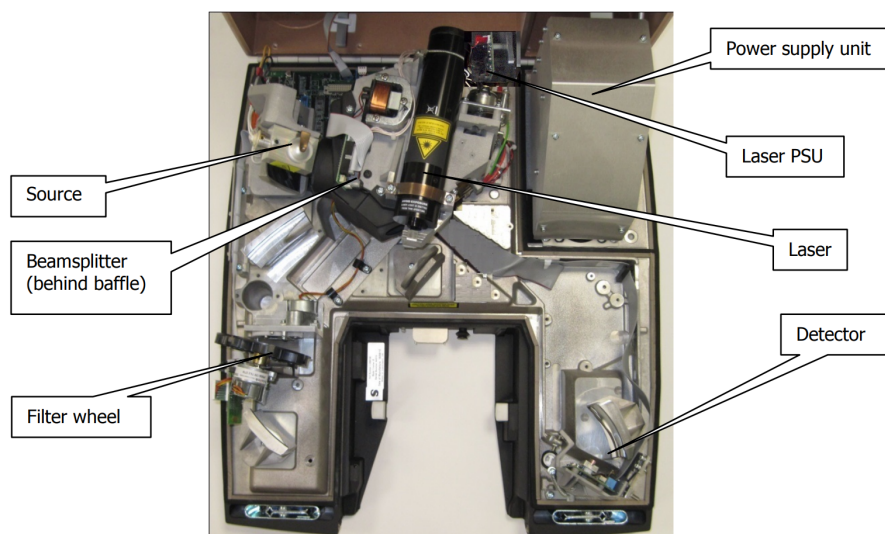


Figure 1.4. An FTIR spectrometer schematic [3].

1.3.1 Light Sources

A luminous blackbody source emits IR radiation, and the beam of radiation travels through an aperture to regulate the energy's amount. IR radiation falls among the range of light sources that can produce radiant energy in the EM spectrum. The simplest and least expensive IR source employed in older devices is an air-cooled source. It normally operates between 1100 and 1400 K . For some applications, sources that cool by air might not have enough IR intensity. The second type of infrared radiation generator is the Globar generator. It is made up of a silicon carbide rod that frequently reaches temperatures higher than 1400 K .

Due to its higher temperature, the Globar IR source emits more IR radiation than older air-cooled sources. An increase in radiation will result in decreased noise and a higher throughput [57]. Today, the most used IR light source is a Globar. According to IEC 60825-1, the spectrum 3 spectrometers are Class 1 laser products. A Class 2 Helium-Neon (HeNe) laser with a maximum output power of 1mW and a visible, continuous wave emission wavelength of 633 nm is found inside the optical module.

1.3.2 Interferometer

An interferometer is the brain of an FTIR spectrometer. An interferometer's function is to divide a light beam into two distinct streams of light and cause one of the light beams to travel a different distance from the other (this is known as optical path difference, or OPD; indicated by δ) [57]. Figure 1.5 depicts the operation of an experimental FTIR spectrometer, which uses a moveable mirror to drive a Michelson interferometer. "Spectral encoding" takes place when the IR wave penetrates the interferometer. For accurate wavelength measurement, control of the mirror position, and duration of data capture the interferometer requires a reference laser. The beam splitter is positioned at the vertex of the right angle and is angled at a 45° with respect to the two mirrors. The interferometer is made up of two mirrors that are positioned at a right angle to one another and are orientated perpendicularly. The incident beam is divided into two equal portions by the beam splitter. One portion travels from the translating mirror through the beam splitter. The remaining half of the beam is reflected by the stationary mirror. The incident beam is reflected by the translating mirror and the stationary mirror. After that, the two streams are merged again and directed toward the detector. If the beam splitter is positioned at the identical distance from the translating mirror as it is from the stationary mirror, then the two light beams will travel the same distance. ZPD, which is represented by Δ , is what is known as zero path difference. Mirror displacements and optical path difference have the following relationship (see in Eq.(1.3)):

$$\delta = 2\Delta \quad (1.3)$$

An OPD can be inserted between the two light beams by moving the translating mirror from its location in relation to the ZPD. The light reflected from the translating mirror will then reflect farther than the light reflected from the stationary mirror. A strong light beam will emerge from the interferometer if the light travels a certain wavelength longer and recombines to form a constructive wave pattern. Since light amplitudes are additive, the two light beams traveling between the stationary and translating mirrors will have amplitudes greater than the sum of their individual amplitudes.

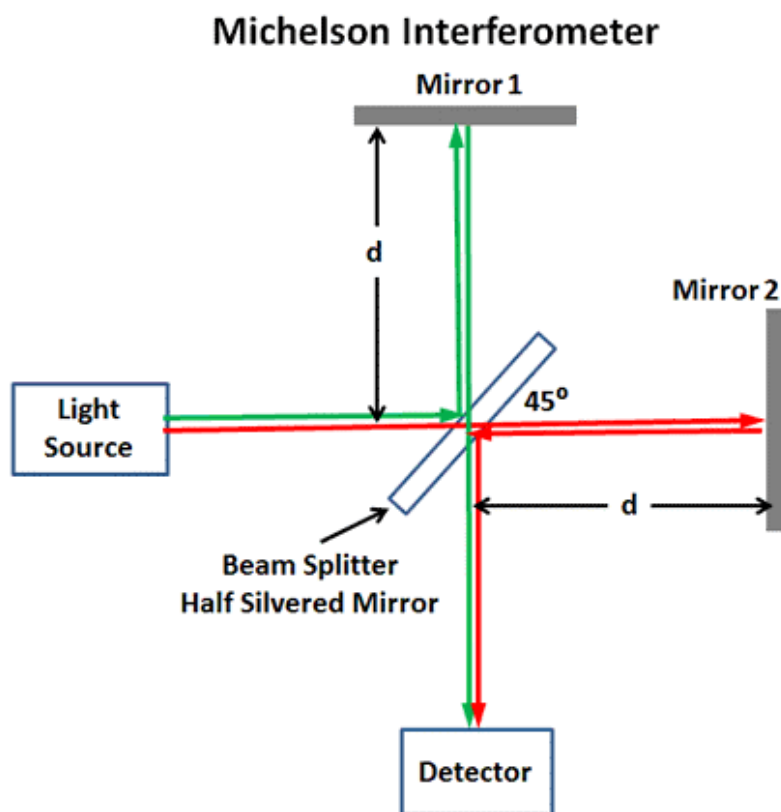


Figure 1.5. Schematic of Michelson interferometer [4]

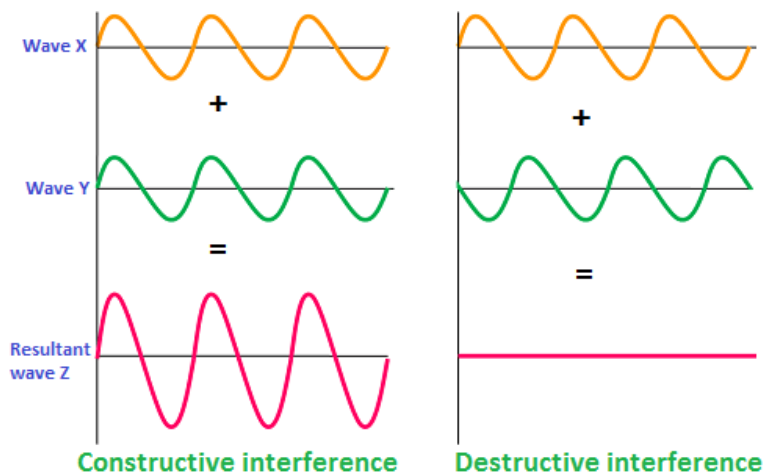


Figure 1.6. Patterns of interference for light going through an interferometer: both constructive and destructive [5].

$$\Delta = n\lambda \quad \text{when } n = 0, 1, 2, 3, \dots \quad (1.4)$$

A constructive wave sequence occurs when OPD equals multiples of λ , while ZPD corresponds to $n = 0$. Nevertheless, if the ZPD is $\frac{1}{4}\lambda$ out of phase, the OPD is going to combine to produce $\frac{1}{2}\lambda$, a destructive wave sequence (i.e., no or faint signal), as a result of Eq.(1.5):

$$\Delta = (n + \frac{1}{2})\lambda \quad \text{when } n = 0, 1, 2, 3, \dots \quad (1.5)$$

There are numerous magnified wave patterns that make up the interferometer that are seen in IR spectroscopy. Figure (1.7)) depicts an interferogram in its conventional form. The greatest spike in the interferogram is the central burst ZPD, which is the addition of the entire constructive wave intensities. The destructive wave trends are displayed in the wings, where the intensities cancel each other out to generate minimal or no signal. This is the signal that FTIR spectroscopy first picked up on. The interferogram is converted to a spectrum using the FT, a mathematical technique. By dividing the interferogram into sine waves for each light wavelength, the conventional spectrum is created.

Once at the detector, the signal undergoes a mathematical Fourier transformation, converting it from an expression of mirror pathway variations to a

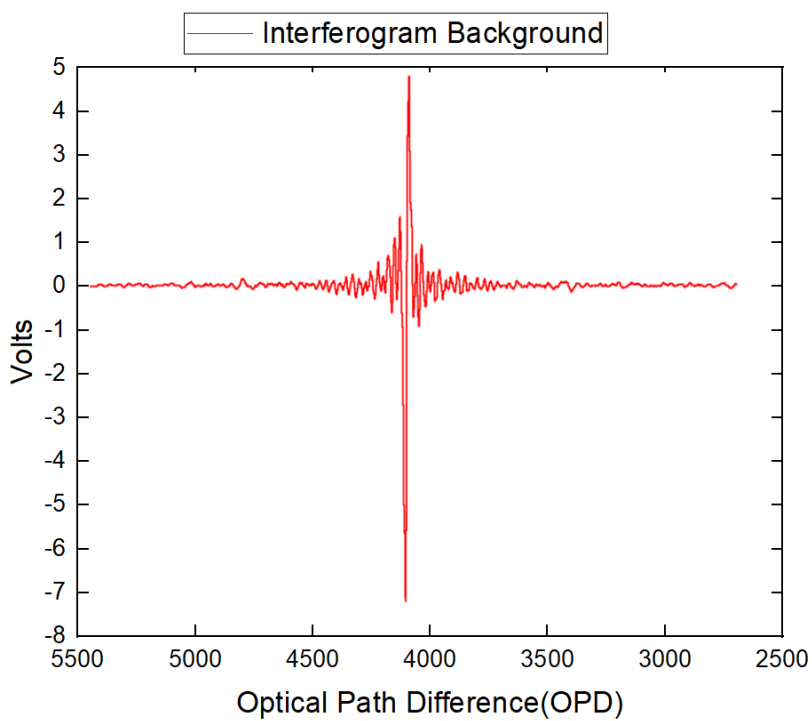


Figure 1.7. OPD is a function of voltage in an interferogram of the background was obtained. ZPD is the constructive wave with the largest amplitude [2].

function of wavelengths and wavenumbers. Depending on how the experiment was conducted, the translating mirror moves at a normal running mirror velocity of 0.475, 0.633, or 0.933 cm/s. The kind of detector used, which performs best in these operating conditions, accounts for the low mirror velocity. The PerkinElmer Spectrum 3 system features gold-coated first-surface optics with excellent reflectivity and an improved rotating Michelson interferometer for fast scanning that self-corrects for tilt and shear-induced variations in dynamic alignment. The PerkinElmer Spectrum 3 uses a proprietary Dynascan interferometer. It is inherently stable and doesn't require dynamic alignment modifications to make up for linear mirror mobility system flaws. An industry-proven interferometer mechanism incorporates a simple, noncritical bearing for unparalleled durability and dependability.

1.3.3 Beamsplitter

A tiny Germanium (Ge) film positioned amid two Potassium bromide (KBr) plates serves as the beam splitter in the mid-IR range; this type of beam splitter is commonly known as a KBr beamsplitter. It functions similarly to a silver mirror that is semitransparent and partially transmits and partially reflects the light source. The Ge is shielded from the environment by the KBr. For the IR beam between 4000cm^{-1} and 400 cm^{-1} , the KBr beamsplitter is transparent. Another potential beamsplitter is cesium iodide (CsI), which operates up to 200 cm^{-1} , lower wavenumbers than the KBr beamsplitter. The CsI, on the other hand, is a soft and very hygroscopic substance that, with time, has a tendency to fog over. It must be anticipated that a CsI beamsplitter will require replacement more frequently than a KBr beamsplitter [58]. The beamsplitter's lifespan is increased by shielding it from a humid environment and purging the spectrometer with dry air. There are two additional beamsplitter choices in the IR region at lower wavenumbers. While the conventional Mylar beamsplitter has been in operation since the 1960s, the solid substrate beamsplitter is a relatively new device, having been in operation since 1998. A very thin polyester film made of biaxially oriented polyethylene terephthalate (boPET) is marketed under the brand name "classic Mylar beamsplitter." As seen in Table 1.1, it can gather spectra in various low wavenumber zones depending on how thin it is. Not all of the specified ranges exhibit the same level of transparency in the Mylar[59]. The Mylar is less transparent at the low and high ends of the ranges indicated.

The Mylar beamsplitter has a number of serious drawbacks. One of the main drawbacks is the need for many beamsplitters with various Mylar thicknesses in order to capture spectra in the entire far IR region at optimal conditions with equal transparency [46] as shown in Figure 1.8, which was created using three distinct Mylar beamsplitters (each with a different thickness) to collect data

for the whole region of 500cm^{-1} - 50 cm^{-1} [6], displays the far IR spectrum of calcite. Another issue is that the Mylar beamsplitter is extremely susceptible to noise vibrations, including those coming from the GPG, because of how thin it is (necessary for purging the spectrometer for water vapors). The Mylar sheet is more vibration-sensitive the thinner it is. The Mylar beamsplitters are still among the most used beamsplitters for the far IR region, despite these issues. The Nicolet solid substrate beamsplitter is the second potential choice for a far IR beamsplitter. The solid substrate beamsplitter is a silicon wafer that is roughly 2 mm thick [60]. Because it is thicker than Mylar, it is less sensitive to noise vibration. Moreover, it only has one working area, which is 700cm^{-1} - 50 cm^{-1} .

With the same efficacy throughout the entire area. The amount of energy absorbed by the two kinds of beamsplitters is another distinction. Due to its greater thickness, the solid substrate may absorb more energy than a Mylar beamsplitter. So, while using the solid substrate beamsplitter, the energy input must be increased. Otherwise, the detector would not be able to adequately register enough output energy [61]. This was done using a Globar IR light source when an air-cooled light source would have sufficed for the Mylar beamsplitter. Next, combine the increased energy output of the Globar light source with the solid substrate beamsplitter in the experimental apparatus. Combining these factors allows for the possibility of obtaining far IR spectra with reduced interference from noise than has ever been described in the literature. Instead of three collections as seen in Figure 1.8, only one spectrum collection is required for the far IR area. It takes no longer than 30 seconds to manually switch beamsplitters from the mid IR to the far IR region. A beam-splitter changing mechanism was used by PerkinElmer in the Spectrum 3 FT-IR, which allowed for automatic switching between the near, mid, and far infrared beamsplitters without the need for manual user involvement. A beam-splitter adjusting system was employed by

Table 1.1. The relationship between PET film thickness and the IR spectrum range. (Reproduced from [46])

Thickness of Film (μm)	Range of Spectra cm^{-1}
6.25	80-450
12.5	40-220
25.5	20-100
50	12-50
100	8-25

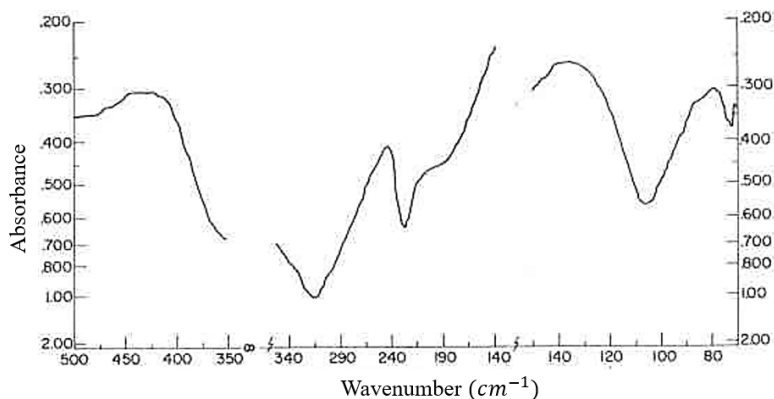


Figure 1.8. Calcite's far IR absorption spectra, as measured with Mylar beamsplitters in the vicinity of $500\text{--}50\text{ cm}^{-1}$. To collect this entire region, the identical sample must be collected three times using different Mylar beamsplitters. (replicating [6]).

PerkinElmer in the Spectrum 3 FT-IR, which allowed automated switching across the near, mid, and far infrared beamsplitters without the need for manual user involvement.

1.3.4 Sample Chamber

The real sample is placed into the sample chamber, where it is examined. Depending on the specifics of the project, either transmission or attenuated total reflection (ATR) spectroscopy will be used to characterize the samples. Samples must be in powder form or immersed in an inert substance to be collected using regular transmission methods. KBr is the material used for the mid IR area, whereas polyethylene is used for the far IR zone. The sample holder is put into the slide holder once the pellet has been put into it. Straight from the sample to the detector, the light travels. When utilizing the IR card for transmission collection, the card is inserted into the slide holder, and powder is applied to the card. In the sample compartment the ATR-attached (UATR see in Figure 1.9 (A)) and FTIR spectrometer spectrum 3 with UATR as seen in Figure 1.3(B). The ATR measurements were carried out using a PerkinElmer universal ATR accessory, which enables direct capturing of ATR spectra on a sample without combining it with an inert substance like KBr or PE. By adjusting the beamsplitter and

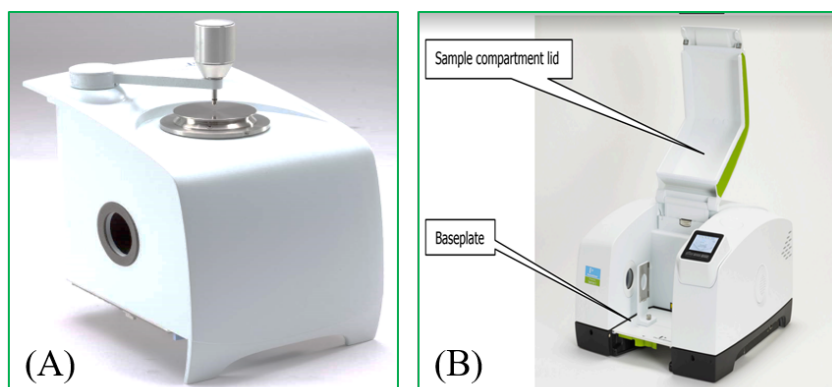


Figure 1.9. The accessories (as seen in (A) and (B) respectively for sample chamber used in ATR spectroscopy as well as transmission [3].

detector, we may collect sample spectra in the far and mid IR ranges. The spectra can be directly collected using the universal ATR on minute fragments, powders, semi-solids, thin films, and liquids. The crystal has a high refractive index and is transparent to the infrared beam; it is an internal reflecting element or IRE. ATR accessories work by monitoring the alterations in a wholly internally reflected IR beam that take place when the beam strikes a sample.

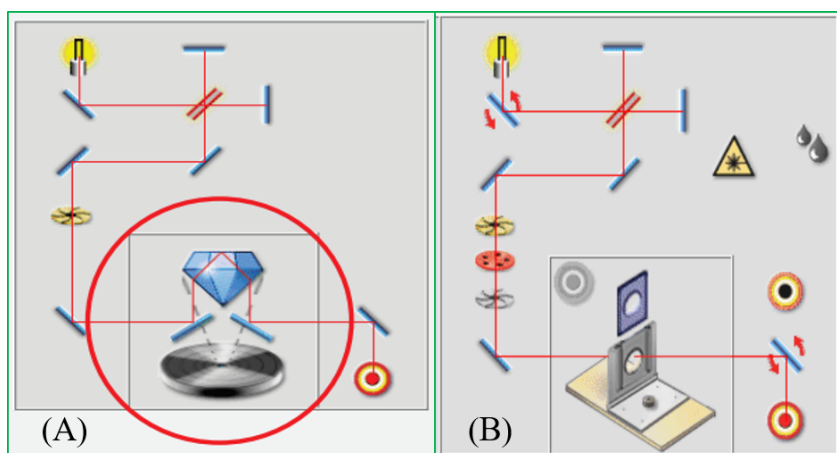


Figure 1.10. Diagram (A) and (B) demonstrating the IR light's journey via the sample chamber for ATR and transmission spectroscopy, respectively [3].

This method solves the two most challenging aspects of IR analysis: sample preparation and spectrum reproducibility. Since the evanescent wave or bubble only reaches a distance of 0.5μ to 5μ beyond the ATR crystal, the sample needs to be in close proximity to it. If the crystal's refractive index is considerably higher than the sample's, internal reflectance will not happen and light will be transferred through the crystal instead of internally reflected. Zinc selenide, KRS-5, Ge, diamond, etc. are common materials used in IR spectroscopy as high refractive index ATR crystals. Refractive indices of ATR crystals typically range from 2.38 to 4.01 at 2000cm^{-1} . It is reasonable to assume that most liquids and solids have significantly lower refractive indices [62]. ATR crystal is a diamond crystal with a transparency range of $45000\text{--}50\text{ cm}^{-1}$ and a refractive index greater than 2.4 is used in this study. The incident beam, which focuses on the crystal surface and usually has an incident angle of 45° , is directed into the crystal by mirrors. After penetrating the crystal, the IR radiation generates a standing evanescent wave. The peculiar property that makes the evanescent wave somewhat bigger than the crystal enables it to pass through the crystal surface by a very little amount. In contact with the crystal, the sample has the ability to come into contact with the evanescent waveform, absorb IR light, and reflect the evanescent waveform back into the crystal and out to the detector in addition to reflecting its own absorption spectrum [58]. To ensure that the evanescent wave enters the sample, the crystal and sample must make good contact. As a result, pressure is frequently used to press the sample against the crystal. In the mid IR range, the evanescent wave enters the sample between $0.1\mu\text{m}$ and $5\mu\text{m}$, whereas in the far IR zone, it penetrates much deeper. The refraction index of the crystal grows with a reduction in penetration depth. In comparison to a ZnSe ($n=2.5$) crystal, a Ge ($n=4$) crystal has a substantially lower depth of penetration. It is feasible to obtain spectra from various depths in the sample if the crystal material is changed while examining the same sample. The term for this is depth profiling. This is particularly helpful when using laminated thin film made of many thin layers. UATR has a diameter of 3mm-5mm and is a single bounce ATR. Due to its superior durability and chemical inertness, it features the most widely used diamond/ZnSe crystal [63].

1.3.5 Detector

FTIR equipment uses DTGS (Deuterated TriGlycine Sulfate) detectors in both the mid IR and far IR regions. A tiny IR transparent window typically shields the detector element from the surrounding factors. Additionally, the sample chamber's signal strength can be reduced by 20% by the window material. To safeguard the detector element, the KBr window must be removed in the mid IR range. But a Polyethylene (PE) window still shields this detector ele-

ment in the far IR spectrum. A pyroelectric bolometer is the detector used by DTGS. It functions by monitoring variations in the amount of IR radiation that strikes the detector element, which causes the DTGS element's temperature to fluctuate. This can be quantified by looking at the variation in capacitance over temperature as measured by the voltage over the detector element. The DTGS detectors are inexpensive, user-friendly, and dependable. The one negative aspect of these detectors is that they are not as sensitive as other current models, like the MCT (Mercury Cadmium Telluride) detector. The translating mirror is limited in its movement compared to an MCT detector when gathering an interferogram. Typical working mirror velocities for the DTGS and MCT detectors are 0.4747, 0.6329, and 0.9329 cm/s and 1.2659, 1.8988, and 2.5317 cm/s, respectively. Because of this, the more modern MCT detector is faster than the DTGS detector. Since DTGS requires collecting time, it is usually only used for 1D point inquiries. On the other hand, 2D IR mapping is done using the MCT detector. A sum of sinusoidal waves, each containing information on the wavenumber of a specific IR peak and the peak strength at that specific mirror site, is called an interferogram[58]. The voltage variation of the detector's temperature fluctuations as a function of OPD is determined using the interferogram. Applying the FT causes it to transform into transmittance as an assortment of wavenumbers. The FT was developed in the 19th century by the French mathematician Joseph Fourier, and it saw major advancements in the 1960s. It is currently often employed in IR spectroscopy[64]. Two DTGS detectors are included in the spectrum 3 instruments [3]; one is meant for the mid IR and the other for the far IR. Earlier research using a DTGS (or even an older type) detector and a CsI beamsplitter characterizes the far IR area as being below 200cm^{-1} , even though this was the threshold level of those detectors & the beamsplitter in earlier studies [65]. The CsI beamsplitter needed more frequent repairs than the KBr beamsplitters, which were more commonly used because their construction was made of a substance that was far softer and more hygroscopic. It has long been believed that the far IR region is below 400cm^{-1} since the KBr beamsplitter has a 400cm^{-1} cut-off limit. Because of this, it became well-liked right away and has been used almost exclusively ever since. The far IR zone is still typically defined in literature as being below 400cm^{-1} [58]. The most recent research, published in 2007, identifies the far IR zone as being below 600 cm^{-1} [66]. This term is directly related to the invention of MCT detectors, which are less time-consuming and more delicate than DTGS detectors, for the purpose of collecting spectra. In advanced spectroscopy, this detector has emerged as the industry standard, particularly in micro-spectroscopy, and has quickly gained popularity. Since MCT detectors have a cut-off limit at 650cm^{-1} – 600cm^{-1} , the far IR region is defined as everything under 600cm^{-1} by the author in [66].

PerkinElmer Spectrum 3 FTIR spectrometers with UATR, which offer sam-

pling flexibility and performance in mid, near, and far IR regions with a single instrument, are utilized in our investigations to enhance innovative product development and research in academia, chemicals, polymers, and pharmaceuticals. You may rapidly go on to your next sample without having to manually reconfigure thanks to computerized set-up and region switching. The completely motorized beam splitter and detector changeover mechanism allows for a quick and simple transition from mid to far IR operation. Regardless of the overall temperature in the laboratory, all DTGS detectors are electronically adjusted to guarantee outstanding reproducibility [3].

1.4 ATR-FTIR Integrated Spectroscopy

The most common sampling method for FTIR spectroscopy is ATR. The DiComp diamond ATR originated about 25 years ago, and it opened the usage of ATR to numerous new applications, such as chemical reaction detection. ATR FTIR has several advantages over other approaches to analysis, particularly molecular-spectroscopy techniques. By harnessing these advantages, scientists and researchers are able to increase chemical innovation. ATR FTIR monitors a wide range of varieties of samples, comprising liquids, solids, powders, semisolids, and pastes, swiftly and conveniently. The IR radiation passes through a crystal, is completely internally reflected at least once across the crystal-sample interface, and the reflected light goes to the FTIR detector during ATR sampling. The ATR-FTIR spectroscopy technique is used in industries such as pharmaceuticals, materials science, forensics, and environmental analysis to identify chemical compounds, study molecular structures, examine surface properties, analyze polymers, investigate biomolecules, monitor chemical reactions, and assess the composition of materials. ATR spectroscopy has found application in examining solid and liquid materials because it can measure spectra without the need for sample preparation or dilution. ATR was first used to acquire the IR spectra of polymer samples and films. The interferogram can be transformed into a spectrum using ATR-FTIR equipment using the Fourier transformation mathematical approach. The conventional spectra are generated by splitting the interferogram into sine waves over each light wavelength. The process comprises integrating the initial information between zero and the greatest path distinction and then converting the signal from intensity across a predetermined time to intensity with regard to frequency. The two primary sampling techniques for FTIR are transmission and reflectance. The transmission method is a simple method that includes transmitting an infrared beam directly into a sample, determining the energy transferred, and constructing a spectrum. Careful preparation of the sample is essential due to the requirement for an extremely thin enough sample (a few m)

to avoid absorption signal saturation, the requirement for sample drying prior to FTIR measurements due to water's strong IR absorption, and the requirement for particular IR transparent sample holders such as barium fluoride(BaF_2) disks. The schematic illustration of the IR light flow in the sample chamber for the FTIR spectrometer with ATR (UATR) (as seen in Figure 1.11).

The IR beam in the reflection technique is reflected from the sample's interaction with another medium, like air or particular substrates before it is detected. When obtaining IR spectra using a non-destructive technique (e.g., dissolution or thin film), the reflection approach is commonly employed. Both internal and external reflections are part of the reflection approach. The most widely used internal reflection is ATR. The IR light in ATR passes through a highly refractive crystal internal reflection element(IRE) beneath the sample. An FTIR spectrum is produced as a result of the evanescent wave's attenuation caused by the sample's reflective properties. Preparation of samples for traditional IR is time-consuming; however, ATR is currently employed in FTIR, so sample preparation is not necessary. Typically, transmission has been used for most IR investigations, wherein IR light passes through a sample directly along a predefined path length. Although sample preparation is easy and reasonably priced, the quality of the delivered data is greatly affected by it.

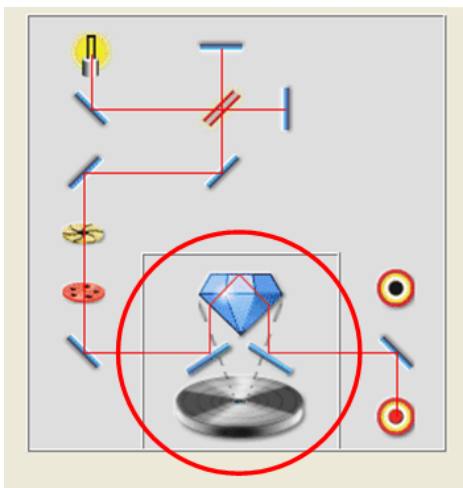


Figure 1.11. The sample chamber's schematic representation of the IR light flow for ATR spectroscopy [3].

ATR offers a potent and oftentimes simpler alternative analytical technique. The efficient path length, d_p , is the depth to which the evanescent wave penetrates

the sample. When incident IR light is oriented correctly, the internal reflecting element of an ATR crystal can reflect it. A part of the energy, known as the evanescent wave, moves along the crystal's surface in the medium with a smaller refractive index, $n(n_{\text{ATR}} > n_{\text{sample}})$, while it does so. Once the sample absorbs a certain quantity of energy, the evanescent wave is attenuated. The Eq.(1.6) represents the wavelength λ of IR light, the ATR crystal's indices of refraction n_{ATR} , the indices of refraction of a sample n_{sample} , and θ , the angle at which it impacts the surface.

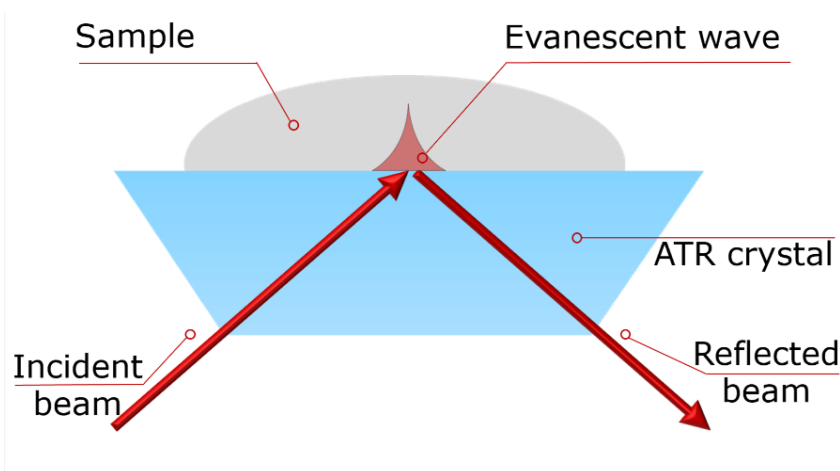


Figure 1.12. Principle of ATR-IR [7]

$$d_p = \frac{\lambda}{2\pi n_{\text{ATR}} \left(\sin^2 \theta - \left(\frac{n_{\text{sample}}}{n_{\text{ATR}}} \right)^2 \right)^{\frac{1}{2}}} \quad (1.6)$$

As the evanescent wave advances deeper into the sample, its intensity decreases exponentially. Therefore, the penetration depth of the ATR spectroscopy is relatively shallow; the exact depth relies on several factors, such as the type of material and wavelength of the light. ATR devices were first developed in the 1970s and have since made significant progress, being certified for use in government and industry operating procedures. ATR is currently the method most often used to obtain an FTIR spectrum. This is because it is more convenient and quicker than other approaches, and the equipment is usually easier to keep safe. Now that ATR is the primary sampling technique, direct measurement of samples for FTIR is achievable. ATR's primary advantage is that it eliminates the need

for sample preparation for both liquid and solid materials. The ATR technique presses the sample up against a high-refractive-index crystal in order to analyze the IR spectrum using IR light that is strongly internally reflected in the crystal. A diamond, ZnSe, or Ge prism is used with the ATR accessory. As the most commonly utilized FTIR method for studying solids and liquids, ATR-FTIR has inadequate sample preparation demands and is non-destructive. The attenuated light gets reflected off the IRE and returned to the detector. Water-containing sample analysis can benefit from the use of ATR-FTIR, a surface characterization technique where IR light passes through a specific ATR crystal [67]. This crystal provides ATR for its internal IR beam. When the crystal comes into contact with the sample, internal reflections of the IR beam are created. These internal reflections result in the creation of evanescent waves that penetrate the sample. When these waves penetrate the sample, they interact with it, releasing IR radiation and creating an ATR-FTIR spectrum of the sample. The fundamental working principles of the ATR-FTIR spectrometer are depicted in Figure 1.12, which also shows the reflection angle and evanescent waves. Surface analysis with ATR-FTIR is possible, and the depth of penetration can be tuned by varying the reflection angle.

Mid-range IR beams are usually employed in ATR-IR due to the fingerprint region. This region, which exhibits molecular vibrations specific to those molecules, can be used to identify the substances in the sample. The sample is prepared more easily with ATR-FTIR than with IR; it is just placed on the crystal, which is an additional advantage. There is relatively little sample needed for this spectroscopic method, and no sample disposal is required. Due to the use of evanescent waves, ATR-sensitivity FTIR's are less sensitive than those using transmission techniques. This can be explained by the fact that waves employed in the transmission methodology enter the sample, whereas waves in the evanescent wave approach only touch the surface of the sample. Because of this, the transmission methodology allows for the study of the entire sample, not just the bulk or surface, whereas the evanescent wave method only looks at a very small section of the sample. ATR has several benefits, one of which is that the preparation of samples for spectral measurements is minimal or nonexistent because of the shallow depth to which IR light penetrates the sample surface. This is a very helpful method for measuring samples that include a lot of water. Specular and diffuse reflection are two methods for achieving external reflection, depending on whether the sample surface is rough or smooth. In situations where a sample's thickness and/or absorptivity are inadequate to generate a spectrum with an acceptable S/N ratio, the reflectance technique may be utilized. When an IR beam passes through a sample, like cells, and is affixed to an IR reflecting device, like a low-e slide, it is reflected back, allowing the beam to travel through the sample again before it reaches the detector. This is known as the reflectance

mode. Signal absorbance is improved by practically doubling the sample's optical path with the use of this approach.

Surface analysis of nanomaterials can be achieved through the qualitative or quantitative application of ATR-FTIR spectroscopy. This is important because the solution scarcely interacts outside the inter-facial area. In order to investigate the surface adsorption of ligands on nanomaterials, such as nanoparticles and nanorods, at the interface between liquids and solids as they relate to biological and environmental conditions, the main emphasis of this study is on ATR-FTIR spectroscopy [68]. There are various instances of using ATR-FTIR spectroscopy to investigate surface associations between ligands and nanomaterials that are significant to the environment and biology. Examining the interactions between the surfaces of nanoparticles and biologically relevant fluids used in cytotoxicity and environmental toxicity investigations is one example of this type of research. The ATR method is a commonly employed approach for surface plasmon excitation.

The two ATR approaches are the Otto setup & and the Kretschmann setup, both of which are shown in Figure 1.13. Both principles are similar, except for the prism location with respect to the metal layer. In the Kretschmann configuration, the second layer is the metal, and the third medium is dielectric; see Figure 1.13 (a). In the Otto configuration, the second thickness is dielectric, and the metal is the third medium (see Figure 1.13 (b)).

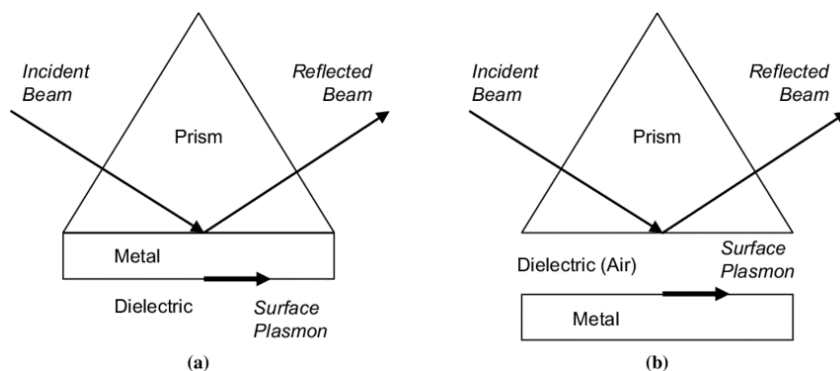


Figure 1.13. Schematics of (a) the Kretschmann setup (b) the Otto setup [8]

An incoming light that is fully reflected at the bottom of a prism, producing an evanescent field, excites a surface plasmon (SP) at the interface between a metal and a dielectric material. The most common configuration (also referred to as the Otto setup) for an internal IR spectroelectro consists of the IRE, so-

lution, and metal electrode. In this setup, the IR beam travels through the IR-transparent IRE with a high index of refraction and entirely reflects from the IRE/solution interaction. The Kretschmann configuration works with just a limited number of electrodes composed of metallic layers that could be placed onto the IRE in a film of a few tens of nm in thickness. Otto configurations are quite wide, but at one angle of incidence and for all mid-IR wavelengths, no such amplification is possible with the Kretschmann design. An Otto configuration-based sensing system might be utilized with a structurally flexible sensor, like one that measures wavelength and air-gap range. Benefits of the Otto setup system include minimal size and real-time compensation for fabrication errors when using the dielectric gap interrogation method. The Kretschmann setup poses flexibility limits for changeable sensing head designs. Although Kretschmann configuration-based SP resonant-based sensing has been developed, real-time metal thickness modification is a difficult task to execute. While tunable resonance qualities are acquired in accordance with a changing air-gap distance, the Otto design, on the other hand, provides the option of reconfiguring. If it is possible to continuously alter the air gap that exists between the thin metal surface and the glass substrate, a SP resonant sensing with the structural flexibility achieved by the Otto setup will be useful. This feature implies that a variety of detection systems may employ the Otto configuration-based sensors [69, 70].

Plasmon Related Surface-Enhanced Infrared Absorption (SEIRA) Spectroscopy

2.1 Plasmonic

Plasmonics is a novel idea in nanophotonics that has drawn a lot of interest because of its interesting characteristics and its potential applications. Plasmon optics restricts light to an oscillating field of free electrons on the Nanoscale scale (surface plasmons (SP)), opening up new possibilities for imaging, sensing, and Nano-photonic devices. Plasmonics is anticipated to become more and more significant in the improvement of numerous technologies as study and technological developments carry on. As free space incident light, "pure" Transverse EM waves do not pair with plasmons because of the longitudinal nature of the excitation. SP can be broadly classified into two categories: those that propagate along a planar metal/dielectric interface, commonly referred to as SP-polaritons (SPPs), or plasmons that are pertinent to applications in plasmonics are known as SPPs, , and those that are localized at metallic nanoparticles, commonly referred to as localized SP (LSP). Despite having similar physical characteristics, SPPs and LSPs have very different appearances. In spite of this, they both show localized EM fields at metallic surfaces that are much stronger than the excitation fields.

Nanoscale optical signal generation, processing, routing, and amplification have potential applications in bio-photonics, optical communications, sensing,

chemistry, and medicine.

2.1.1 A quick history: remember the past to create the future

One of the trendiest areas of photonics nowadays is plasmonics. The study of EM waves' interactions with free electrons in metals is known as plasmonics. More than a century ago, German physicist Paul Karl Ludwig Drude [71, 72] anticipated this kind of behavior. Understanding of light as an EM wave at a high level is thought to be a wonderful place to start when attempting to explain and comprehend plasmonics. The term "plasmonic resonance" refers to the coupled density wave oscillation of free carriers (electron clouds), mostly present at the metal/dielectric interface, and incoming photons. The application of these collective electron density waves has attracted a lot of attention. They could combine to produce light under certain circumstances and are referred to as SP. SP can have incredible effects on optical characteristics. Plasmonics is an intriguing subject of study because of its potential to modify and manipulate local light fields as well as interact with light at wavelengths far longer than those of nanostructures.

Based on Maxwell's equations, a classical framework provides a solid understanding of how metals interact with EM fields. Initially, Somerfield investigated (1916) EM surface modes on metal wires theoretically. He determined how waves would propagate around a cylindrical metal surface by solving Maxwell's equations [73]. It should be noted that these surface modes, also referred to as surface waves for radio waves, are electromagnetically equivalent to and therefore are the direct precursors of SPPs in the visible spectrum. A solid mathematical basis for the scattering of light on microscopic spherical particles was developed by Gustav Mie in 1908, almost ten years later [74]. Eventually, this formalism was used as a basis by its descendants to describe LSP resonances in metallic nanoparticles.

Moreover, plasmonics today encompasses all of the research on the invention, production, and use of plasmon-based nanostructures, having been inspired by Richard Feynman's 1959 vision "There's Plenty of Room at the Bottom". Plasmonics is moving from a lab curiosity to useful applications as a result of the recent blossoming of nanotechnology[75], which has brought with it a multiplicity of approaches for building structures at the nanoscale. Potential uses for plasmonics in solar cells[76, 77], biosensing[78], gas sensing[79, 80], optical computing[81], and even early cancer detection and therapy [82, 83] are being investigated [84].

In the classical illustration, plasmons are explained in terms of the metals Drude model. The metal is viewed as a three-dimensional crystal consisting of positively charged ions, with a delocalized electron gas circulating within the ion grid's periodic potential. Metals' optical characteristics are largely determined by plasmons. The Drude model, a basic model contained in the Lorentz model

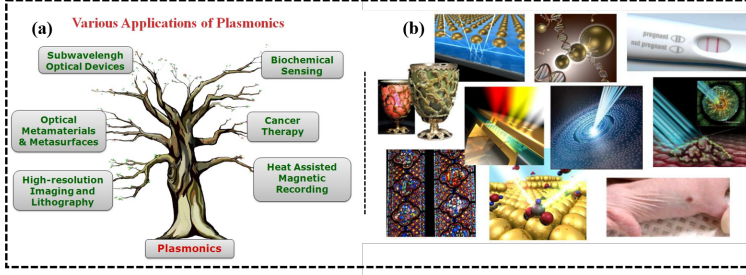


Figure 2.1. (a) Various applications of plasmonics [9].(b)Biophotonic applications of plasmons [10]. Important plasmonic features: Localized light at nano(sensing, trapping, and curing applications), Strong EM field (enhancement of molecular emission and absorption(fluorescence spectroscopy,surface-enhanced Raman (SER) and SEIRA spectroscopy)), Sensitivity to local environment (SP-resonance (SPR) sensors)

extension, provides the dielectric function $\varepsilon(\omega)$, which describes a material's response to an EM field. The metal's Drude model permittivity can be expressed as in Eq.(2.1).

$$\varepsilon(\omega) = \varepsilon_{\infty} \left(1 - \frac{\omega_p^2}{\omega(\omega + i\gamma)} \right) \quad (2.1)$$

The plasma frequency as well as damping parameter, also known as the collision frequency, are denoted by ω_p and γ , respectively. The material permittivity at high frequencies is ε_{∞} [85]. These factors are critical in attempting to comprehend the nature and origin of the plasmonic modes. However, a COMSOL Multiphysics will be used to compute these quantities numerically in Chapter 3.

2.2 Biosensors: general aspects

This section will provide an overview of the biosensors field. Biosensors use various methods, such as optical or electrical, to convert biological signals into physical signals. Here, the main concentrate of the discussion is on optical sensing techniques, particularly those utilizing Plasmonics. The identification of tiny compounds at ultra-low concentrations and the development of tiny gadgets for point-of-care (PoC) examination are the primary problems in the rapid, A real-time, label-free method for testing biologically relevant substances using plasmonic biosensing. The exceptional capacity of biosensors to identify a biological event on a transducer device through a signal-based measurement of the binding

reaction response has made them gadgets of great interest to academia, industry, and research labs [86]. Leland Charles Clark Jr. initially described biosensors in 1962. He saw the potential to show off the elements of a biosensor as well as the method for combining a transducer device with a bio receptor[87]. It's crucial to keep in mind that every biosensor is made up of a transducer that will amplify the resulting signal and a bio-recognition layer. The biosensor's key component is the signal transducing element. There are several transducer kinds that are researched, including optical, electrical, optical, gravimetric, and acoustic transducers. Of these, we will concentrate on the optical transducer. Here, the pinning of the evanescent wave at the metal/dielectric interface allows for the light-matter interaction by multiple techniques, including SPR, LSP resonance, SEIRA, and SER. Biosensors track illnesses and microorganisms that cause them in biological solutions such as blood, urine, saliva, tears, and perspiration. The research domain of biosensors has expanded its uses in recent years, bringing with them new possibilities in fields such as ecological surveillance, the farming industry, defense, and security, as well as medical analysis, healthcare, pharmaceutical research, and food safety. Biosensors have been added to the Internet of Things (IoT) recently. Examples include sensors that are integrated into vehicles to notify drivers when their tire pressure is low and the COVID-19 quick detection kits that are available right now [88]. They may also incorporate different point-of-care uses, like medication administration, forensics, & the quality of water. They have been used in the highly sensitive identification of analytes, even with minimal quantities, due to their interactions between high-affinity bio-samples. The addition of microfluidic channels to the miniature devices could enhance their capacity to precisely regulate, synchronize, and alter micro-fluid volumes for enhanced mass and heat transfer. For the creation of vital platforms in biological diagnosis, this is absolutely necessary [86]. Nowadays, everyone is interested in device downsizing, especially for biosensing analysis. In fact, many biomarkers relating to biological samples like blood, urine, and saliva can be detected sensitively and noninvasively in a fast, low-cost, repeatable, and dependable manner by packing and integrating devices into a single interface. Miniaturized biosensors have been developed and manufactured using a variety of techniques, such as design optimization, characterization, and testing. The following are the primary barriers to biosensor development such as the effectiveness of tracking biorecognition signals, including auditory, optical, electrical, gravimetric, and electrochemical ones, the enhancement of the transducer's capabilities, including its low detection limits, quick response time, repeatability, and ability to detect individual samples. The biosensor device's integration and size reduction utilizing micro- and nanotechnologies for mass manufacturing. The primary resolution to all these issues lies in the nanostructuring of materials that function as transducer elements. The following sections will address the structures' design and composition in more

detail later on. Additionally, the signal strength is highly sensitive to the spacing between samples and the transducer elements since the nature of the signal augmentation reliant on the E around the plasmonic structure. Accordingly, surface chemistry has a vital role in the identification of target analytes. As a result, substrates can be made functional by incorporating a biorecognition component (such as antibodies or other tiny molecules made to bind to the intended analyte selectively) to encourage a molecular interface for focused detection. The signal that is measured will vary as a result of the analyte attaching to the biorecognition element [89]. Notably, according to Minopoli et al., surface lattice (SL), SERS spectroscopy, SEIRA spectroscopy, and plasmon-enhanced (PE) fluorescence are classed as external signal amplification-based biosensors, SL is classified as inherent resonance-based biosensors [90].

SPP can be used in conjunction with a variety of spectroscopy techniques, like SEIRA, to increase its functionality and broaden its range of applications. SPP and SEIRA have been shown to work together to characterize ultrathin films [91, 92], identify particular biological analyte fingerprints [96], and associate with molecules vibrational oscillation [93, 94]. The majority of SEIRA active substrates, which are covered in the SEIRA state-of-the-art section, use LSP to strengthen vibrational signals in IR spectra. When using LSP to create SEIRA active substrates, these structures typically take the form of nanoscaled metal islands, spheres, or nanoantennas on the surface. Prior research has indicated that vibrational characteristics of polymer films could potentially be enhanced by using an angle-tunable grating structure [95]. Only a small number of experimental examples have looked into this area, but [95, 96], indicates that there is still room for improvement and that this technique can offer greater flexibility in SEIRA applications. By modifying coupling conditions, propagating SPP can directly modulate the increased electric field in the infrared region, giving SERIA active substrates greater control and reproducibility than confined surface plasmons.

2.3 SEIRA Sensing

2.3.1 Introduction

Spectroscopy is an effective photonic and optical method. The vibrations of IR fingerprints are a rich source of molecular information because they establish a direct correlation between the vibrational properties and the configuration, chemical bonds, and molecular substances. IR spectroscopy provides direct molecular structure characterization with chemical specificity exclusive to this spectral region, it is commonly acknowledged as the gold standard in chemical analysis. Hence, it is feasible to identify compounds in a clear, non-destructive method for

detecting proteins, lipids, and DNA, among other biological building blocks, and label-free manner, which makes IR spectroscopy a very effective and vital instrument. Figure (2.2) illustrates the absorption bands in the IR spectrum caused by molecular vibrations. In this sense, the functional groups and chemical bonds of a molecule provide a "vibrational fingerprint" in this spectral region.

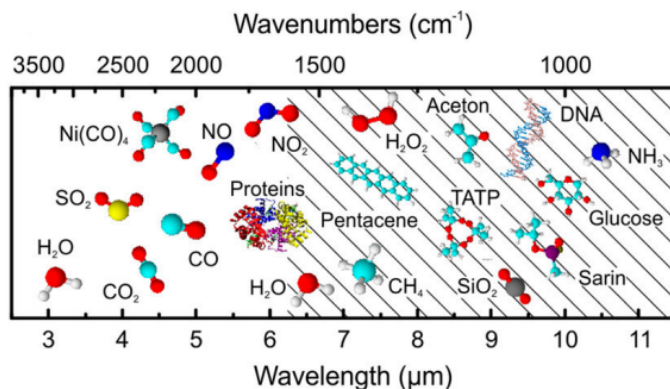


Figure 2.2. (a) Different IR vibrations of certain kinds of molecules. The area of the fingerprint that contains skeletal vibrations is indicated by the hatching portion [11].

As a result, IR measurements offer extremely precise and quantifiable chemical, structural, and compositional data regarding the components of samples in any state of matter [97, 98]. The low sensitivity linked to tiny molecular absorption cross sections hinders the broad use of conventional IR methods for practical trace analysis (e.g., extremely thin films, modestly sized samples, ultrarare concentrations, etc.), despite its benefits and promise. Furthermore, IR spectroscopy is frequently employed to identify compounds in forensic, food, safety, pharmaceutical, and health applications. However, the use of conventional IR spectroscopy in the field of trace molecular detection is restricted by the limited IR absorption cross-section of molecules. To achieve significant IR absorption, some compounds need a long absorption path or a high target molecular density. As a result, a rather high threshold for the minimal number of species investigated is necessary for molecular fingerprint identification using FTIR spectroscopy. It is utilized for fast and routine structural studies of chemical compounds, process monitoring, and material identification in a variety of academic, industrial, and other applications [99, 100]. Beer's law, often known as the Beer-Lambert law, [50], provides an explanation for this restriction (governs IR absorbance). In general,

the Beer-Lambert law can be stated as follows:

$$Abs = \varepsilon cL \quad (2.2)$$

where c is the material's concentration, L is the span of the light's passage throughout the substance (absorbing material's thickness), Abs is its absorbance, and ε is known as the molar absorptivity. It can be observed from Eq.(2.2) that the Abs is proportional to the L and c . Conventional spectrometers are unable to detect detectable absorbance in situations when the analyte's thickness is extremely thin or its concentration is extremely low. Unfortunately, the low IR absorption cross sections prevent their employment in spectroscopic examination of small amounts of materials, e.g., in sensing applications [101]. The poor detection ability, particularly in the identification of molecule traces, is caused by the low molecular absorption cross sections [102]. A drawback of IR spectroscopy is its weak signal intensity and extremely undesired background and noise since all thermal things in our surroundings always emit light (IR); this leads to reduced S/N and signal-to-background ratio [103]. A fresh approach is desperately required to address this issue in order to further the advancement of IR spectroscopy technology and raise the detection sensitivity of conventional IR spectrometers [104].

Increased IR absorption has been used to show chip sensors with integrated photonic devices, including Fabry-Perot interferometers [105], ring resonators [106], photonic crystal slot waveguides [107], and mid-IR photonics (Heterogeneously integrated silicon photonics) [108]. Still, an issue for engineering applications is light coupling into waveguide-based integrated photonic devices. There are numerous approaches to solving this issue, including by improving the IR source, creating ultrasensitive IR detectors, and applying SEIRA [104]. The detection sensitivity of IR spectrometers can be increased using brighter IR light sources and more sensitive IR detectors, although these upgrades are frequently more expensive. As an alternative, SEIRA spectroscopy is an economical and efficient way to improve interactions between matter and light [11, 109]. The idea of SEIRA was first put forth by Hartstein et al. in 1980 [100] and Hattar et al. [110] in 1982. A relatively inexpensive, low-noise, and efficient method of enhancing the detection capability is SEIRA innovation. It takes advantage of the strong light-matter interaction and sub-wavelength localization made possible by plasmonic resonances of metallic nanostructures. To overcome these limitations, signal-amplifying strategies can be adopted, and the use of SEIRA is the most commonly used solution. On inexpensive disposable substrates, a novel method for spectroscopic trace analysis is given that combines external reflection techniques with SEIRA spectroscopy [111].

Rough surfaces made of metal [112], metallic island films [113], and metallic

nanoparticles [114, 13] were the main subjects of the early SEIRA research. Nonetheless, the haphazard arrangement and dispersion of these metallic nanostructures as resulted in rather broad extinction spectra and difficult-to-control plasmonic resonance frequencies. The application of rationally patterned metallic nanostructures, such as nanowire [115, 103], nanoshell [116], nano size gap [117, 110], meta-surface [118], nanohole [119], strip grating [120], Nano-disk [121], cross-shaped perfect absorber [122], nanoantennas (NA) fashioned like fans [22], Nano crescents [123], and triangle-shaped NA [124], to SEIRA has been increasing in recent years. The Nanostructures achieve exact resonant wavelengths and narrow extinction spectra through their interaction with dipoles. Recently, Neubrech et al. presented a comprehensive study of plasmonic Nanostructures for SEIRA. The only usage of SEIRA in use now, meanwhile, is for mid-IR sensing of macromolecules like polymers or proteins found in bio-materials [11].

Resonant metal NA based SEIRA spectroscopy, or simply "resonant SEIRA," gets around this restriction. When metal nanostructures are activated resonantly, they exhibit plasmons, which are collective oscillations of electrons that produce enormous EM fields at the nanoscale. The molecules situated in these fields have their IR vibrations amplified by an order of magnitude, which allows for an unparalleled level of sensitivity in spectroscopy. The oscillating dipole of the surface-adsorbed molecule interacts with the induced dipole of the metal when IR radiation excites the composite medium. As a result, the metal's dielectric function changes, and the effective medium's absorbance increases at the adsorbate's vibrational frequency. The metal layer's increased absorptivity and volume fraction cause the effective medium absorption to dominate the surface enhancement process. It is important to remember that the amplifying seen by SEIRA spectroscopy is largely dependent on the shape of the metal nanostructure [125]. By utilizing customized metallic structures, which combine free-space rays into sub-wavelength-sized areas, SEIRA can further increase its sensitivity. Light can be effectively coupled into sub-wavelength areas using resonant antennas. Significant local electric field increases can be achieved in these areas, allowing molecules positioned in these so-called "hot spots" to absorb more energy. Thus, it is possible to enhance traditional infrared spectroscopy beyond monolayer sensitivity. The fundamentals of SEIRA spectroscopy are covered in this chapter, along with an explanation of how infrared light interacts with metal surfaces and structures.

Numerous innovative biosensor platforms have been developed as a result of the growing need for biosensors that are more dependable and affordable [126]. The advantages of optical sensors, like their cost-effectiveness, multiplexing capabilities, and immunity to electromagnetic interference, have drawn a lot of interest. Surface plasmon collective excitation has been used to improve the vibrational signals of thin molecule layers using SEIRA, a potent vibrational label-free analytical method. SEIRA has drawn a lot of research attention as a potential al-

ternative biosensor platform because of the surface plasmon phenomenon, which produces an amplified vibrational signal. In recent years, continuous SEIRA sensing systems have emerged [127, 128, 129]. This chapter primarily focuses on resonant SEIRA and its physics, namely the resonant coupling between molecule and NA excitations, as well as their spatial extent and frequency scaling. Different strategies to maximize SEIRA gain are presented based on these fundamentals; these strategies include choosing the right nanostructures, geometries, arrays, and materials. Furthermore, the SEIRA principle is delineated, specifically focusing on theoretical frameworks that offer comprehension of the light-plasmonic nanostructure interaction and the coupling of nanostructures with vibrating molecules. Common active SEIRA substrates are covered in this context, along with optimization strategies for them that range from material selection to geometric design and standard fabrication processes. There will also be a discussion of SEIRA analytical application advancements and the sensor platform's near-term potential.

2.4 State of the art for SEIRA

Using the powerful near-field enhancement of subwavelength nanoantennas, nanophotonics can get over this restriction. Enhancing the molecule-resonator coupling can cause a change in the resonance's intensity or frequency, which can then be used to extract the chemical fingerprints when they are spectrally overlapped with the absorption fingerprints. SEIRA has been implemented on a number of plasmonic platforms, the most basic of which is the use of rod-type antennas [11, 26, 23]. These NA configurations focus incoming light into hotspots for EM fields, leading to a substantial light-matter interplay and the detection of typically modest absorption signals, such as those found in protein monolayers [130, 131] (Figure 2.3(a)). Many sensing applications in various domains, including chemical engineering, pharmaceutical research, materials science, environmental monitoring, and human health, have been become feasible by techniques using SEIRA spectroscopy [11]. SEIRA spectroscopy has proven especially useful in biosensing, where it is crucial to distinguish between and detect with high sensitivity the absorption signatures of the fundamental components of life, such as proteins, lipids, and nucleic acids (Figure 2.3(b)). Furthermore, IR spectroscopy's non-invasive and label-free characteristics make it possible to observe chemical interaction kinetics in real-time and in situ during intricate bioassays or biological membrane processes. The shape, material choice, and layout of nanostructured antenna assemblies determine their limits of detection and, in turn, the sensitivity of SEIRA spectroscopy. Some of the key design principles for very surface-sensitive resonators and their uses are highlighted in the section

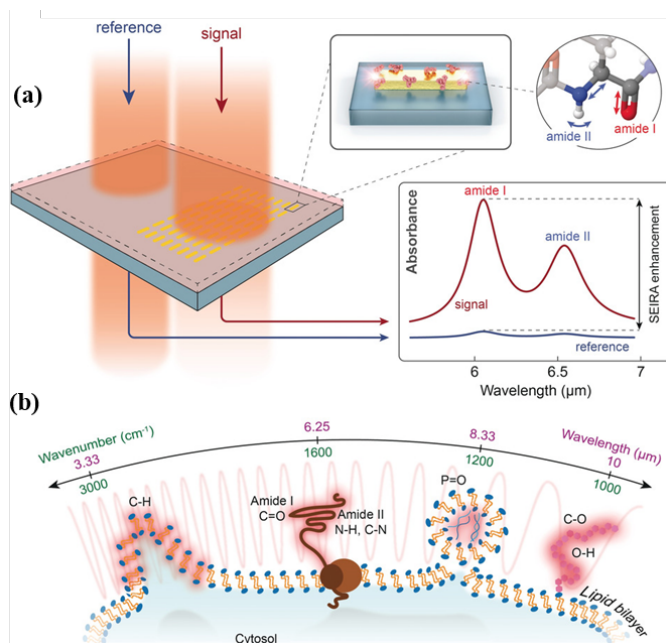


Figure 2.3. SEIRA spectroscopy. (a) The distinctive vibrational bands of molecules connected to their chemical bonds are optically detected by IR absorption spectroscopy. Stronger absorption signal increases can be obtained from resonant nanoantennas by accessing biological analytical and compositional information from monolayers and few-molecule systems and enhancing these fingerprints. (b) Because SEIRA spectroscopy techniques can distinguish between a wide range of key biologic components, including (fat-containing substances) lipids, proteins, carbohydrates, and nucleic acids, they are essential for comprehending complicated biological systems, like membranes as well as cells contact mechanisms[12].

that follows [132]. Silver (Ag), aluminum (Al), and gold (Au) are examples of plasmonic materials that have been used to create the metasurfaces for SEIRA spectroscopy thus far. Strong dipole moments and tight electromagnetic field confinement are provided by the rod-type nanoantenna design, which is one of the most straightforward and widely utilized resonator geometries for SEIRA sensing. The absorbance signals are improved by orders of magnitude at the antenna tips due to greater light-matter interaction [11]. Furthermore, by carefully adjusting the plasmonic metasurfaces' unit cell periodicities, the signal improvement can be further increased [133]. In Figure 2.4(a) left, the authors have demonstrated the realization of gold nanorod metasurfaces with a nanoantenna length of $2.2\mu\text{m}$ [13]. The authors also provided evidence of submonolayer sensitivity for chemically specific protein detection (see Figure 2.4(a) right). Higher resonance quality factors (Q-factor) can be achieved by using resonant geometries with higher Q-factors [134] or more sophisticated resonator designs, such as nanogap nanoantennas [26, 27]. According to L. Dong et al.'s work, near-field enhancements up to 10^7 enable the detection of as few as 500 4-nitrothiophenol(4-NTP) molecules [26]. Figure (see Figure 2.4(b)) shows an additional nanogap antenna design that the authors have demonstrated using coaxial metasurface designs. It's interesting to note that standard laser lithography nanofabrication techniques and Al_2O_3 atomic layer deposition were able to consistently produce nanogaps as tiny as 7nm. In comparison to standard nanorod designs, these metasurfaces offer signals of protein thin layers that are more than ten times greater [14].

In addition to surface sensitivity, having near-field enhancement throughout a broad spectral range is critical for simultaneously targeting many chemical species. The most significant absorption bands of proteins, for example, are found in the spectral range of 1450cm^{-1} to 1750cm^{-1} , whereas the highest absorption bands of lipids are seen in the vicinity of 3000cm^{-1} . Consequently, using a single resonant metasurface to target both molecular species is not feasible. Multiresonant nanoantennas have recently been introduced [15] as a means of tracking real-time protein and lipid interactions. Figure 2.4(c) shows how the authors were able to identify lipid vesicles containing cargo molecules and then puncture them with melittin peptide to release the cargo analytes via liposome puncturing. The ability of such a label-free metasurface-based detection mechanism to study biological interactions between proteins and cell membranes is striking, and it can be applied to a wide variety of lipid vesicles, including exosomes, synaptic vesicles, and liposomes, across cancer diagnostics and treatment, pharmaceutical research, and neurodegenerative diseases [15]. Fascinatingly, infrared spectroscopy may reveal details about the secondary structure and conformation of proteins in addition to enabling the differentiation of different biological building blocks like proteins, DNA, and lipids. The hydrogen bonds that hold adjacent amino acid residues in polypeptide chains together preserve the native transform

of the protein's secondary structure.

The secondary alpha helices and beta sheets of proteins are the main constituents of the secondary structure. Because it controls a protein's functionality and interactions with other biological macromolecules, the secondary structure of proteins is very significant. Parkinson's disease, Alzheimer's disease, Huntington's disease, and numerous other degenerative and neurodegenerative illnesses are thought to be primarily caused by changes in the secondary structure of proteins [135]. As a result, it is crucial to use high-sensitivity and label-free approaches to monitor the protein states. According to Dordaneh et al., SEIRA is a good choice for tracking protein misfolding and the secondary structure of small amounts of analytes. In Figure 2.4(d), the authors demonstrate the dynamic monitoring of β -sheet to disordered conformation transitions in a monolayer of α -synuclein protein associated with illness. Furthermore, SEIRA can be applied to the detection of tiny molecules, including volatile organic chemicals and gases. Gold-(Au)-based metasurfaces with a metal-organic framework for the simultaneous detection of multiple gas species have been demonstrated by H. Zhou et al. In this case, the metalorganic framework is required to focus the tiny gas molecules to the surface close to the plasmonic antenna tips, where the strongest localization of electromagnetic fields occurs. Furthermore, other materials, such as highly doped semiconductors [136] and two-dimensional materials like graphene [137], can be used to create plasmonic metasurfaces. The optical response of the 2D materials is greatly disrupted following molecule adsorption, which makes them very intriguing for gas sensing. In order to investigate the SO_2 , NO_2 , N_2O and NO rovibrational modes, H. Hu et al. used graphene nanoribbon metasurfaces [17]. Figure 2.4(e) depicts the experimental gas cell with an integrated metasurface. The devices that were presented have a sensitivity of 800 zeptomoles per $1 \mu m^2$ and rapid response times (less than 1 minute). These devices have the potential to be employed in breath analysis and volatile organic compound monitoring. As shown in Figure 2.4(a-c), the plasmonic-based SEIRA strongly amplifies chemical absorption signals over a wide spectrum range, with the nanoantennas' resonance bandwidth being substantially greater than the molecular absorption bands' full-width at half maximum (FWHM). Resonance bandwidths covering the spectral band of the molecule absorption are necessary for the operation of techniques like vibrational circular dichroism spectroscopy and SEIRA spectroscopy. Thus, in this context, a relatively broad-band resonance may be helpful. However, the large spectral resonance bandwidth means that, in order to read out the chemical fingerprints of the target analytes, more sophisticated and costly tools like FTIR and tunable quantum cascade laser sources are still required. In theory, these restrictions might be circumvented by metasurfaces that permit spectrally selective resonances, which would simultaneously provide more spectral information about the chemical absorption bands and amplify the absorption signal. A summary of

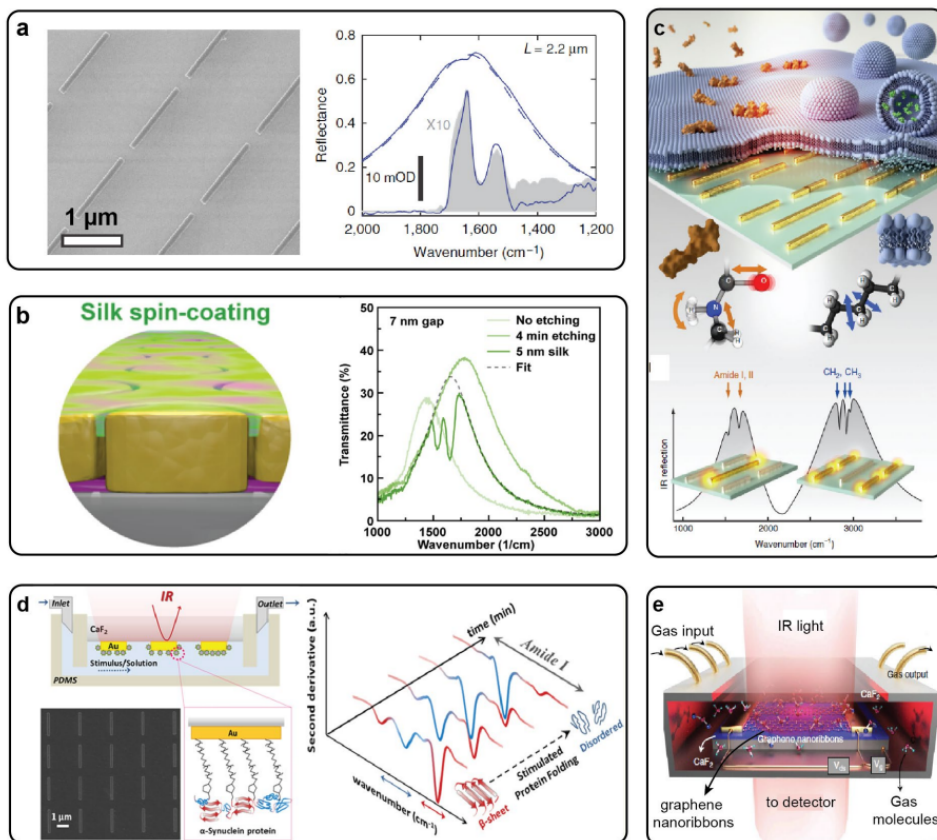


Figure 2.4. Plasmonic antennas for enhanced surface spectroscopy. (a) Surface-bound streptavidin monolayer absorbance signals in relation to rod-shaped gold nanoantennas. Reproduced from reference [13]. (b) For stronger SEIRA signals, use coaxial nanogap antennas. Inspired by reference [14]. (c) Gold(Au) nanoantennas with multiple resonances for the simultaneous detection of proteins and lipid bilayers. Taken from reference [15]. (d) The identification of conformational state transitions and secondary structure in proteins. Taken from reference [16]. (e) Graphene nanoribbon metasurfaces for gas sensing Taken from reference [17].

the developments of SEIRA active substrates over the last ten years is illustrated in Figure 2.5, which highlights four key trends: materials, increased bandwidth, enhanced sensitivity, and applications.

Here, Figure 2.5(a) presents a plasmonic chip-based device that addresses these issues and permits real-time, high-sensitivity in-situ monitoring of the interactions between proteins and nanoparticles, including the ability to see minute amounts of water displacement during binding events. Determine an enhancement factor of 13,800 for the electric field intensity. Samples were created using the lift-off process on calcium fluoride and electron beam lithography. Figure 2.5(b) dipolar rod antenna for polymethyl methacrylate (PMMA) identification that is manufactured using EBL and has the ideal absorber arrangement. Diagrammatic representation of a simulated near-field intensity enhancement (identifying Amide I and II) using a gold nanoring antenna on a silicon nitride nano pedestal (using the EBL method); see Figure 2.5(c). An arrangement of tip-to-tip dimers made of gold nanoantennas (using EBL and enhancement factor 10^4) is shown in Figure 2.5(d). In order to achieve maximum SEIRA enhancement (10^3), an Au rod with a 4,4'-bis(N-carbazolyl)-1,1'-biphenyl layer was constructed (EBL) at calcium fluoride (Figure 2.5(e)). For the detection of zeptomoles of octadecanethiol, the fan-shaped Au structure in Figure 2.5(f) produced by photo-lithography (nanolithography) had a SEIRA enhancement factor of 10^5 . Aluminum antenna (with the EBL technique) with acrylamide functionalization (see Figure 2.5(g)) and Figure 2.5(h) to examine the behavior of organic monolayers bonded to sputter-coated, ultrathin gold (Au) layers on calcium fluoride substrate. The SEIRA enhancement factor is 50. For PMMA detection, colloidal lithography based on Al and Au nanoantenna arrays atop substrates made of Si (see Figure 2.5(i)) Bowtie antenna with a theoretical SEIRA EF is 10^7 that is self-aligned (using beam lithography) and has a gap above an Au film with a SiO_2 spacer layer for 4-nitro thiophenol and 4-methoxythiophenol molecules (see Figure 2.5(j)).

For protein investigations, grating order-coupled nanogap Antennas (Rod) at calcium fluoride Substratum (20–100 nm) in 2.5(k). By examining its optical response using a polymethyl-methacrylate film and a thin protein bilayer, the perfect absorber platform (used EBL) was discovered in Figure 2.5(l). For the detection of thin poly(methyl methacrylate), a novel crooked nanoantenna with an enhancement factor of 2.8×10^4 and a calcium fluoride substrate was employed with EBL (see Figure 2.5(n)). To improve trace chemical detection and 10% enhancement, an Au ring resonator with SiO_2/Si substrate (used EBL) and an FTIR-ATR equipment were utilized. By using EBL different arrays of closely spaced gold-insulator-metal resonators, 2,4-dinitrotoluene was deposited (SiO_2 as a dielectric layer, for separated layer as chromium adhesion), see Figure 2.5(o). Titanium adhesion layer and Au nanoantennas manufactured (by

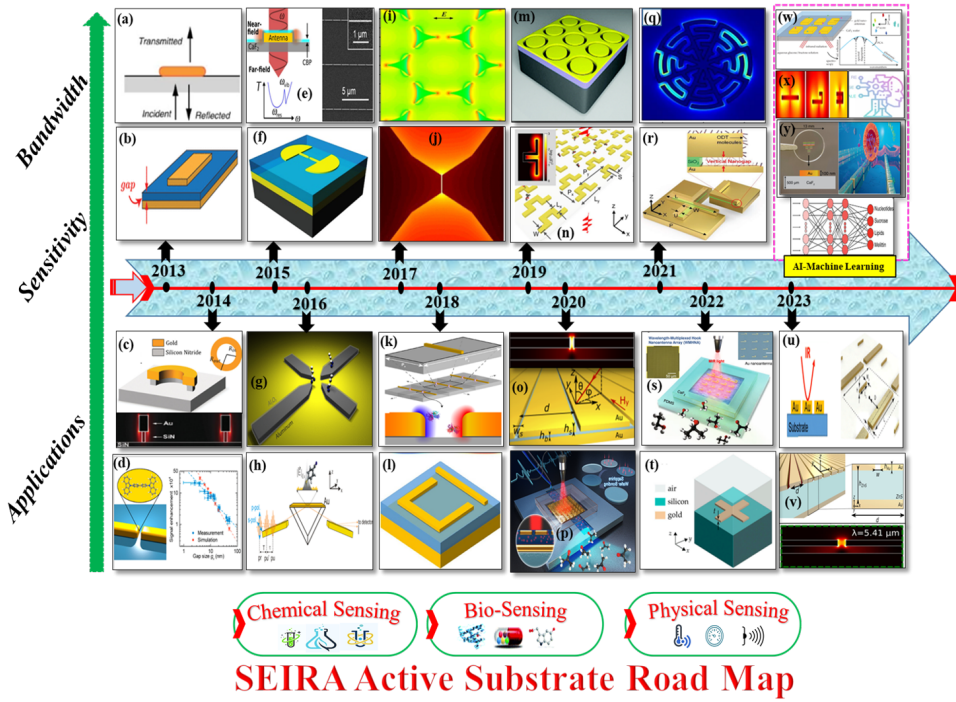


Figure 2.5. SEIRA sensing applications roadmap over the previous ten years for optimizing and utilizing SEIRA active substrates. (a) adapted from reference [13]. (b) adapted from reference [18]. (c) and (d) are adapted from references [19, 20], respectively. (e) and (f) are adapted from [21, 22], respectively. (g) and (h) are adapted from [23, 24], respectively. (i) and (j) are adapted from [25, 26], respectively. (k) and (l) are adapted from [27, 28], respectively. (m) and (n) are adapted from [29, 30], respectively. (o) and (p) are adapted from [31, 32], respectively. (q) and (r) are adapted from [33, 34], respectively. (s) and (t) are adapted from [35, 36], respectively. (u) and (v) are adapted from [37, 38], respectively. For the relation of AI Deep Learning (Machine Learning) and SEIRA in (w-y) and adapted from [39, 35, 40]

focused ion beam) on Al_2O_3 substrate make up the hybrid nanofluidic-SEIRA, see Figure 2.5(p). A resonant metamaterial liner was created by patterning a gold disc with thin wires or gaps along its edge using EBL (for CO_2 sensing as seen in Figure 2.5(q)). Using a thick vertical nanogap, a metamaterial absorber (nanoimprint lithography) is used to target 1-octadecanethiol molecules (see Figure 2.5(r)). Provide a machine learning method for deriving complementary chemical as well as physical data from biologic samples (PMMA) by hooking nanoantennas to calcium fluoride(Glass) and see Figure 2.5(s)). Cross-shaped nanoantenna with 10^4 SEIRA enhancement factor (used EBL) for protein identification (see Figure 2.5(t)). Breast cancer detection and enhancement up to 10^3 using a sensor chip based on metallic nanorod structures (Used EBL) (see Figure 2.5(u)). Between the mirror layer and gold ribbons (which employed EBL), there is a zinc sulfide dielectric layer that is utilized to identify 2,4-dinitrotoluene (see Figure 2.5(v)). Views on anticipated developments in SEIRA innovation are covered in this section., (see in Figure 2.5(w-y)).

This section's goals are to give a general introduction of SEIRA innovation and highlight four key trends: materials, enhanced sensitivity, enhanced bandwidth, and applications as seen in Figure 2.5. Sensor networks, wearable devices, and the Internet of Things have posed new challenges for the miniaturization and integration of IR spectroscopy systems and chips throughout recent years. In order for SEIRA technology to continue to grow, IR spectroscopy downsizing as well as system integration have emerged as critical objectives. A more intelligent device design and analysis of data can be achieved by leveraging machine learning (ML). Furthermore, the emergence of ML has given SEIRA technology a fresh life. More intelligent data analysis and device design can be made possible by leveraging ML.

2.5 SEIRA Principle

The fundamental components of SEIRA, which establish their sensitivity, are their nano/micro designs. The characteristics of substrates with nano- and micro-structure are crucial to macro-optical designs. The primary focus of SEIRA spectroscopy is the quantity of photons absorbed by the IR molecule; photon absorption itself is the only mechanism measured. External reflection and transmission geometries have shown this phenomenon since its discovery [138]. The SEIRA enhancement mechanism for resonant nano antenna spectra before and after coating with the absorbing bio-analyte vibrations is shown in Figure 2.6(a). The band of heightened bio-analyte absorption is correlated with the severe dips in the resonant nanoantenna. A plasmonic nanostructure simulation displaying hot spots (near-field confinement) at the crooked nanoantenna boundaries with

bio-analyte as seen in 2.6 (b). These so-called "hot spots" contain molecules that will couple to the resonance, a significant increase in their absorptivity cross-section. The local field augmentation of incident light is directly proportional to the molecules' increased absorption intensity [139]. A standard parameter is needed to measure SEIRA's sensitivity. The quantity of molecules that are involved in the enhanced vibrational signal, the molar concentration of molecules adsorbed at hotspots divided by their weight, and the enhancement factor (EF), which connects increased signal intensities to conventional IR strategies (transmission, reflection), have all been determined in a number of studies. Generally, these "sensitivity" values are reported for each NA, even though many arrays of NA are examined. As a result, Eq.(2.3) [140, 96, 141] defines SEIRA EF as follows:

$$SEIRA_{EF} = \frac{\Delta R}{\Delta R_0} \times \frac{A_0}{A_{SEIRA}} \quad (2.3)$$

Where ΔR and ΔR_0 are reflection changes as a result of the bio-analyte on the nanoantenna and, conversely, as a result of the bio-analyte on the flat layer of nanoantenna material. The ratio of ΔR and ΔR_0 is called SEIRA gain [142]. A_0 is the portion of the nanoantenna unit cell that is exposed to light. A_{SEIRA} is effective area of nano antenna (Where the field is localized).

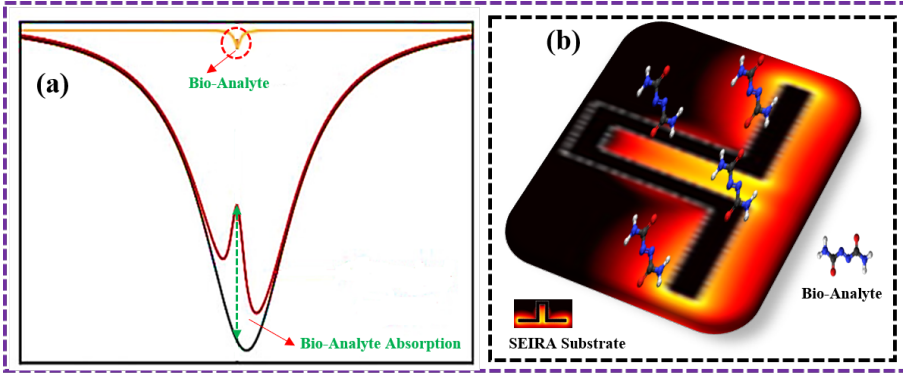


Figure 2.6. A plasmonic meta structure-based illustration of the SEIRA enhancement principle. (a) Vibrational bands of bio-analyte absorbed on plasmonic nanostructure are amplified (red curve), and plasmonic resonance is tuned (black curve) to match the vibrational bands of bio-analyte. On top of the unaffected resonance (black), in orange (un-enhanced bio-analyte absorbance), adapted from [41]. (b) crooked nanoantenna with bio-analyte [29].

The bio-analyte's reaction with the stronger E at the surface is what causes

the heightened signal in the spectra according to the SEIRA approach. Conventional electromagnetic theory describes the link between the bio-analyte and the electric field (E). Two different mechanisms contribute to the overall enhancement of SEIRA (chemical and electromagnetic mechanisms) [132]. The local augmentation of an adsorbate's vibration is thought to be estimable with respect to the electromagnetic enhancement effect. The following Eq.(2.4) can be used to express how the intensity of the E and the rate at which the bio-analyte dipolar moment changes relate to the absorption strength in IR spectroscopy.

$$IR(Absorption) = \left| \frac{\partial \mu}{\partial Q} \cdot E \right|^2 = \left| \frac{\partial \mu}{\partial Q} \right|^2 |E|^2 \cos^2 \theta \quad (2.4)$$

According to Eq.(2.4), the bio-analyte dipolar moment's changing rate could be increased, the electric field could be strengthened, and the $\cos^2 \theta$ value could be raised to achieve an improvement in the IR signal. where E signifies the analytical substances' local electric field of excitation, whose substrate surface luminosity $|E|^2$ differs from the incoming photon field's; The angle connecting $\partial \mu / \partial Q$ and E is shown by θ ; as well as the dipole moment derivation with regard to the normal coordinate (Q), or the dipole moment μ across the normal path [143, 144].

2.5.1 Chemical Enhancement Mechanism

The orientational substrate bio-analyte interaction at the interface forms the chemical boosting mechanism's foundation, which is linked to a rise in $|\partial \mu / \partial Q|^2$ (that is, the coefficient of absorption). This generally indicates that certain chemical exchanges that occur between bio-analytes and the signal-enhancing active substrate or surface augmentation the IR signal by active substrate; however, the fundamentals of chemical mechanisms are still not well understood [145, 146]. Chemical processes are contingent upon the nature of the contact between chemisorbed molecules and the substrate surface. These mechanisms are typically limited in scope since the probed species must be residing in close proximity to the substrate surface to facilitate chemical interactions[132]. A graphic illustration of the chemical enhancement mechanism is shown in Figure 2.7.

Usually, the charge transfer mechanism explains chemical enhancement. Chemisorption is the process by which bio-analytes on a metal surface take on new electronic states. Prior research has indicated that molecules that have chemisorbed on the metal surface display a more robust signal compared to ones that have adsorbed physically [147]. In contrast to the collective electron resonance coupling observed in SEIRA spectroscopy, Osswa et al.'s discovery [148] that the signals of p-nitrobenzoic acid chemisorbed on isolated silver island films were enhanced in the IR region suggests that the enhancement is related to a chemical mechanism

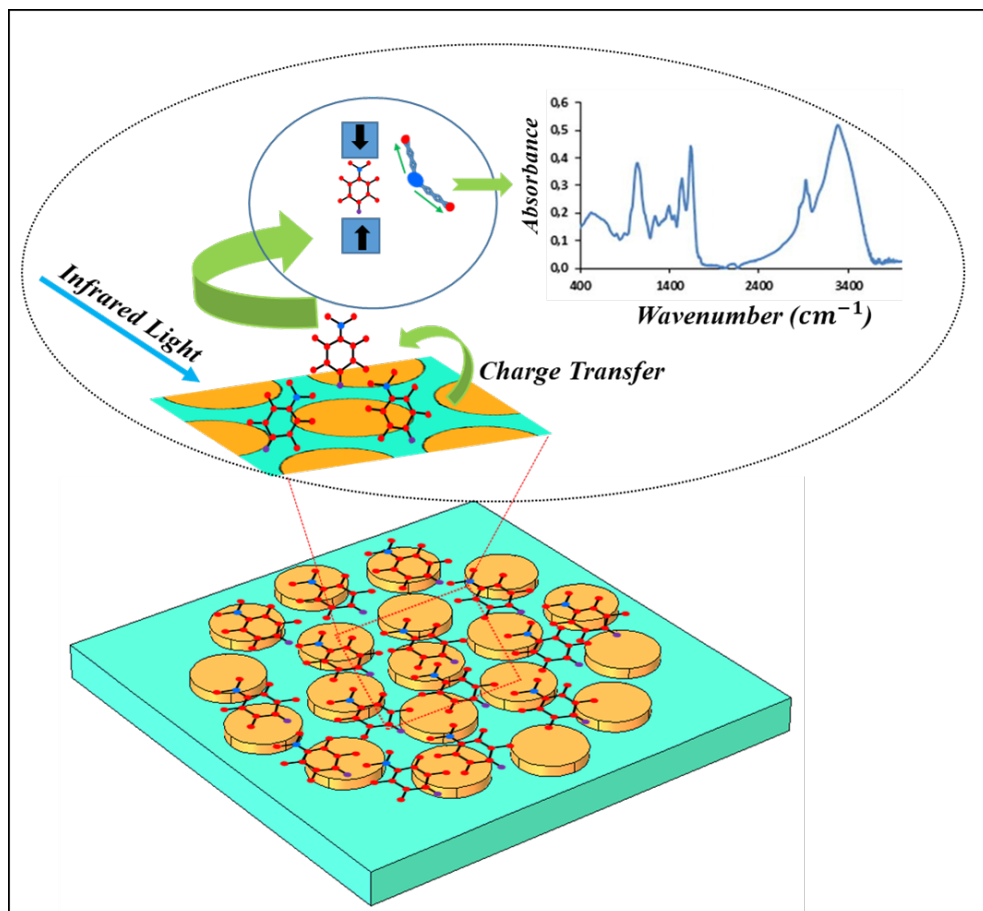


Figure 2.7. SEIRA spectroscopy's chemical enhancement mechanism

present in SEIRA spectroscopy rather than the electrical enhancement mechanism. It is thought that charge oscillations between molecular orbitals and the metal surface can raise the absorption coefficient of chemisorbed molecules, producing a stronger vibrational signal [149]. The adsorbed molecules and the atoms adsorbed around the metal surface would interact to produce a specific chemical effect. When an electric field activates the electron that filled the metallic stage on the outermost layer of metal, it moves to the agitated molecular orbital of the molecules that have been adsorbed. Additionally, electrons can go from the occupied metal level to the vacant molecule orbital. When an energy gap in the electron transport among molecules that are adsorbed and the metallic surface is filled by incoming photons, resonance is achieved. This causes the adsorbed molecules' oscillating dipole to increase. Consequently, it is possible to enhance the IR signal [150].

Furthermore, the magnitude of the signal can also be influenced by the molecular interactions [151]. The transfer of charges from metal states below the Fermi level to vacant molecule orbitals is linked to the mechanism of chemical amplification. It can be affected by a variety of elements, including electrical structure, molecular structure, and the binding effect between the molecule and the substrate. The enhancement of molecules chemisorbed on a metal surface is greater than that of molecules physisorbed, indicating covalent interactions between the molecules and surfaces [148]. Evidence that the SEIRA spectra rely on the analyte's molecular geometry supports the molecular process. Although covalent attachment is not necessary for surface enhancement, interactions between the dipoles of adsorbed molecules alter band intensities and locations, as demonstrated by the presence of enhancement on ATR-FTIR measurements [151]. The nanoparticles' local optical field distribution is random. The effect of these randomly oriented localized fields on the vibrational intensities is comparable to that of an unbound or freely rotating molecule. Consequently, there is no polarization dependency in the enhancement.

2.5.2 Electromagnetic (EM) Enhancement Mechanism

Local SPPs are the cause of the EM mechanism. On the other hand, the enhancement of the EM mechanism in SEIRA is proportional to the square of the local EM field and is caused by amplified local E upon the surface of the substrate (Enhancement Factor = $|E|^2$).

$$|E_{loc}(\omega_o)/E_o(\omega_o)|^2 \quad (2.5)$$

In Eq.(2.5), the terms E_{loc} and E_o stand for the incident E severity at wavelength ω_o of the IR active vibration and the local E severity near the molecule, respectively [152]. Surface plasmon resonances, or aggregate vibrations of un-

bound conduction electrons and Charge carriers are found in conducting media that are in resonance with an incoming EM field, are the primary cause of EM enhancement. When the incoming light meets with the boosting substrate material's free conduction electrons, a collision takes place. The SEIRA effect is most likely influenced by EM enhancement [153]. Theoretical investigations of SEIRA on metal island substrates can simplify the nanostructures as uniformly sized and shaped elongated ellipsoids [143, 154]. A greater local EM field is produced by the caused dipole (ρ) in the metallic island than by the incoming photon field surrounding the island (as seen in Figure 2.8). Changes in vibrational states can be brought about by interactions between adsorbed molecules and this amplified EM field. Every point on the island's surface experiences an induced local increased EM field that is basically polarized in relation to the surface normal; the intensity of this field decreases drastically as the distance to the metal exterior increases.

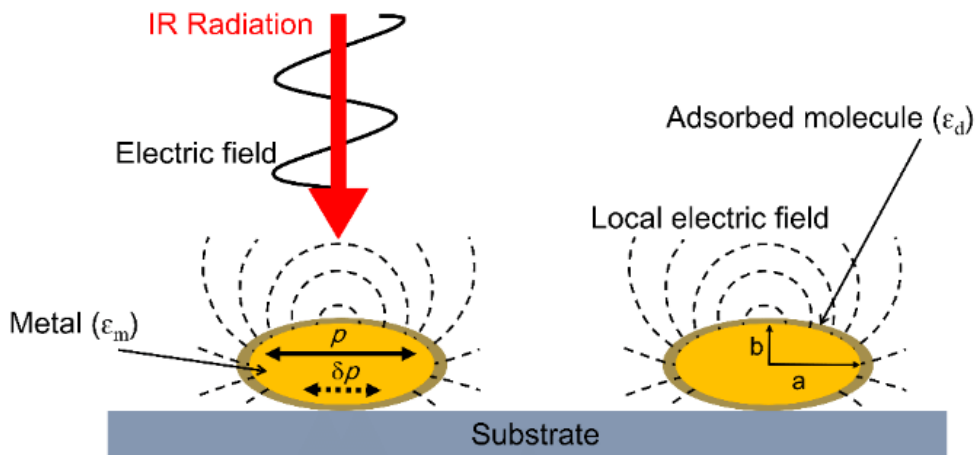


Figure 2.8. Diagrammatic depiction of the SEIRA EM operation on metallic island film. The metal film's optical characteristics are affected by the electromagnetic mechanism[42].

The near-field effect, which explains the comparatively limited amplification, and the theory of surface selection are easily explained by this process. It is anticipated that the effective enhancement distance is 8–10 nm due to the EM field's drastically declining intensity [154]. The metal islands' primary radius, denoted by a , is specified by its parallel alignment with the surface. While " b " refers to the smaller radius, which is angled in relation to the surface of metal.

The islands' aspect ratio can be expressed as $\eta = a/b$. It is expected that the monolayer of adsorbed bio-analyte covers the metal islands uniformly. ϵ_m and ϵ_d represent the dielectric function of the adsorbed bio-analyte and the metal islands, respectively. In the transmission measurement, the primary radius "a" of the ellipsoids has an E that is parallel to the surface, its due to the incident infrared light. Localized surface plasmon resonance (LSPR) occurs when IR rays impinges on the metallic island films, polarizing the metal islands and generating a point dipole (ρ) by excitement of cumulative electron resonance. When a metal nano particle's valence electrons vibrate collectively, LSPR happens [155]. This is caused by the incident light's frequency resonance. Figure 2.8 illustrates how an increased local E surrounding the metal nanostructures is produced by LSPR excitation. The metal island's dielectric function may fluctuate as a result of dipoles that oscillate within the molecules being adsorbed or inducing dipoles ($\delta\rho$). The metallic island film's spectrum should resemble the molecule's spectrum almost exactly since the disturbance should be greatest at the vibrational frequencies of those molecules. The incidence electric field is significantly weaker than the enhanced E surrounding metallic islands, but it is not constant. Where the radius of curvature is highest near the point of the islands, the strongest field is found, and where the curvature is least, the weakest field is found [156]. As one moves away from the substrate, the augmented localized electric field's magnitude rapidly drops. It is also believed that the elevated localized electric field has a role in amplifying the vibrational signals of adsorbed molecules in SEIRA spectroscopy [157]. In order for electromagnetic mechanisms to be amplified, incident light must interact with free conduction electrons within the amplifying substrate material, causing SP resonances (i.e., Free conducting electron bursts/carriers of charge in conducting media in resonance with in coming EM field). In the case of the IR spectrum, they can occur at the of plasmonic NA's [158], which produce a local EM field that is greater than the incoming photon field that molecules in proximity to the surface perceive [159, 146]. Stated otherwise, the plasmonic substrate's localized, hot spot-like highly amplified EM field is the outcome of the connection between the substrate surface and the incident photon field. Consequently, there are amplified infrared absorption signals at the vibrational dipoles of the molecules inside these hot areas [160, 161].

Furthermore, the enhanced field diminishes rapidly as one moves away from the substrate surface; in other words, EM mechanisms are amplified only in close proximity to the surface [143, 159, 132]. Increasing dissonance between the rate of vibration and the plasmon frequency generally results in a decrease in the EM enhancement effect in SEIRA [162, 163]. Therefore, in order to obtain substantial EM amplification of the processes, the excited SP needs to be resonant with the frequency of the vibration of the target biologic substance [164]. In many instances, EM and chemical mechanisms overlap. However, because EM

mechanisms often contribute far more to the overall SEIRA augmentation than do chemical mechanisms, it can be challenging to distinguish between the two contributions in a single experiment. According to SEIRA's "surface selection rule" [165, 166], vibrations of molecules associated with derivatives of dipole moments (i.e., shifts in dipole) that are not parallel to the surface of the substrate are preferred for amplification. The molecular dipole moment change is correlated with the strength of the vibrational signal in the IR spectrum. The metal islands produce an enhanced electric field, which can be used to amplify IR absorption signals in IR spectra. A stronger local electric field squares with the corresponding intensity of amplified IR absorption signals. Currently, most SEIRA research is focused on metallic structures and materials that enhance signals, particularly noble metals like silver or gold. Metal plasmonics, however, have significant losses, particularly in the IR spectrum. Therefore, well-defined metallic nanostructures, such as nanoscale-dimensioned metamaterials, nanoparticles, nanoislands, NA's (such as Rod, shells), etc., are constructed in order to realize substantial plasmonic enhancement in the mid IR [11, 167, 158, 168]. In an ideal scenario, certain plasmonic nanostructures should exhibit distinct resonances that provide light retention and robust nearfield advancements in a sub-wavelength container with low energy loss in a more consistent manner [169]. Light-matter interactions can be enhanced by matching the target vibrational frequencies with the severity of plasmon resonances dependent on a substrate. This means that the EM enhancement effects are largely reliant on the surface morphology and composition of the plasmonic material as well as the dielectric properties of the surrounding environment [170]. Typically, molecules exhibit several vibrational bands in the region of the fingerprint. While it is possible to improve the design of customized substrate structures in advance to bring the plasmonic resonance closer to a desired vibrational frequency, this may not be convenient or sufficient for clearly detecting and characterizing different chemical species on a vast scale. Furthermore, the metallic substrate that is usually utilized lacks external tunability because its plasmon frequencies are locked after manufacture.

2.6 ATR-SEIRA

Attenuated total reflectance SEIRA spectroscopy is also known as ATR-SEIRA spectroscopy. In order to enhance the IR signal in a manner similar to SEIRA, but with the added advantage of ATR, ATR-SEIRA uses a surface (often a prism or crystal) where the sample is in contact with the surface. The IR signal in SEIRA is amplified when the molecules under investigation, or analytes, are adsorbed onto surfaces with nanostructures, such as metal nanoparticles. The

analyte's vibrational modes interact with the surface plasmons of the nanoparticles to intensify the IR signal. Using the SEIRA effect will greatly increase the signal-to-noise ratio. This phenomenon takes place on the nano island-like Ag, Au, or Cu metal layer at the internal reflection element (IRE)/examined sample interfacing, and it has the ability to significantly increase the IR signals of absorbed biologic samples [171]. Hartstein et al. used the ATR methodology to identify this occurrence for the first time [100]. After that, the Osawa group used ATR-SEIRA to carry out a number of important related studies, including those on the fundamentals of immediate enhancement [148], the history of absorption enhancement as well as the surface selection rule [154], dynamic process investigations in electrochemical reactions [172], and so forth [173].

At the metal/air interface, surface plasmon polaritons are excited by the evanescent wave. ATR measures the attenuation of the evanescent wave, a technique used to study samples at or near a material's surface [100]. Time-resolved vibrational spectroscopy is a good application for ATR-SEIRA spectroscopy because of its great sensitivity. Comparable to the extremely advanced SER spectroscopy systems is the detection limit in ATR-SEIRA spectroscopy. ATR-SEIRA spectroscopy has great promise for biological event monitoring due to its trace-level observation capabilities. In terms of sensitivity and depth of analysis, SEIRA allows for the detection and examination of monolayers or thin films by offering increased sensitivity for surface species or molecules that are near the nanostructured surface. While combines the advantages of ATR with SEIRA, allowing greater sample penetration than typical SEIRA while providing improved sensitivity for surface species. ATR configuration allows ATR-SEIRA to probe a little bit deeper into the sample, allowing a wider range of applications beyond surface examination. Essentially, ATR-SEIRA combines the benefits of both ATR and SEIRA methods, providing enhanced surface species sensitivity and allowing analysis at somewhat deeper sample depths than traditional SEIRA. The basic setup for ATR-SEIRA spectroscopy consists of efficiently designed substrate placed on top of prism (that is with high index of refraction) with a flat surface [174]. The metal film is used to produce the local EM field augmentation, and the prism is utilized to meet the ATR requirement and support the metal film. Target molecules in the evanescent wave zone will exhibit greatly increased and detectable IR absorption.

An IR beam would entirely reflect at the interface between the sample and the internal reflecting element (IRE, such as a diamond, Ge, or ZnSe with a refractive index greater than 1.5), as seen in Figure 2.9 [175]. Physical and chemical changes, such as those in the target molecules' type, concentration, location, orientation, and rotation, are frequently observed in conjunction with active biological events. The exact location of the peak and intensity of IR emissions may vary as a result of these modifications. A thorough and comprehensive under-

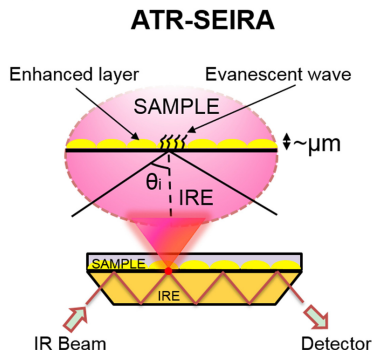


Figure 2.9. ATR-SEIRA schematic representations[43].

standing of the biological processes taking place at interfaces can be achieved by directly gathering and interpreting the IR data of target molecules. ATR-SEIRA spectroscopy provides an excellent way to see and comprehend intricate biological processes as they happen in real-time. Bio-systems occasionally need crucial external habitats constructed on prisms in order to survive. Therefore, selecting a prism can be tricky and requires meeting a number of unique requirements, such as: (1) having a high refractive index and minimal absorption at its targeted wavelength; (2) having a high level of physical as well as chemical stability in the identifying environments; (3) not having any unneeded chemical reactions between the prism and bio-molecules; (4) having good bio-compatibility; and (5) being inexpensive and simple to process.

Use antibodies and aptamers (DNA/RNA) as capture molecules to ATR SEIRA experimentally demonstrate the immunoassay's distance-dependent signal intensity [176]. Fatty acid analysis on silver nanoparticles was explored using ATR SEIRA [174]. Analyzing the electro-oxidation mechanism of C_5 furanics derived from biomass on platinum electrodes via ATR-SEIRAS investigation [177].

2.7 Summary

The field of nanostructure-based SEIRA technology has advanced rapidly over the last few decades, moving from basic research to a wide range of real-world uses. A number of theories, including the Fano-resonance principle, coupling harmonic oscillators, and temporal coupling mode theory, have evolved since the first SEIRA demonstration to provide intuitive physical insights into SEIRA spectroscopy. Meanwhile, there is a continuing push to make nanofabrication

technology more sophisticated, precise, and affordable. Physical, chemical, and biosensors are among the many SEIRA-based sensing applications that have been steadily developing thanks to this theoretical understanding and cutting-edge nanofabrication techniques. Numerous attempts have been made to optimize SEIRA performance, spanning from structural design and material selection to the use of machine learning algorithms, in order to further enhance sensing performance. The number and species of analytical substances as well as the sensing methodologies and sensing efficiency (sensitivity, identification limit, etc.) of SEIRA-based sensors have all improved significantly as a result of these initiatives. However, there continue to be several obstacles standing in the way of SEIRA's development and sensing applications: (1) Large-scale, economical fabrication. It is intended that SEIRA will get past this obstacle and move toward useful industrial applications; (2) consistently refine SEIRA augmentation and enhance sensing performance through the creation of novel, efficient methods; (3) enhance the detection limit by integrating a bright light source, an effective detector, and SEIRA technologies; (4) creating ultra-narrow band as well as ultra-broadband SEIRA with strong absorption enhancement in the future; (5) the in-situ & extremely sensitive detection of minute amounts of analytes; an example of this would be the detection of minute amounts of proteins and gasses in their natural liquid environments; (6) developing strategies that are more effective and appropriate for SEIRA sensing applications.

Design and Optimization of Plasmonic SEIRA Substrate

3.1 Introduction of COMSOL Multiphysics

Finite element modeling (FEM) has been utilized by photonics researchers to achieve some noteworthy optical discoveries. To examine the electromagnetic (EM) field impacts on plasmonic nanostructures, numerous teams of researchers have recently turned to the commercial software "COMSOL Multiphysics". A solver for partial differential equations (PDEs) based on FEM is called COMSOL Multiphysics. FEM is a numerical modeling-based solution that simplifies a much more complicated and big problem into a number of smaller ones, or "finite elements," making the problem easier to analyze overall. One of its many strengths is its simultaneous solution of any physical challenge ranging from one-dimensional geometry to three-dimensional geometry using either spherical or Cartesian coordinate systems. The fundamental idea behind FEM is to divide a continuous domain with unknown functions specified into several sub-domains with straightforward interpolation techniques described. FEM's primary benefit is its simple handling of intricate geometries using dispersive materials. Each of the frequencies associated with interest is generated by FEM in a single run, but the other two produce a wide-band response each time. In the field of engineering, the FEM tools are thoroughly examined and used. COMSOL Multiphysics is a widely used commercially available program that simulates surface plasmon formations in the frequency domain by utilizing a FEM solver [178, 179, 180]. COMSOL Multiphysics covers a wide range of physical systems, including chemical engineering, earth science, electrics, acoustics, structural mechanics, heat transfer, micro-electro-mechanical systems, and radio-frequency. Engineering profession-

als, researchers, and students are increasingly using COMSOL Multiphysics for educational or professional applications because of its easy-to-use computer-aided design applications [181].

The EM waves interface is the sole COMSOL Multiphysics physical model employed during this chapter for numerical modeling. A simulation procedure can be carried out using the EM model found in COMSOL. A valuable and efficient method for researching the tiny EM response is simulation (numerical modeling). A microscopic EM investigation by analytical computation is extremely challenging, if not impossible, due to the intricate boundary value issues involved. It is anticipated that the in-homogeneity of the micro-structure in this study—that is, the combined structure of the dielectric material and the metal-semiconductor nanocomposite—can be analyzed through simulation of in a particular model (geometry and physical system) that reflects the actual state.

The numerical modeling of the suggested structure provides insight into the design outcomes and helps to prevent squandering time and resources on poorly thought-out solutions. More computing power is available for simulation programs thanks to recent developments in chip technology. The simulation results of today are nearly identical to real-world data and are therefore more trustworthy. This chapter will present results and simulations for the creation of new frequencies via optical intensity enhancement on a gold nanoantenna based on a glass substrate that has localized surface plasmons.

This chapter explains the theoretical work, and as such, this chapter is devoted to a detailed description of the numerical modeling as well as the implementation of a model simulating a SEIRA substrate. Throughout the work, the commercial software COMSOL Multiphysics was utilized, in particular, the Wave Optics Module (WOM) for FEM simulations of gold nanoparticles interacting with light. MATLAB was used for calculations of changes in permittivity, as well as the visualization of data. The section is structured into multiple parts. First, the general approach of the simulation methodology used is described. Thereafter, the processes of the FEM simulation of the light interacting with GND's.

Here, we further explain why we chose the array-based plasmonic nanostructure as GND. For rich optical properties, such as LSPR, sensitivity, repeatability, uniformity, tuneability, affordability, and ease of fabrication are all dependent on the plasmonic Nano structure's design (Shape) and make it essential. Numerous plasmonic nanostructures have been proposed with varying methods of plasmon resonance tuning. There are still obstacles to be solved, such as the necessity for wavelength tuning, ineffective local gap distance adjustment, and the inherent radiation-dampening characteristic of the confined plasmonic mode. Moreover, there are complicated synthesis techniques for creating nanostructures, including nanorods. The aforesaid problems can be simultaneously resolved by

plasmonic nanostructures based on GND array arrays [182]. Biosensors, Nanomedicine, and optoelectronic devices can all benefit from the flexible plasmonic features of Nanoarrays, which have created a wealth of potential for EM augmentation and light management. Specifically, the combined actions of plasmons within gold nano-arrays generate a coherent optical response that results in distinct and intense spectrum characteristics[183]. The size, form, and periodicity of the Nanostructure determine the optical spectrum of a GND, offering plasmon and optical features tremendous flexibility and tunability. An extremely stable and well-organized structure, the GND closed-packed array nanostructure can increase the area accessible to light management and electromagnetic enhancement. An additional benefit of GND's array-based plasmonic nanostructure over the Nanoprism arrangement is that, because the mode is dispersed throughout the nanostructure, the sensitivity to small molecules is less reliant on the exact location of the molecule's binding in relation to the surface of the GND. It indicates that the amount of molecules required to produce a discernible signal are in the zone where the mode of detection is strong, even at lower concentrations of molecules. GNDs benefit from the local field distribution in the following significant ways: One advantage of using nanodisk array sensors over nanoprism arrays is that the former is more appropriate for use with active chemical substances, which require stable structural properties nanostructures, while the latter is affected negatively by the potential existence of an adhesion layer [184] .

3.2 EM Waves, Frequency Domain Interface Model in COMSOL Multiphysics

The electric field issue for the time-harmonic domain (THD) in the linear medium is intended to be resolved by the EM waves, frequency domain interface model. This model can do the following investigations (Numerical modeling): mode assessment, boundary mode assessment, eigenfrequency, and frequency-domain analysis. The solution can be found using one or more input frequencies by using the frequency domain analysis. When dealing with cavity difficulties, eigenfrequency research can determine the resonance frequency and its eigenmodes. Finding permitted propagating modes and the corresponding transmission line for 2D cross-waveguides is possible with the use of mode modeling. After that, the borders that represent waveguide ports are studied using boundary mode evaluation, and the TH-equation can only be solved in its electric field variation. In order to create a simulation for our plasmonic SEIRA substrate model, we have chosen the frequency domain study to represent the plasmonic SEIRA substrate at various EM wave (light) frequencies.

The basis of EM waves and the frequency domain interaction model used to

solve the electric field (E) are the Maxwell Equations. The time-harmonic as well as eigenfrequency are determined by the regarding Maxwell equation (Eq.) as seen in Eq.(3.1).

$$\nabla \times (\mu^{-1} \nabla \times E) - k_0^2 (\varepsilon - i\sigma/\omega\varepsilon) E = 0 \quad (3.1)$$

$$k_0^2 = \omega \sqrt{\varepsilon_0 \mu_0} = \omega/c_0 \quad (3.2)$$

$$c = 3 \times 10^8 \text{ m/s} \quad (3.3)$$

$$\omega = 2\pi v \quad (3.4)$$

Where:

μ = Relative Permeability

ε = Relative Permittivity

σ =Conductivity

c =Speed of light in air/vacuum

v =Frequency of EM wave [Hz]

For nonmagnetic and linear materials with ($\mu = 1$),and ($\varepsilon = n^2$),where n is the refractive index of material, (3.1) can be written in (3.2).

$$\nabla \times (\nabla \times E) - k_0^2 n^2 E = 0 \quad (3.5)$$

3.2.1 Geometry of the Plasmonic SEIRA Substrate

The geometrical model in the COMSOL Multiphysics numerical modeling goal is to model the actual state of the plasmonic SEIRA substrate properties (or the metal nanoantenna) and its interaction with EM waves. It is composed of four layers and the SEIRA substrate layers are sandwiched between two perfect matching layers (PML) at the z-axis. An acoustic model (modalities of propagation and evanescence) can have a domain or layer termed PML (also known as a sponge layer) included in it to simulate an open, non-reflecting infinity domain [185]. In place of non-reflecting border conditions, it establishes a perfectly absorbing domain. The PML is compatible with many forms of waves, not just plane waves. By applying a complex-valued coordinate conversion to the chosen domain in the frequency domain, the PML essentially renders it absorbing at a sustained wave impedance, hence removing reflections at the point of interaction. In the time domain, the PML is used to solve auxiliary equations for inverse Laplace transformation equations. In order to completely absorb outgoing waves at any frequency and angle of incidence, PML might be the most effective technique[186].

The ATR technique is employed as Otto configuration for the functionalization of plasmonic SEIRA substrate. Even without surface enhancement, the

ATR method has enough sensitivity to identify a monolayer. Figure (3.1) shows the description of model geometry for plasmonic SEIRA substrate with metallic nanoantenna. When an IR probe beam is used to irradiate the backside of a prism, it serves as an IRE. The ATR element and the metallic nanoantenna surface are separated by a thin layer of AIR/Water Gap (or Otto Gap). If the thickness of Otto Gap is of the order of the IR radiation, the evanescent wave penetrates the metallic nanoantenna and senses the species therein. The technique is known as Otto configuration, and its sensitivity is enhanced compared to external reflection spectroscopy [187].

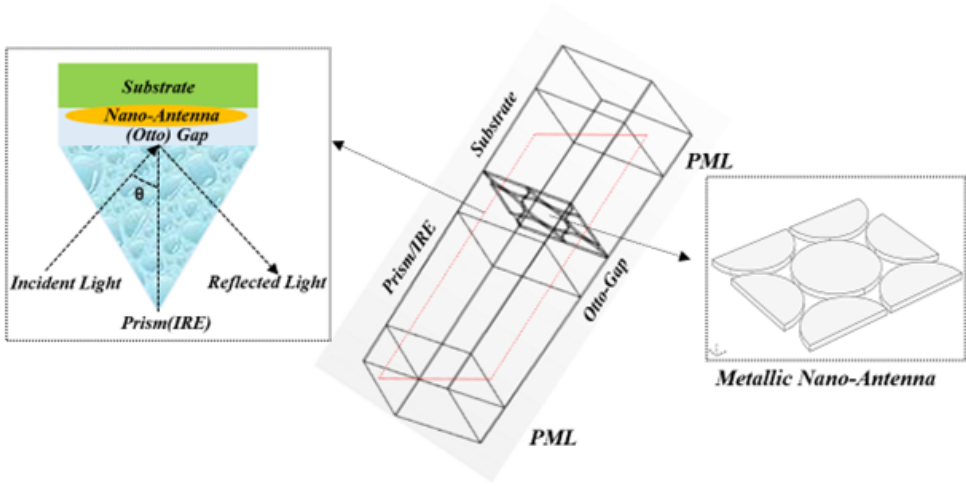


Figure 3.1. Geometry Model of the plasmonic SEIRA substrate with ATR-Otto Configuration

3.2.2 Closed Packed Array of GND-based Unit Cell Antenna Design

Nano disks arranged in closed packed array are integrated into the substrate. The side lengths of the unit cell are P_x and P_y . Figure(3.2) shows the unit cell where the gap between Nano disks is G . The diameter and thickness of the Nano disks are D and t_m , respectively. Nano disk associations were designed by geometrical considerations and Table 2.1 shows the spatial coordinates (x , y , and z , respectively). In Table (3.1) $R=1/2(D+G)$ is the sum of half the diameter of the nanodisk and half of the gap between Nano disks. The side lengths P_x

(Width) and P_y (Depth) are calculated by using the simple expression as $4 \times R$ and $3.5 \times R$, respectively.

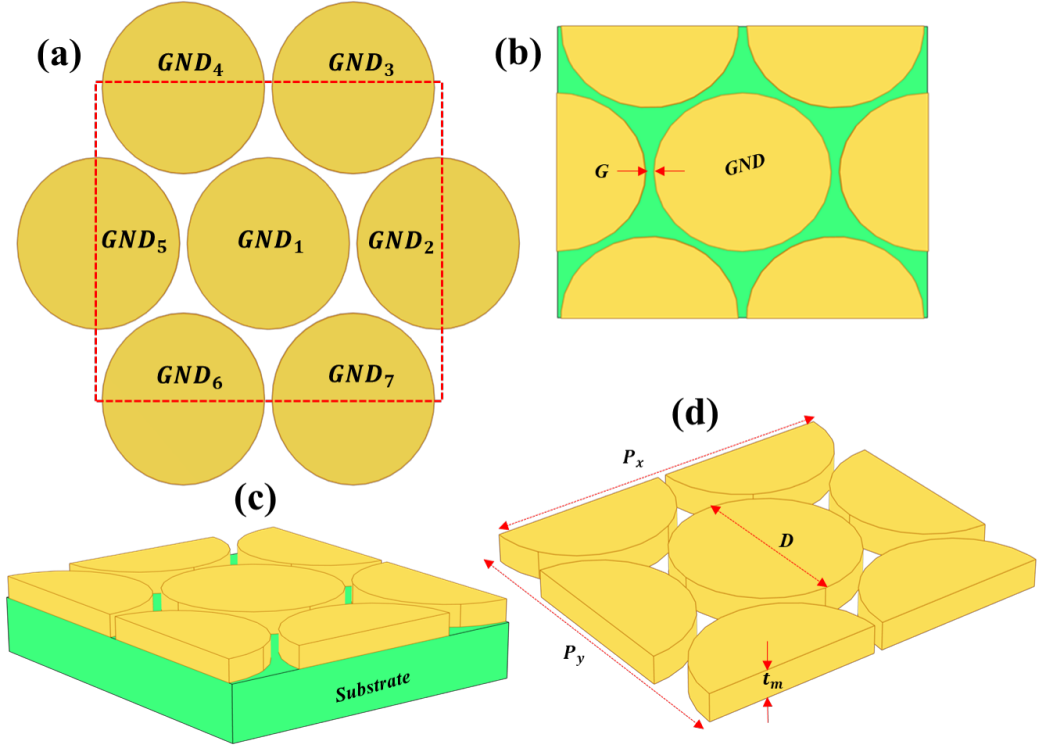


Figure 3.2. Schematic representation of Unit cell. GND=Gold Nano Disk

3.2.3 The Plasmonic SEIRA Substrate Model of Materials

The WOM in COMSOL Multiphysics was selected for our simulation. With optical frequencies or wavelengths in the nano-to-micrometer range, the WOM resolves issues related to EM waves. The settings of material attributes that are most crucial. The majority of non-conductive materials can be distinguished using the displacement field model applied to the material in COMSOL Multiphysics, as well as their refractive indices ($n = n + ik$), real (n), and imaginary (k). The energy loss during wave propagation is represented by the value of k , which is often positive. If the dielectric material's refractive index is disper-

sive over the desired frequency, its frequency-dependent n_r and k can be determined from the metrology of the material, such as ellipsometry or Spectrophotometer [188]. The resulting data sets for refractive indices can be imported into COMSOL Multiphysics and will be adapted for simulation by a generalized multi-coefficient function. Since Ohm's Law ($J = E/\sigma$) can now be used to directly compute the current density for conductive materials like metal. Thus, $(\varepsilon(f) = 1 + i\sigma/(2\pi f\varepsilon_0))$ can be used to calculate the permittivity of conductive materials. It is obvious that the loss of the metal in this relationship is inversely correlated with its conductivity. This is consistent with the idea that low-frequency EM waves will be blocked by metal. To represent the electric displacement field in COMSOL Multiphysics, the metallic region must be chosen using "real permittivity," with the real component of permittivity as well as permeability configured as 1, and a certain electrical conductivity. The unit cell of the sample contains an ATR element (Diamond crystal is used as IRE) layer with a refractive value range between 2.4 and 2.65. A Nobel metal is utilized in the implementation of the nanoantenna in this study. The Drude model is commonly employed to simulate the optical characteristics of metals, with gold (Au) serving as the nanodisk for Nobel metals. Typically, the Drude model is employed to simulate the optical characteristics of metals, with gold (Au) serving as the Nobel metal for nanodisks. For every Nano disk in the unit cell, the material contents of Gold (Au) have been assigned as 0,1, and ε_{Au} (or(Epsilon) ep_{Au}) for electric conductivity, relative permeability, and permittivity, respectively. The Drude Model [71] depicts the permittivity of gold (ε_{Au}) as represented by Eq. (3.6) [189], which has a dispersion relation with regard to the frequency of EM wave.

$$\varepsilon_{Au} = \omega_p^2 / \omega(\omega + j\gamma_{Au}) \quad (3.6)$$

Table 3.1. Spatial coordinates (x, y and z, respectively) of GND

Thickness of Film (μm)	Range of Spectra
GND_1	$P_{x,y,z} = (0, 0, 0)$
GND_2	$P_{x,y,z} = (2 \times R, 0, 0)$
GND_3	$P_{x,y,z} = (R, \sqrt{3} \times R, 0)$
GND_4	$P_{x,y,z} = (-R, \sqrt{3} \times R, 0)$
GND_5	$P_{x,y,z} = (-2 \times R, 0, 0)$
GND_6	$P_{x,y,z} = (-R, -\sqrt{3} \times R, 0)$
GND_7	$P_{x,y,z} = (R, -\sqrt{3} \times R, 0)$

Where:

$$\varepsilon_{\infty} = 1$$

$$\omega_p = \text{Here the plasma frequency} = 1.2 \times 10^{16} \text{ rad/s}$$

$$\gamma_{Au} = \text{Here the collision frequency} = 10.5 \times 10^{13} \text{ rad/s}$$

For the solution of the Maxwell Equation given in Eq. (3.1), the three material components (properties) of electric conductivity, relative permittivity, and relative permeability in the EM waves interaction model must be entered in properly. When the built-in materials (those specified in the COMSOL material's library) are chosen, COMSOL Multiphysics instantly includes these components. It is also up to the users to independently specify their material and attributes. In Figure 3.1 the unit cell contains the Otto gap layer which is the water layer and the material properties of the water layer are represented with the water refractive index $n = 1.33$. For the Glass (Quartz) layer, the material modeling of the substrate depicted in Figure (3.3) is utilized. The Glass (Quartz) layer is chosen as the substrate material with the refractive index $n = 1.5$. Its material composition is derived from pre-built materials in the COMSOL material library that have the following properties: relative permeability, permittivity, and electric conductivity: $1, 1e^{-14}[S/m]$, 4.2, and $1, 1e^{-14}[S/m]$.

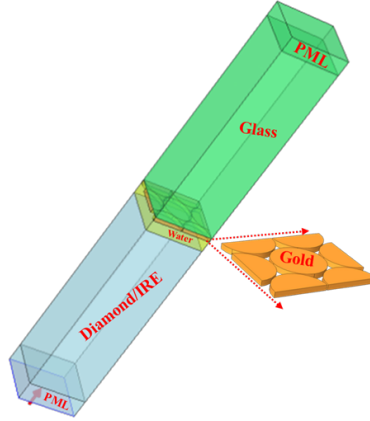


Figure 3.3. The unit cell's COMSOL Multiphysics numerical model with material representation. The water gap between the prism and nanoantenna was used to confirm the diversity of the reflectance characteristics associated with the Otto configuration and its suitability for bio-sample detection.

3.2.4 Boundary Conditions (BC)

Since the boundaries established in the simulation model are crucial to solving Maxwell's equations, the outcome will be significantly impacted. In certain instances, the desired design can also be made simpler in the simulation model by using the appropriate BC's, which can save a significant amount of simulation time.

Scattering BC

To simulate the state of an electric field resulting from incident (incoming) light and scattered (outgoing) light, scattering BC's are employed. The assumption behind scattering BC is that the boundaries serve as a transparent medium for both entering plane waves normal to the boundary and scattered waves. The Eq.(3.7) gives the expression for the scattered plane wave of the electric field.

$$E = E_{sc}e^{-jk(n.k)} + E_0e^{-jk(k.r)} \quad (3.7)$$

In Eq.(3.7) E_{sc} and E_0 are the scattered (outgoing) light and incident plane waves that travel in the direction k respectively. In the geometry model, two scattering BC's are used: one for incoming light and one for leaving light. In the PML layers, light from both sources—incoming and outgoing—is scattered.

Periodic Boundary Conditions

SEIRA substrate layer and PML layers in the x and y axes are bound by periodic BC's. Use periodic BC to make the solution equal on two different (but usually equally shaped) boundaries. Floquet periodic BC was imposed on the side walls.

3.2.5 Meshing the SEIRA substrate Geometry Model

Importantly, adaptive meshing is required for periodic BC to work accurately. Thus, an exact meshing scheme on the opposite side walls was imposed. The model of the SEIRA substrate in COMSOL Multiphysics uses free triangular mesh on the opposite side walls and free tetrahedral mesh (For inside the walls and Nano disks (Nanoantenna)) between the PML layers. PML layers are meshed by using the swept option (Distribution-based mesh).

3.3 Simulation Study for SEIRA substrate

The SEIRA substrate is designed to enhance the IR absorption of molecules adsorbed on its surface, allowing for sensitive detection and analysis of these molecules. To achieve a rigorous solution to Maxwell's equations, computational EM models in COMSOL Multiphysics are used. The WOM in COMSOL Multiphysics was selected for the simulation of SEIRA substrates. In the frequency domain, the SEIRA substrate study is simulated for several wavelengths of EM waves. COMSOL Multiphysics provides the capability to perform parametric sweeps for each parameter. An infinite film of close-packed nanoparticles (Nano Disks) is incident on by an incoming wave in the $\theta = 45^\circ$ incidence configuration, and the wave source is defined as a periodic port. The unit cell of the SEIRA substrate consists of a dielectric layer that functions as a diamond crystal. This dielectric layer possesses a refractive index of 2.53. The dielectric layer, with its high refractive index, plays a crucial role in facilitating the enhancement of IR absorption in the SEIRA substrate. By precisely controlling the thickness and properties of this layer, researchers can optimize the SEIRA substrate's performance for various applications, such as chemical sensing, and spectroscopy. Overall, the dielectric layer with a refractive index of 2.53 in the SEIRA substrate acts as a key component in enabling highly sensitive IR absorption measurements and opens up new possibilities for advanced molecular analysis and characterization. Since the thickness of the diamond crystal and glass(Quartz) substrate is much larger than the maximum wavelength, PML conditions are all applied at the z-axis whilst the BC's for the x-axis and y-axis are defined as periodic. The Poynting vector can also be integrated at the port of entry and exit to determine transmission or reflection. Without complicated sample preparation, the ATR offers the ability to analyze a variety of liquid samples. As seen in Figure (3.4), the ATR crystal (Diamond), which is typically an IR transparent material with a high refractive index and a polished surface, is the important component of the UATR module that measures ATR. At the crystal-to-sample contact, the IR beam is incident on the ATR crystal at an angle that is larger than the critical angle and is completely reflected. Due to the light's wave-like characteristics, it is not reflected immediately on the boundary surface but instead travels a short distance inside the sample that is in close contact with the crystal, taking the shape of an evanescent wave. The wavelength, refractive indices of the ATR crystal and sample, and angle of the incoming laser beam all affect the penetration depth, which is typically a few microns. The IR beam leaves the ATR crystal after interacting with the sample and is ultimately pointed at the IR detector. The diamond crystal used in this ATR unit has a refractive index in the waveband that interests us approximately 2.53. While the wave injects $\theta = 45^\circ$ of incident angle onto the diamond crystal, which is far more than the theoretical critical

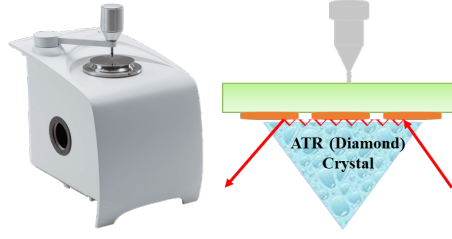


Figure 3.4. (a) UATR module with Diamond/ZnSe [12], (b) Schematic diagram of the mechanism of ATR measurement.

angle and ensures the entire internal reflection, the wave's theoretical critical angle for the wave impinging from the air/water on a crystal is 23.29° , 31.73° , respectively.

3.3.1 The Characterization of EM Responses and Tunability Confirmation

A completely three-dimensional FEM approach is used for the numerical simulations (in COMSOL Multiphysics). A linearly polarized wave impinges on the structure at a 45° incidence in the simulations. In the IR spectrum, the substrate is taken to be lossless with a refractive index of 1.5 (i.e., glass). To investigate the EM response of such a unit cell of SEIRA substrate design (as seen in Figure(3.2)), we start our simulation by fixing at $|E_0| = 1V/m$ the value of the E of the incoming EM radiation and the optical attributes of the SEIRA substrate have been evaluated by employing a linearly polarized EM plane wave with $E_0 = E_{0,y}$ and $E_0 = E_{0,x} + E_{0,y}$ (with $E_{0,x} = E_{0,y}$) for the closed packed array of GNDs. The resulting closed-packed array of GNDs-based unit cell reflection coefficient is defined as $abs(ewfd.S11)^2$, where *ewfd* is EM waves, frequency domain. S11, or scattering parameters, is the reflection coefficient at the input port, and *abs* stands for absolute values. Changing the size, shape, and composition of the nanostructures will allow you to tune the plasmon resonance to specific wavelengths. The reflection spectrum can be controlled through this tuning. It is possible, for instance, to design nanostructures that strongly reflect light at a specific wavelength or within a specific wavelength range. Utilizing plasmonic nanostructures to manipulate the reflection spectrum offers several uses, including sensing, imaging, and improving solar cell efficiency. The reflection spectrum of plasmonic sensors, for example, can be monitored to detect changes in the environment (e.g., a change in refractive index). We carried out a parametric numerical study using the unit cell Nano antenna design parameters, such as P , D , t_m , G , etc., to confirm the

tuneability of EM responses for the proposed closed-packed array of GND-based Nanoantenna. In order to verify the response(as reflectance) tuneability over the P, three ($P=500\text{nm}$, 750nm , and 1000nm) distinct P-based designs were first selected. As is well known, P (Distance from one GND half to other GND half in unit cell as we see in Figure 3.2 (d)) is the sum of GND D (Diameter of GND) and G (Gap between to GND). The reflection spectrum shows a Lorentzian line form as seen in Figure (3.5)(a). We changed the GND design parameters such as D and G for each design, and we fixed the P and t_m . We can clearly observe the influence of the change in D on the resonance shift in Figure 3.5(a), which shows the reflection spectra for the proposed nanoantenna with varying D and G, and While $P=500\text{nm}$, $t_m=30\text{nm}$ as fixed parameters. A change in D refers to a change in the length of the unit cell sides such as P_x and P_y , for instance, and because of an increment or decrement in D, the area of the unit cell will change accordingly.

When $P=500\text{nm}$, the resonance peak shifted from $5.915\mu\text{m}$, $5.32\mu\text{m}$, $5.055\mu\text{m}$,

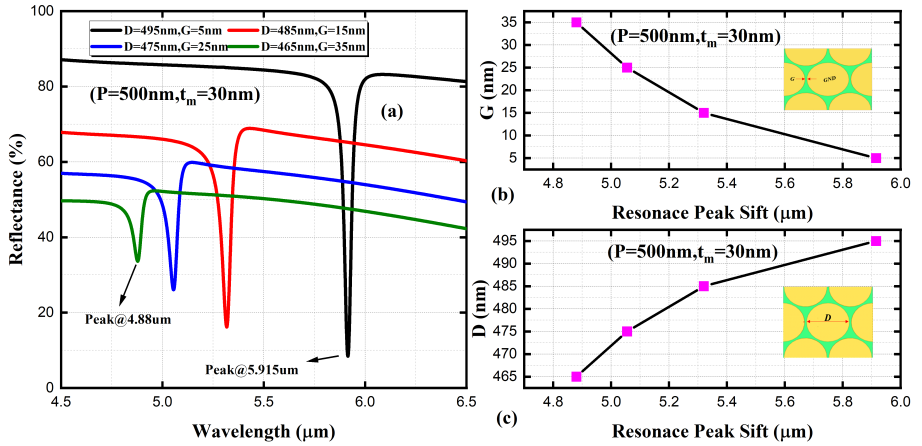


Figure 3.5. The reflection spectra with an azimuth angle $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) The influence of D and G on the reflection spectrum. (b) and (c) 2D representation for resonance peak shift as a function of G and D, respectively. While Here $P=500\text{nm}$ and $t_m=30\text{nm}$ are constant.

and $4.88\mu\text{m}$. To keep P constant, D varied from 495nm , 485nm , 475nm , and 465nm , while G varied from 5nm , 15nm , 25nm , and 35nm , respectively. Figure 3.5(b) is a two-dimensional line graph that represents the resonance peak shift as a function of D. Figure 3.5(c) is a two-dimensional line graph that represents the resonance peak shift as a function of G. When $P=500\text{nm}$ the unit cell sides length are respectively $P_x=1\mu\text{m}$, $P_y=0.88\mu\text{m}$. The 2D surface plot representation seen in Figure 3.6 clearly illustrates the influence of G and D on the resonance peak

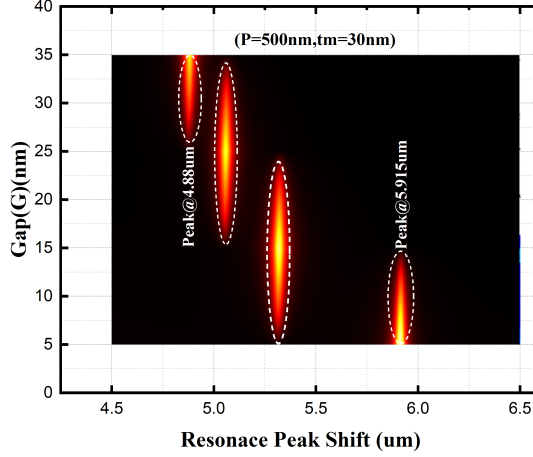


Figure 3.6. Resonance peak shift using a function for G is demonstrated numerically in COMSOL(as 2D surface plot). P and t_m are fixed in this case, whereas G and D are variable.

as shift. The resonance peak shifts from $4.88\mu m$ (at $G=35nm$) to $5.915\mu m$ (at $G=5nm$). A SEIRA biosensor is likely to make use of hot-spot (At "hot-spots" on the nanoscale, the local dispersed EM field can be significantly enhanced thanks to noble-metal nanostructures) engineering and surface plasmon localization. A localized electric field hot spot will have a larger surface enhancement effect on SEIRA signals. Because of these enhanced signals, bio-markers can be detected with greater sensitivity. Using SEIRA spectroscopy and discrete dipole approximation scattering (SEIRA nearfield enhancement) calculations, we have studied the effect of gap on electric field enhancement in GND closed packed arrays with gaps varying from 5 to 35 nm. Smaller gap sizes resulted in higher nearfield enhancement as shown in Figure 3.7. In order to confirm the tuneability response of our proposed GND-based Nano antenna in the fingerprint region, we used the second value of $P=750nm$ in our numerical analysis. We can clearly observe the influence of the change in D on the resonance shift in Figure 3.8(a), which shows the reflection spectra for the proposed nanoantenna with varying D and G , and While $P=750nm, t_m=30nm$ as fixed parameters. When $P=750nm$, the resonance peak shifted from $6.17\mu m$, $5.78\mu m$, $5.53\mu m$, and $5.36\mu m$. To keep P constant, D varied from $745nm$, $735nm$, $725nm$, and $715nm$, while G varied from $5nm$, $15nm$, $25nm$, and $35nm$, respectively. Figure 3.8(b) is a two-dimensional line graph that represents the resonance peak shift as a function of D . When $P=750nm$ the unit cell sides length are respectively $P_x=1.5\mu m$, $P_y=1.32\mu m$. The 2D surface plot

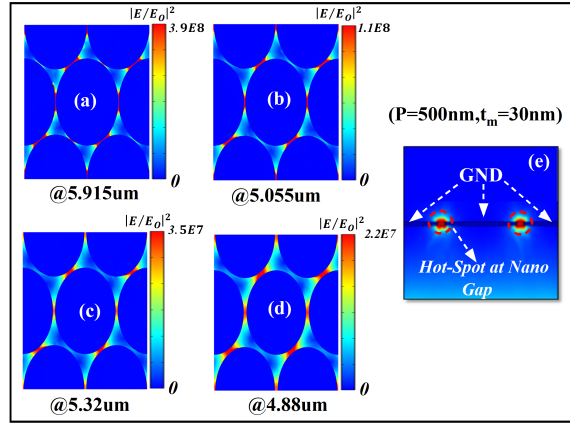


Figure 3.7. Near-Field Enhancement for When G and D vary to make sure P is constant as 500nm . Near E-field confinement with Hot-Spot created by coupling between GND are clearly visible between the Nano gap (Between Nano disks) as seen in figure (a-e).

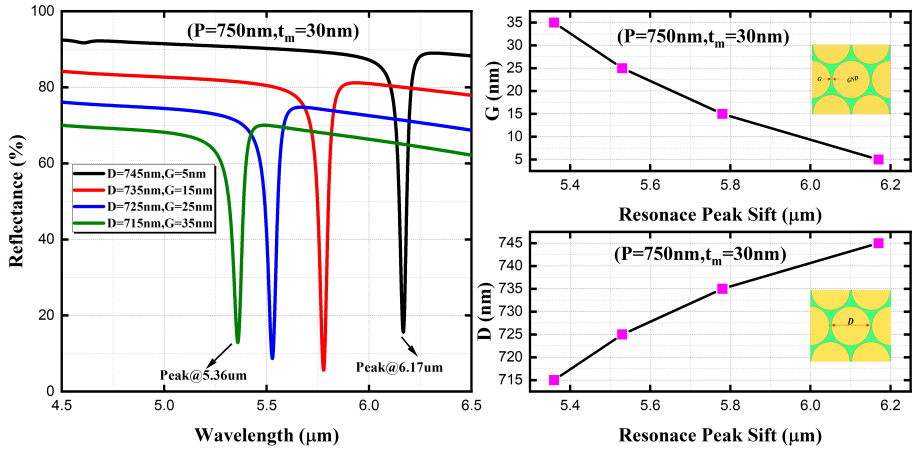


Figure 3.8. The reflection spectra with $\phi=0^\circ$ and an incidence angle of $\theta=45^\circ$. (a) The influence of D and G on the reflection spectrum. (b) and (c) 2D representation for resonance peak shift as a function of G and D , respectively. While Here $P=750\text{nm}$ and $t_m=30\text{nm}$ are constant.

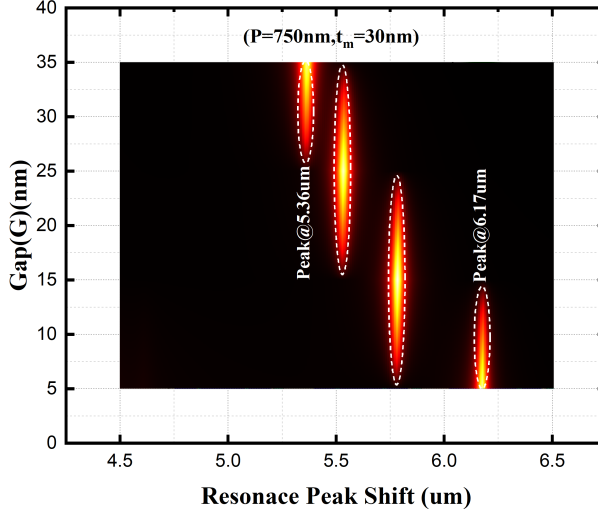


Figure 3.9. Resonance peak shift using a function for G is demonstrated numerically in COMSOL(as 2D surface plot). P and t_m are fixed in this case, whereas G and D are variable.

representation is seen in Figure 3.9 that clearly illustrates the influence of G and D on the resonance peak as shift. The resonance peak shifted from $5.36\mu m$ (at $G=35nm$) to $6.17\mu m$ (at $G=5nm$). Next, we employed the 3rd value of $P=1000nm$ in our numerical analysis to confirm the tuneability response of our proposed GND-based nanoantenna in the fingerprint region. We can clearly observe the influence of the change in D on the resonance shift in Figure 3.11(a), which shows the reflection spectra for the proposed nanoantenna with varying D and G , and While $P=1000nm, t_m=30nm$ as fixed parameters. When $P=1000nm$, the resonance peak shifted from $6.31\mu m$, $6.02\mu m$, $5.83\mu m$, and $5.7\mu m$. The 2D surface plot representation seen in Figure 3.12 clearly illustrates the influence of G and D on the resonance peak as shift. The resonance peak shifted from $5.7\mu m$ (at $G=35nm$) to $6.31\mu m$ (at $G=5nm$). Hence, the geometry of the structure can influence the resonant frequencies of reflection peaks, and selective frequencies can be obtained. Here, we use three different P values ($500nm$, $750nm$, and $1000nm$) for a GND-based unit cell to illustrate the efficacy of this tuning process. D and G are varied to maintain a constant P value. To conclude, tuning the periodicity of the unit cell array (or the sides length change) can have a dramatic effect on the resonance peak shift, whereas here t_m of GND is fixed. One of the design parameters for the proposed GND-based nanoantenna is also (t_m). In the

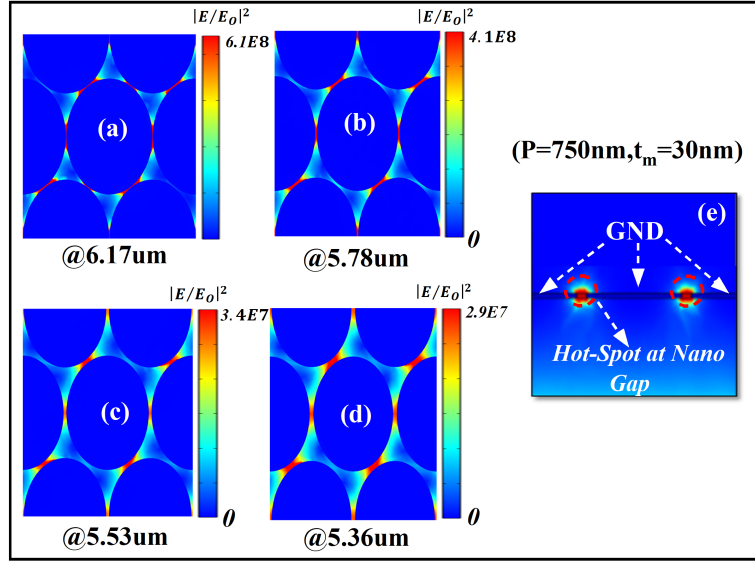
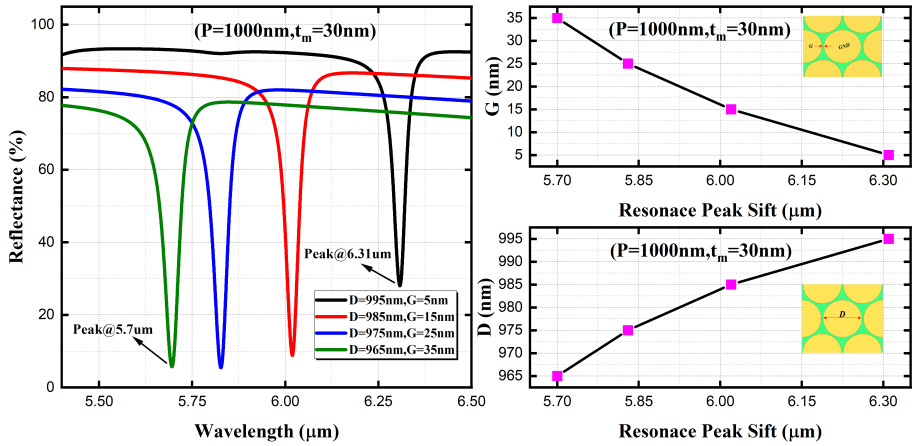


Figure 3.10. Near-Field Enhancement for When G and D vary to make sure P is constant as 750nm. Near E-field confinement with Hot-Spot created by coupling between GND is clearly visible between the Nano gap (Between Nano disks) as seen in Figure (a-e).



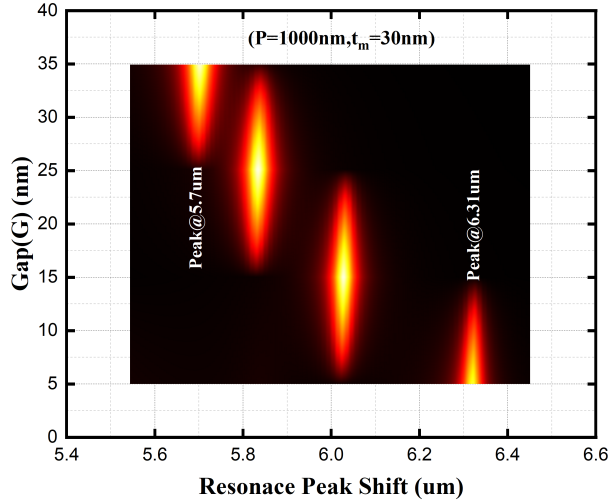


Figure 3.12. Resonance peak shift using a function for G is demonstrated numerically in COMSOL(as 2D surface plot). P and t_m are fixed in this case, whereas G and D are variable.

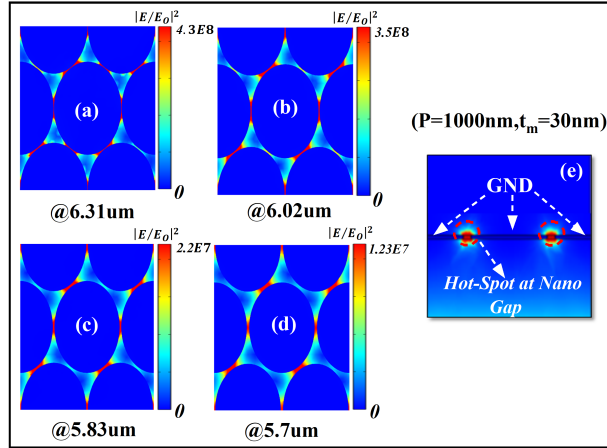


Figure 3.13. Near-Field Enhancement for When G and D vary to make sure P is constant as 1000nm. Near E-field confinement with Hot-Spot created by coupling between GND are clearly visible between the Nano gap (Between Nano disks) as seen in figure (a-e).

prior analysis, we selected three P's (500 nm, 750 nm, and 1000 nm), but t_m is fixed in every case. G and D, however, vary to maintain a constant P. The t_m of the nanoantenna, which can have a big impact on its optical characteristics, can be examined using the reflectance spectra. In this section, we check the influence (tuneability) of t_m on resonance peak shift for all three P's. SP, which are collective oscillations of electrons at the metal surface, is a common target for nanoantenna design. The resonance wavelength can be adjusted by adjusting the antenna t_m . The SP frequency may vary, which could alter the reflectance spectra.

It is feasible to adjust the Nano antenna's optical response to wavelengths by adjusting its t_m . This can be useful in situations when the reflectance spectra are designed to pick out and accentuate light wavelengths, like in spectral filtering applications. The nanoantenna t_m can also influence its interaction with the surrounding dielectric environment. Variations in t_m can influence the effective refractive index that incident light experiences, which can impact the resonance wavelength and the reflectance spectra as a whole.

We carried out the numerical simulation design parametric analysis for various values of t_m such that 20nm to 100nm with 20nm meter step in order to validate our proposed GND array-based Nano antenna tuneability over the GND t_m . In the first case, we choose the fixed P as 500nm vary the t_m , and observe the tuneability. Figure 3.14 clearly illustrates how t_m affects the resonance peak with the shift. In Figure 3.14(a), which shows the reflection spectra for the proposed nanoantenna with varying t_m , and While P=500nm, D=485nm, G=15nm as fixed parameters. When P=500nm, the resonance peak shifted from $5.22\mu m$, $5.42\mu m$, $5.58\mu m$, $5.71\mu m$, and $5.8\mu m$. Figure 3.14(b) is a two-dimensional line graph that represents the resonance peak shift as a function of t_m . The 2D surface plot representation seen in Figure 3.14(c) clearly illustrates the influence of t_m (at fixed parameters such as P=500nm, G=15nm, D=485nm) on the resonance peak as shift. The resonance peak shifting from $5.22\mu m$ (at $t_m=20nm$) to $5.8\mu m$ (at $t_m=100nm$). In Next, When P=750nm while t_m varies. In the second case, we choose the fixed P as 750nm vary the t_m , and observe the tuneability. Figure 3.15 that clearly illustrates how t_m affects the resonance peak with the shift. In Figure 3.15(a), which shows the reflection spectra for the proposed nanoantenna with varying t_m , and While P=750nm, D=735nm, G=15nm as fixed parameters. When P= 750nm, the resonance peak shifted from $5.71\mu m$, $5.86\mu m$, $5.96\mu m$, $6.03\mu m$, and $6.07\mu m$. Figure 3.15(b) is a two-dimensional line graph that represents the resonance peak shift as a function of t_m . The 2D surface plot representation seen in Figure 3.15(c) clearly illustrates the influence of t_m (at fixed parameters such as P=750nm, G=15nm, D=735nm) on the resonance peak as shift. The resonance peak shifting from $5.71\mu m$ (at $t_m=20nm$) to $6.07\mu m$ (at $t_m=100nm$). Next, when P = 1000 nm while t_m varies. In the second case, we

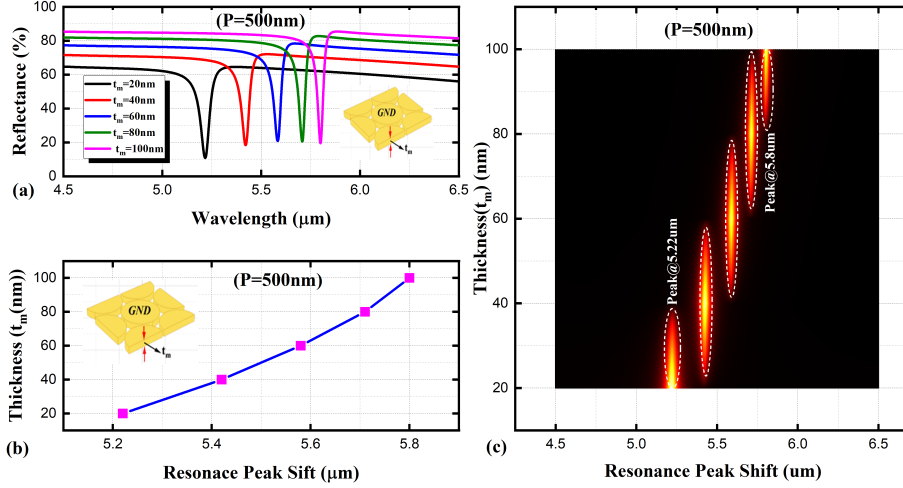


Figure 3.14. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) The influence of GND t_m on the reflection spectrum. (b) 2D Representation for resonance peak shift, and here $P=500\text{nm}$, While G and D are constant. While t_m varies from 20nm to 100nm with a 20nm sweep step size.

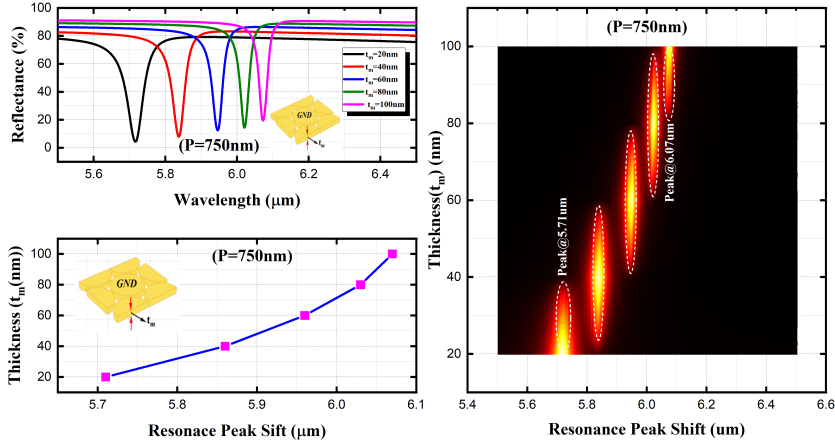


Figure 3.15. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) The influence of GND t_m on the reflection spectrum. (b) 2D Representation for resonance peak shift, and here $P=750\text{nm}$, While G and D are constant. While t_m varies from 20nm to 100nm with a 20nm sweep step size.

choose the fixed P as 1000 nm, vary the t_m , and observe the tuneability. Figure 3.16 that clearly illustrates how t_m affects the resonance peak with shift. Figure 3.16(a), which shows the reflection spectra for the proposed nanoantenna with varying t_m , while $P = 1000$ nm, $D = 985$ nm, and $G = 15$ nm as fixed parameters. When $P = 1000$ nm, the resonance peak shifted from $6.01\mu\text{m}$, $6.06\mu\text{m}$, $6.15\mu\text{m}$, $6.19\mu\text{m}$, and $6.21\mu\text{m}$. Figure 3.16(b) is a two-dimensional line graph that represents the resonance peak shift as a function of t_m . The 2D surface plot representation is shown in Figure 3.16(c) which clearly illustrates the influence of t_m (at fixed parameters such as $P = 1000$ nm, $G = 15$ nm, and $D = 985$ nm) on the resonance peak as a shift. The resonance peak shifts from $6.01\mu\text{m}$ (at $t_m = 20$ nm) to $6.21\mu\text{m}$ (at $t_m = 100$ nm). The parametric study presented above

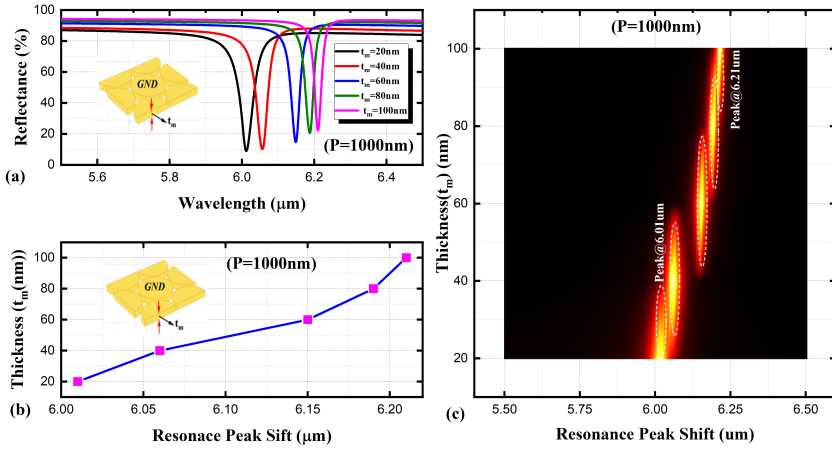


Figure 3.16. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) The influence of GND t_m on the reflection spectrum. (b) 2D Representation for resonance peak shift, and here $P = 1000$ nm, While G and D are constant. While t_m varies from 20 nm to 120 nm with a 20 nm sweep step size.

provides proof of the resonant peak's tuneability throughout a range of t_m for three distinct P values (500, 750, and 1000 nm). To confirm that P is fixed, the other two design parameters, D and G , are kept unchanged while t_m fluctuates for all three of these P 's. In all numerical analyses, G was filled with water ($n = 1.33$). As we know, an analytical device called a biosensor can detect and quantify biological molecules or chemical compounds by converting a biological response into a measurable signal. On the other hand, materials or structures known as nanostructures have dimensions at the Nanoscale, that are often smaller than 100 nm (as seen in Figure 3.17) [27]. Because of their small size, Nanos-

structures can have special qualities and purposes. The use of Nanostructures in biosensing has enhanced biosensor performance in several ways and created new opportunities (such as enhanced sensitivity, improved selectivity, miniaturization, faster response times, multi-analyte detection, and long-term stability). In the field of biosensors, the gap between Nanostructures and biosensing can be defined as the intersection between Nanotechnology and biosensors. A gap in the reflection spectrum between nanostructures shows how light may be engineered and controlled to interact with nanoscale structures, opening up a wide range of useful applications in photonics and optics. Research & development in the region, brimming with possibilities for use in food safety, environmental monitoring, medical diagnostics, and more, is found in the space between nanostructures and biosensing. We already know that our proposed GND-based Nano antenna (self-assembled SEIRA substrate) is tunable across the design parameters (such as P, D, G, and t_m) based on earlier numerical research. In Next Here, we performed the parametric numerical analysis for design parameter G (gap varies between the GND) over the sensitivity (impact on absorbance due to artificial bioanalyte) for all three P's. Unit cells having non-equal periodicities P_x and P_y make up the GND array. When G is changed, and G is directly related to the area of a unit cell. This geometric arrangement (as seen in Figure(3.2) causes the nanogaps to develop between adjacent unit cells along the x and y axes of the array. Here in this next section, we performed the geometric parametric analysis with different values of G (fill the gap or replace the water gap with a bio-sample (artificial bioanalyte)) for a better understanding of the performance of SEIRA substrate in terms of absorption. The G between GND was filled up with a material of complex permittivity to model its dispersive optical behavior. This material permittivity is determined using a Drude-Lorentz oscillator model[71]. An Eq.(3.8) for Drude-Lorentz that describes the relative permittivity of the bio-sample [190]. An oscillator with amplitude is used to imitate absorption, While eigenfrequency is ω_0 . Hence, the parameters we chose to determine the permittivity of the bio-sample in MATLAB are $A(\text{Amplitude}) = 10^{-5}$, $\varepsilon_\infty = 1.8$ and $\gamma(\text{Damping factor}) = 2.8 \times 10^{11}$. To reach the biosample's [190] absorbance band, these parameters have been specified.

$$\varepsilon_\omega = \varepsilon_\infty + \frac{A\omega_0^2}{\omega_0^2 - \omega^2 - i\gamma\omega} \quad (3.8)$$

Thus, a permittivity model for bio-sample is established for $6.293 \mu m$ or ($1589 cm^{-1}$). The both real(n) & imaginary(k) part of the index of refraction, as $n^\sim = n + ik$, are shown in Figure 3.18. Here is Figure (3.19) illustrating the simulated reflectance spectra for different values of G between the close-packed array of GND. The values of G vary from 5nm to 35 nm, and here G is filled with

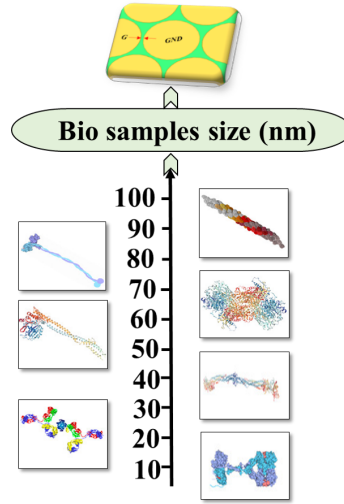


Figure 3.17. Scale representation of example Bio Samples structures from 10 nm to 100 nm in the bottom panel [27]. Above panel: 3D-proposed GND array-based unit cell with G used in the numerical simulations. And G was filled with an artificial bioanalyte.

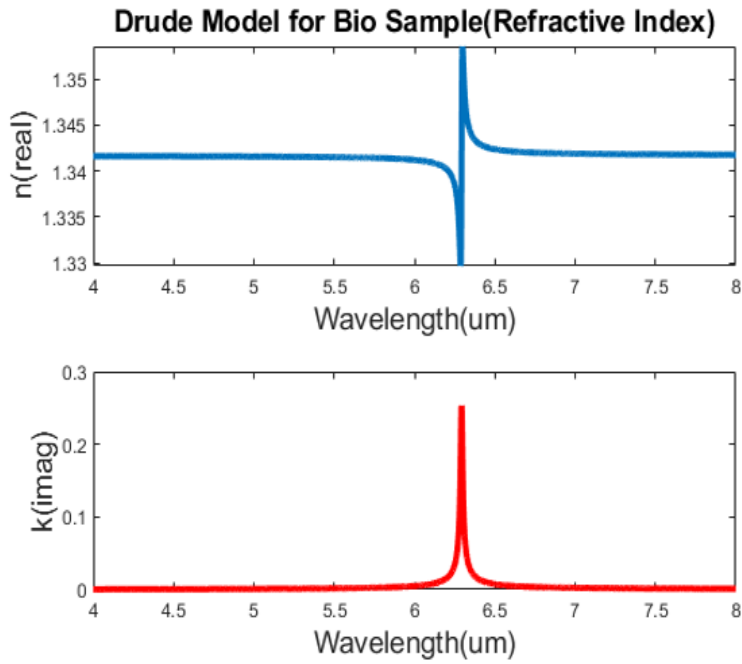


Figure 3.18. Real (n) & imaginary (k) part of the index of refraction of the bio-sample as a function of the wavelength.

an artificial bio sample as a replacement for water. We can see the absorbance dip (magenta dashed box) decreasing with an increment in G . The thickness of G is equal to Nanoantenna thickness, and the unit cell surface is also covered with an artificial bio-sample monolayer. The higher the dipper absorbance dip, the more important it plays in SEIRA gain (in terms of sensitivity). While D and G vary to maintain the P constant, $P = 500$ nm and $t_m = 30$ nm are used in stimulation as parameters that correspond to Figure (3.19) for reflectance spectra. We observe an absorbance dip as a result of the investigated artificial bio-sample monolayer, which is reduced as G increases. Figure (3.19) illustrates the inverse relationship between G and absorbance drop.

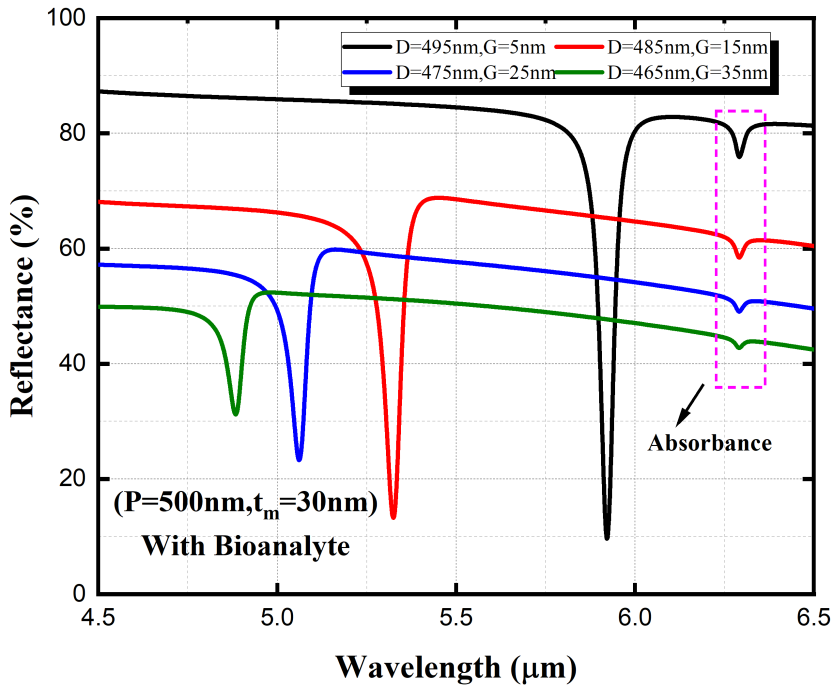


Figure 3.19. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) Simulated reflectance spectra for different values of G with an artificial bio-sample. The dashed box indicates the impact of G (5nm to 35 nm) at absorbance dip. Absorbance dip appeared due to an artificial bio-sample that is established for $6.293 \mu m$ or $(1589 cm^{-1})$.

The absorbance dip is strongly related to G , and this analysis gives us a clear idea of choosing a suitable G value for the proposed close-packed array

of GND-based SEIRA substrates. Figure (3.20) represents the clear idea about the influence of G on absorbance dip as a change in reflectivity. We studied the SEIRA gain, which is defined as a ratio of $\frac{\Delta R}{\Delta R_0}$. SEIRA gain has a direct relationship with the SEIRA enhancement factor. Where ΔR and ΔR_0 are the changes in reflectivity of the met surface and of a flat, unstructured metal sheet, respectively, determined in the presence and absence of the adsorbed analyte. As we probed the adsorbed analyte at $(6.293 \mu m)$ and we calculated the ΔR (it's a difference in reflectivity due to the presence and absence of the bio-sample) for different values of G . For different values of G , the absorbance dip appeared due to an artificial bio-sample that was established at $6.293 \mu m$ or (1589 cm^{-1}) .

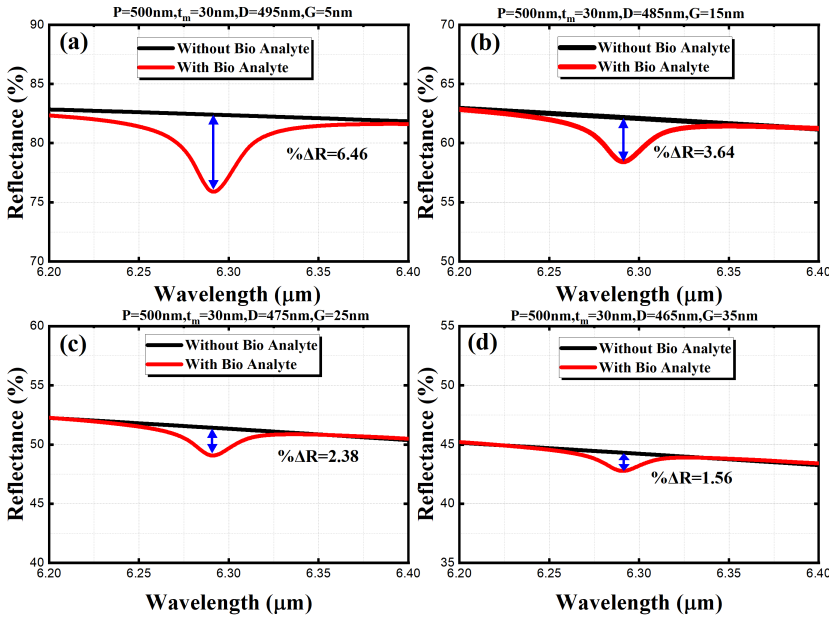


Figure 3.20. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a-d) Simulated reflectance spectrum for different values of G without (black) and with (red) artificial bio-sample. The blue arrow indicates the impact of varying G (5nm, 15nm, and 35nm) and we calculate this impact as ΔR (change in reflectivity due to artificial bio-sample).

Figure (3.21) shows the variation in reflectivity caused by the artificial bio-sample at $P=500 \text{ nm}$ for various values of G as a function of G and ΔR . The expression $(\Delta R = R(\text{without adsorbed artificial bio analyte}) - R(\text{with adsorbed artificial bio analyte}))$ have be used to compute the ΔR . In order to observe how

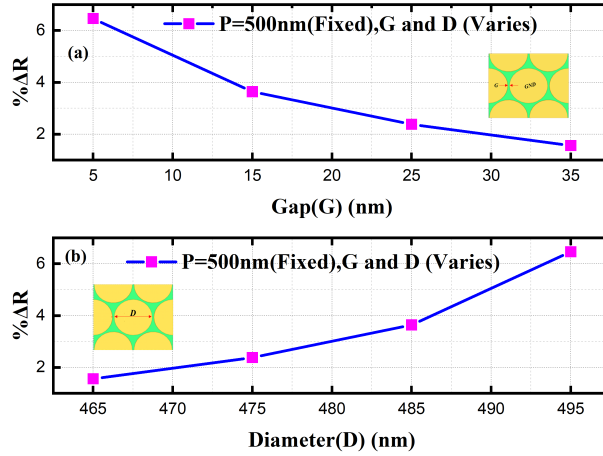


Figure 3.21. (a) 2D representation of changes in reflectivity (ΔR) as a function of the G between GND. G varies from 5nm to 35nm. (b) 2D representation of changes in reflectivity (ΔR) as a function of the D . GND D varies from 495nm to 465nm. P is fixed in all scenarios, with D and G varying to keep P constant, while $t_m = 30$ nm.

varying G affected the artificial bio-sample absorbance dip, we performed the analysis for $P = 750$ nm. The absorbance dip decreases with the increase in G . A G -affected artificial bio-sample absorbance decrease was detected. Here, $t_m = 30$ nm and $P = 750$ nm are fixed, but D and G are changing to maintain the P fix. As can be observed in the figure, the absorbance drop is deeper for low values of G and shallower at high values of G . It fluctuates in this analysis from 5 nm to 35 nm, while D varies from 745nm to 715nm in order to maintain P as a fixed parameter. An artificial bio-sample with an established value of $6.293 \mu m$ or (1589 cm^{-1}) caused the absorbance dip to emerge for varying values of G . Figure (3.21) shows the variation in reflectivity caused by the artificial bio-sample at $P = 750$ nm for various values of G as a function of G and ΔR . To see how G affected the third value of $P = 1000$ nm. Since D likewise ranges from 995 nm to 965 nm, the effect of G 's various values on the artificial bio-sample absorbance—such as 5 nm, 15 nm, 25 nm, and 35 nm—confirms that P is fixed at 1000 nm. The figure represents the influence of G on the absorbance dip. Figure (3.21) shows the variation in reflectivity caused by the artificial bio-sample at $P = 1000$ nm for various values of G as a function of G and ΔR .

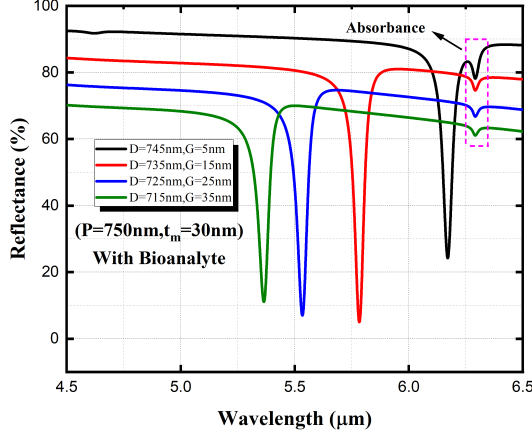


Figure 3.22. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a) Simulated reflectance spectra for different values of G with an artificial bio-sample. The dashed box indicates the impact of G (5nm to 35 nm) at absorbance dip. Absorbance dip appeared due to an artificial bio-sample that is established for $6.293 \mu\text{m}$ or (1589 cm^{-1}). Here $P=750\text{nm}$ and $t_m=30\text{nm}$ as fixed parameters.

3.3.2 SEIRA Gain and SEIRA EF

In order to assess the sensitivity of the proposed GND-based SEIRA substrate, we carry out the calculations for SEIRA gain and SEIRA EF for each of the three P 's (500nm, 750nm, and 1000 nm), as previously reported in our preliminary numerical study. In order to determine the precise SEIRA substrate sensitivity in this case, we compare the signal intensity obtained from molecules adsorbed on a GND-based antenna to the signal obtained from the same molecules in the absence of a GND-based antenna (flat layer with the same t_m), or, in other words, SEIRA gain. SEIRA gain is defined as $(\frac{\Delta R}{\Delta R_0})$, as far as we know. where the differences in reflectivity of the SEIRA substrate and a flat, unstructured metal layer, respectively, are represented by (ΔR) and ΔR_0 , which are estimated with the adsorbed artificial bio analyte present and absent. Here, We describe the reference calculation to derive ΔR_0 . In the previous subsection, we had performed the numerical computation as ΔR for all P 's using the proposed GND-based SEIRA substrate (such as in Figures (3.20,3.23,3.26, respectively). We swapped out the GND-based antenna in numerical design for a flat gold layer with the same $t_m=30\text{nm}$ value as the proposed Nanoantenna in order to do the ΔR_0 measurements. We calculate the ΔR_0 by using this expression ($\Delta R_0 = R_0(\text{without}$

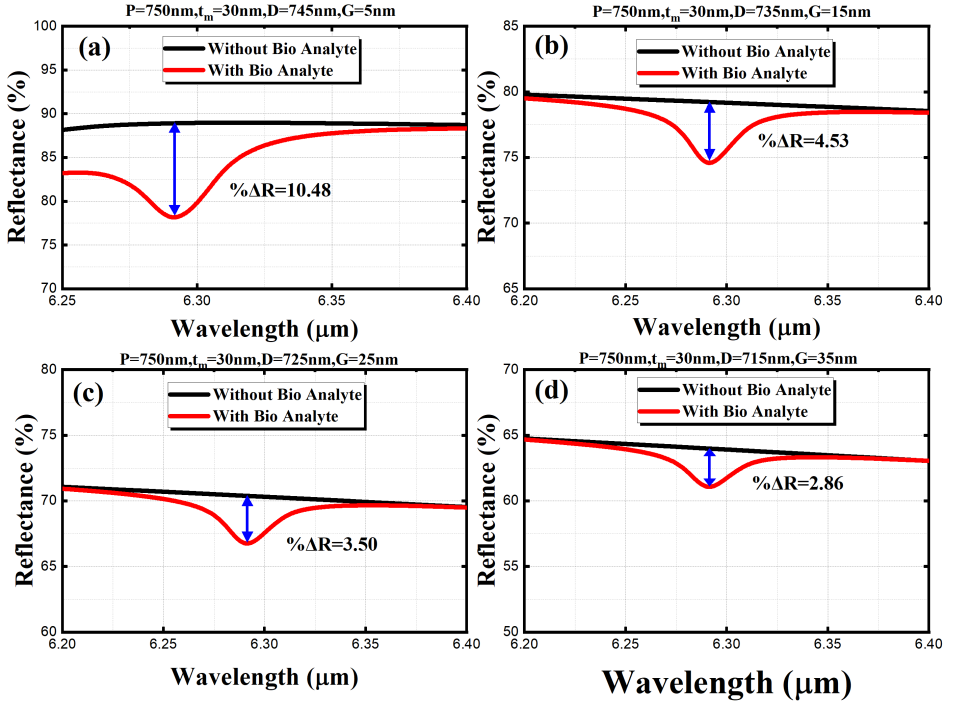


Figure 3.23. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a-d) Simulated reflectance spectra for different values of G without (black) and with (red) artificial bio-sample. The blue arrow indicates the impact of varying G (5nm, 15nm, and 35nm) and we calculate this impact as ΔR (change in reflectivity due to artificial bio-sample). Here $P = 750$ nm and $t_m = 30$ nm as fixed parameters.

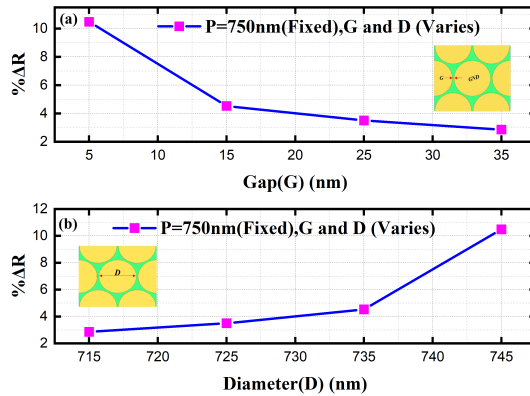


Figure 3.24. (a) 2D representation of changes in reflectivity (ΔR) as a function of the G between GND. G varies from 5nm to 35nm. (b) 2D representation of changes in reflectivity (ΔR) as a function of the D . GND D varies from 745nm to 715nm. P is fixed in all scenarios, with D and G varying to keep P constant, while $t_m=30\text{nm}$.

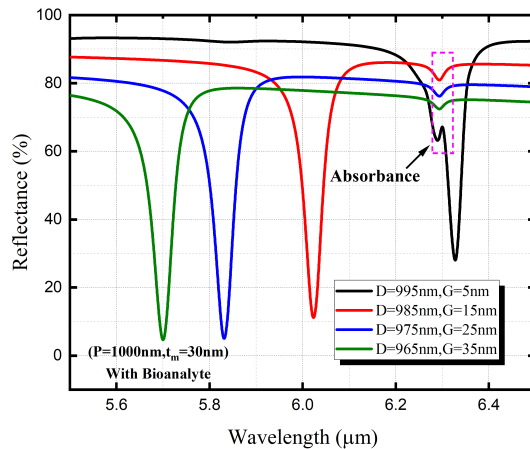


Figure 3.25. The reflection spectra with $\phi=0^\circ$ and an incidence angle of $\theta=45^\circ$. (a) Simulated reflectance spectra for different values of G with an artificial bio-sample. The dashed box indicates the impact of G (5nm to 35 nm) at absorbance dip. Absorbance dip appeared due to an artificial bio-sample that is established for $6.293 \mu\text{m}$ or (1589 cm^{-1}). Here $P=1000 \text{ nm}$ and $t_m=30\text{nm}$ as fixed parameters.

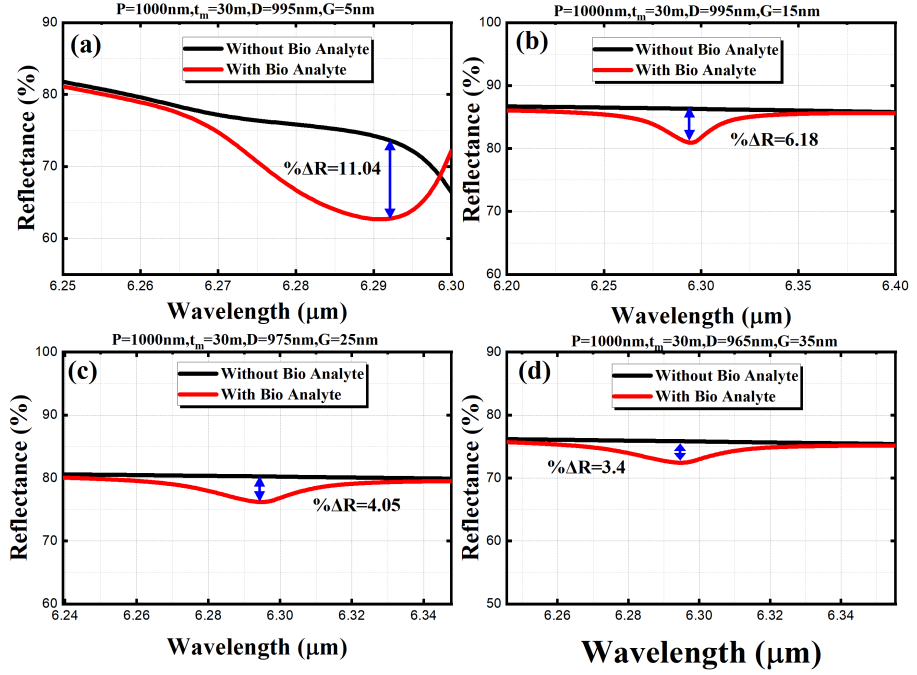


Figure 3.26. The reflection spectra with $\phi = 0^\circ$ and an incidence angle of $\theta = 45^\circ$. (a-d) Simulated reflectance spectrum for different values of G without (black) and with (red) artificial bio-sample. The blue arrow indicates the impact of varying G (5nm, 15 nm, and 35 nm), and we calculate this impact as ΔR (change in reflectivity due to artificial bio-sample). Here $P = 1000$ nm and $t_m = 30\text{nm}$ as fixed parameters.

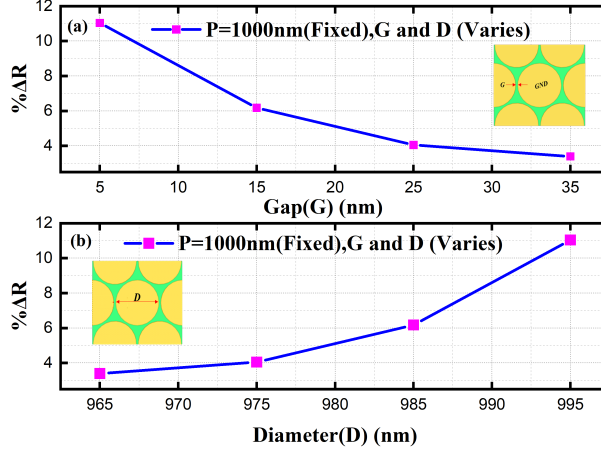


Figure 3.27. (a) 2D representation of changes in reflectivity (ΔR) as a function of the G between GND. G varies from 5nm to 35nm. (b) 2D representation of changes in reflectivity (ΔR) as a function of the D. GND D varies from 995nm to 965nm. P is fixed in all scenarios, with D and G varying to keep P constant, while $t_m=30$ nm.

adsorbed artificial bio analyte)- R_0 (with adsorbed artificial bio analyte)). Figure 3.28 represents the numerical analysis for ΔR_0 measurement. Here, we see the reflection spectrum as a function of wavelength for a flat gold layer in the presence (Red, absorbance dip) and absence (Black, no absorbance dip). A bio-sample monolayer has a $t_m=30$ nm, which is the same as the thickness of our nanoantenna. In Figure 3.29 (a) and (b) SEIRA gain is expressed as a 2D function of G and D when $P = 500$ nm and $t_m=30$ nm(as fixed parameters), respectively. As we can see in (a) and (b), the SEIRA gain increases in proportion to G. The SEIRA gain values fluctuate (2.3×10^3 , 1.3×10^3 , 8.5×10^2 , and 5.6×10^2 , respectively) when G changes from 5 nm to 35 nm. In Figure 3.30 (a) and (b) SEIRA gain is expressed as a 2D function of G and D when $P = 750$ nm and $t_m=30$ nm(as fixed parameters), respectively. As we can see in (a) and (b), the SEIRA gain increases in proportion to G. The SEIRA gain values fluctuate (3.7×10^3 , 1.6×10^3 , 1.25×10^3 , and 1.02×10^3 , respectively) when G changes from 5 nm to 35 nm. In Figure 3.31 (a) and (b) SEIRA gain is expressed as a 2D function of G and D when $P = 1000$ nm and $t_m=30$ nm(as fixed parameters), respectively. As we can see in (a) and (b), the SEIRA gain increases in proportion to G. The SEIRA gain values fluctuate (3.94×10^3 , 2.21×10^3 , 1.45×10^3 , and 1.2×10^3 , respectively) when G changes from 5 nm to 35 nm. As a result, as we can see in the last section (Figures

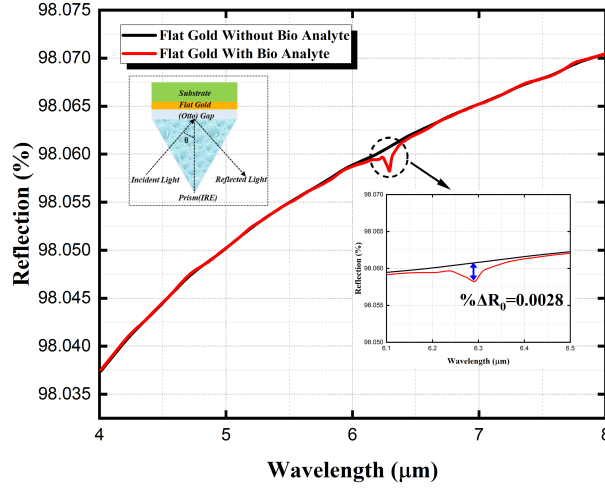


Figure 3.28. Illustration of a reference design with a thin Gold layer deposited on a Glass substrate and the corresponding reflection coefficient calculated using FEM-based COMSOL Multiphysics as a function of the wavelength.

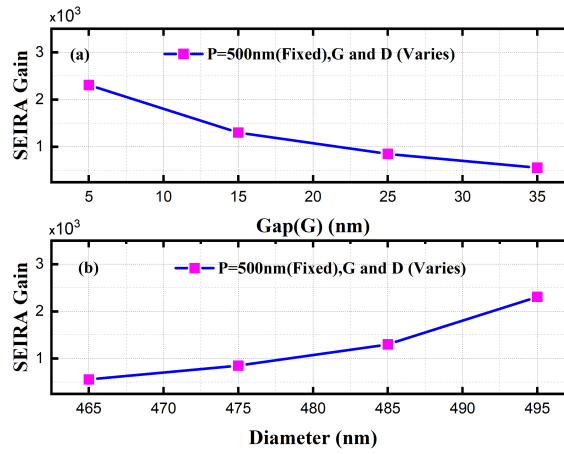


Figure 3.29. (a) The SEIRA gain as a function of the G between GND. (b) The SEIRA gain as a function of D. While $P=500\text{nm}$, $t_m=30\text{nm}$

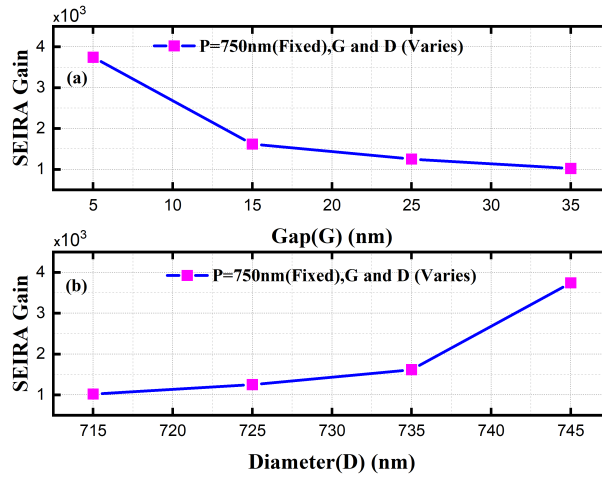


Figure 3.30. (a)The SEIRA gain as a function of the G between GND.(b)The SEIRA gain as a function of D.While $P=750\text{nm}, t_m=30\text{nm}$

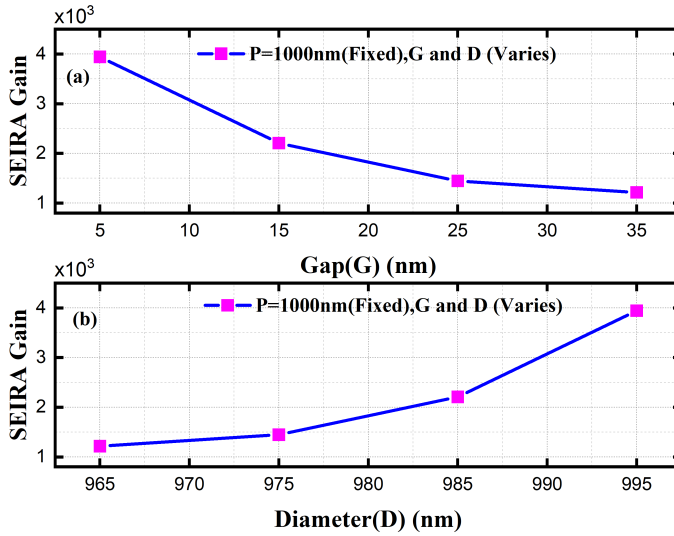


Figure 3.31. (a)The SEIRA gain as a function of the G between GND.(b)The SEIRA gain as a function of D.While $P=1000\text{nm}, t_m=30\text{nm}$

(3.20,3.23,3.26) for impact of G on absorbance dip due to artificial bio-sample, the SEIRA gain is also observed to have an influence on variance in G. When G is low, SEIRA gain values are more appropriate than when G is large. Because the SEIRA gain arises from the interaction between the molecular vibrations of adsorbed species and the LSP's (collective electron oscillations) on a GND array-based antenna (or SEIRA substrate). In other words, the interaction is inversely proportional to G, or it is more at minimal values of G. Figures (3.29,3.30,3.31) are the numerical evidence of this explanation. In the case of low G values compared to high G, the molecule vibrational signals are enhanced greatly when IR light interacts with a GND array-based antenna.

In next we performed the SEIRA EF calculation on behalf of our numerical analysis for different values of P's. As we studied expression such as $SEIRA\ EF = \frac{\Delta R}{\Delta R_0} \times \frac{A_0}{A_{SEIRA}}$ or $SEIRA\ EF = SEIRA\ gain \times \frac{A_0}{A_{SEIRA}}$. To quantify the exact SEIRA substrate sensitivity we require comparing the signal intensity obtained from molecules adsorbed on GND based antenna to the signal obtained from the same molecules without the presence of GND based antenna (flat layer with the same t_m), or In another word SEIRA gain. A_0 is an area of the unit cell (Nano antenna) exposed to light. While A_{SEIRA} is an effective area of Nano Antenna (where the field is localized). The EF can vary for different vibrational modes of molecules and different experimental setups. The Figure 3.32 (a) and (b) illustrate the 2D representation SEIRA EF for

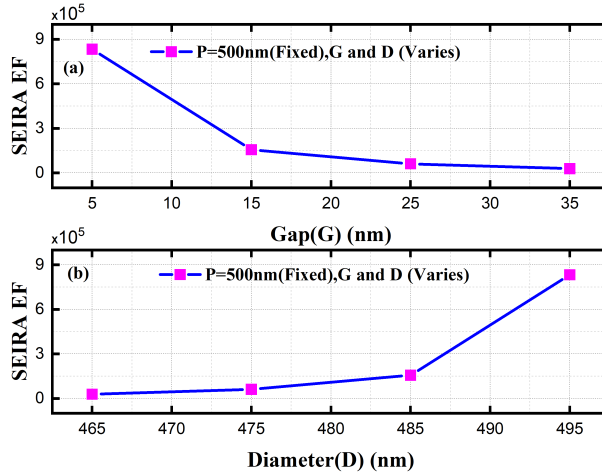


Figure 3.32. (a)The SEIRA EF as a function of the G between GND.(b)The SEIRA gain as a function of D.While $P=500\text{nm}$, $t_m=30\text{nm}$

$P=500\text{nm}$. When $t_m=30\text{nm}$, SEIRA EF values such as 8.33×10^5 , 1.56×10^5 ,

6.1×10^4 , and 2.87×10^4 are reported for varying values of G (5nm, 15nm, 25nm, and 35nm, respectively) or D (495nm, 485nm, 475nm, and 465nm, respectively), to maintain P as fixed. Figure 3.33 (a) and (b) illustrate the 2D repre-

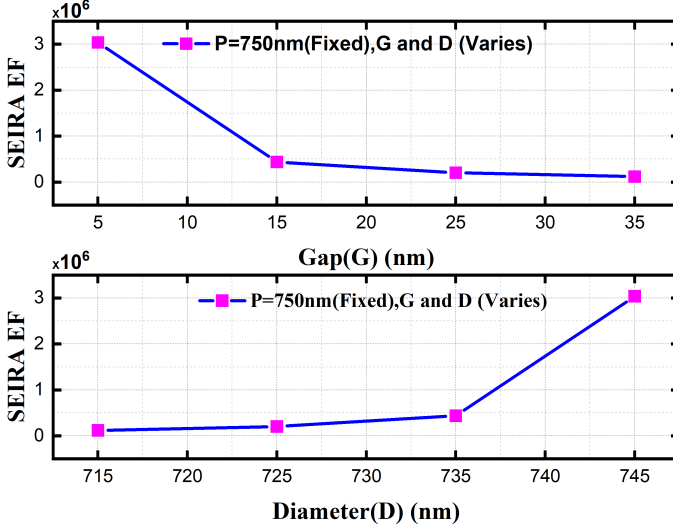


Figure 3.33. (a)The SEIRA EF as a function of the G between GND.(b)The SEIRA gain as a function of D.While $P=750$ nm, $t_m=30$ nm

sensation SEIRA EF for $P=750$ nm. When $t_m=30$ nm, SEIRA EF values such as 3.04×10^6 , 4.4×10^5 , 2.03×10^5 , and 1.19×10^5 are reported for varying values of G (5nm, 15nm, 25nm, and 35nm, respectively) or D (745nm, 735nm, 725nm, and 715nm, respectively), to maintain P as fixed. Figure 3.34 (a) and (b) illustrate the 2D representation SEIRA EF for $P=1000$ nm. When $t_m=30$ nm, SEIRA EF values such as 5.69×10^6 , 1.06×10^6 , 4.18×10^5 , and 2.5×10^5 are reported for varying values of G (5nm, 15nm, 25nm, and 35nm, respectively) or D (995nm, 985nm, 975nm, and 965nm, respectively), to maintain P as fixed.

The proposed nanoantenna is composed of a Nano Disk Au structure with a Nano gap that is positioned atop a reflective substrate to form a cavity. In this work, precise geometrical constraints were obtained by numerical analysis, resulting in a regular pattern of strong hotspot-containing nanogaps. This 3D shape effectively confines incident mid-IR radiation within its narrow junction, resulting in a hot spot that can be tailored to span the range of frequencies relevant to SEIRA and has SEIRA EF of 10^5 .

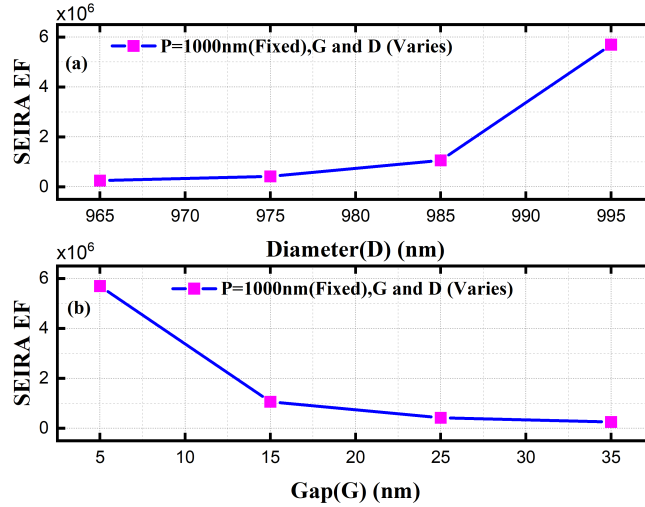


Figure 3.34. (a) The SEIRA EF as a function of the G between GND. (b) The SEIRA gain as a function of D. While $P = 1000 \text{ nm}$, $t_m = 30 \text{ nm}$

3.4 Summary

This chapter focuses on the design and optimization of plasmonic SEIRA substrates, and it will primarily deal with the design of the structure using COMSOL Multiphysics (FEM) numerical simulations, which describe the periodic arrays of gold Nano disks (GND). An artificial bioanalyte was employed to test the SEIRA substrate sensitivity, and the calculations were done using SEIRA gain and SEIRA EF. An extremely stable and well-organized structure, the GND closed-packed array nanostructure can increase the area accessible to light management and EM enhancement. An additional benefit of GND's array-based plasmonic nanostructure is that, because the mode is dispersed throughout the nanostructure, the sensitivity to small molecules is less reliant on the exact location of the molecule's binding in relation to the surface of the GND. The proposed Nano antenna consists of a Nano Disk Au structure with a Nano gap, positioned to create a cavity above a reflective substrate. This 3D geometry tightly confines incident mid-IR radiation into its small junction, yielding a hot spot with a theoretical Near-field enhancement factor is 10^8 and SEIRA EF is 10^5 , which can be designed to span the range of frequencies useful for SEIRA. In this work, precise geometrical constraints were obtained by numerical analysis,

resulting in a regular pattern of strong hotspot-containing nanogaps.

Chapter 4

SEIRA Substrate Fabrication and Morphological Analysis (Experimental Methodologies)

This chapter describes the first portion of the experimental tasks carried out in this work. The key objectives of this chapter are to introduce the fabrication process and the instruments that are used to examine the fabricated samples for morphological characterization. A cost-effective method for creating large-area periodic nanostructures with tunable nanostructure size, period, and material is called Nano-sphere lithography, or NSL. Additionally, NSL is a very flexible technique for creating different periodic nanostructures, including Nano-meshes and Nano-holes. The NSL approach is used to create single layers of nanoscale features in patterns that are identical or hexagonally close-packed. The scanning electron microscope (SEM), a popular microscopy tool for evaluating Nanoscale objects, is introduced.

4.1 Introduction

The community of Nano-scientists and Nano technologists is faced with substantial difficulty in the development of methods that can generate immobilized metal nanostructures at a reasonable cost. Periodic Nano-structured superlattices with symmetry breaches throughout the surface and thickness are of paramount relevance in plasmonic research because of their enormous potential in drug delivery, medicinal, and environmental sensor applications. The structures have several optical anisotropies and EM hotspots that increase the device's

sensitivity. The creation, development, application, and study of all sciences and technologies applied at the Nanoscale is known as nanotechnology. This refers to measurements that are meters in size, or Nano measures. The nanotechnology scale ranges from 1nm to 100nm and thus opens a wide range of possibilities, including the manipulation of simple atoms or molecules as well as viruses, bacteria, and organisms. Professor Richard Feynman introduced the idea of nanotechnology in 1959 during a meeting on the future of technology held at the California Institute of Technology (Caltech) [191]. Although nanotechnology is

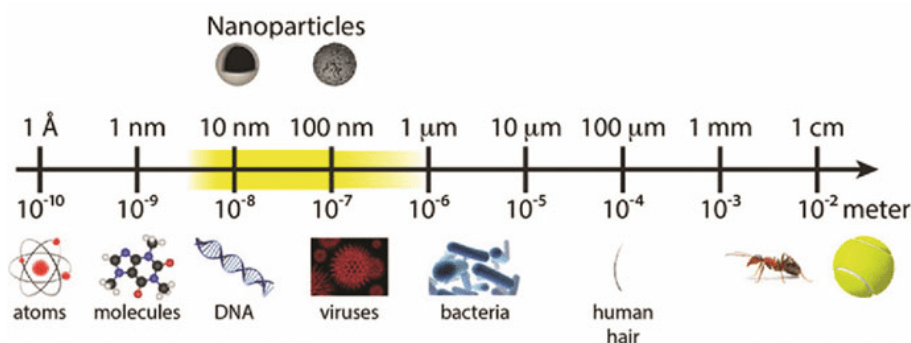


Figure 4.1. Comparing substances of various sizes with nanoscale dimensions. Nano-material Applications in Biomedical Engineering.[44]

a rather recent field of study, there are numerous manufacturing processes and equipment available to produce nanomaterials, such as nanostructured surfaces, nanoparticles, etc. The two categories of nanotechnology fabrication techniques are top-down(TD) approaches and bottom-up(BU) methods. On the one hand, there are top-down procedures that involve removing material from a bulk substrate until the desired Nano material is obtained. This group includes printing techniques. On the other hand, BU techniques accomplish precisely the reverse; they begin at the atomic or molecule level and piece together the Nano-material bit by bit until the intended structure is generated.

4.2 Fabrication Method

A TD fabrication technique, such as NSL, was used to fabricate the SEIRA substrate. Recent years have seen a lot of study on NSL, a promising lithography process that is cost-effective, scalable, and easy to use. Modern NSL formalism uses methods like anisotropic etching and multi-step shadow mask deposition

to create 2D and 3D nanostructures with precise supervision over their size, form(shape), inter-structural Nanogap, aspect ratio, precision, and vertical uniformity. Using mono-disperse PS as a mask, NSL is a well-liked and economically advantageous method for fabricating uniform shapes of nanoscale objects on a substrate. This approach involves forming one or more layers of Nano-spheres onto a substrate, followed by the application of a tiny monolayer or multilayered coating of the target material, such as metals and polymers.

The self-assembling PS beads that may be bought commercially are the foundation of NSL. In the NSL method, a group of Nano-spheres placed on a surface is used as a mask. The orderly arrangement of the Nano spheres' self-assembly depends on the surface properties and kind of media used in the colloid. Colloids are liquids in which Nano-spheres are distributed. Generally, relatively flat Nano patterns are created by utilizing the space between the Nano-spheres, which is present regularly throughout the entire surface. When a material such as gold is sprayed onto the Nano sphere pattern, which serves as a mask, a consistent dot pattern is left in its wake. Nowadays, NSL has evolved into a method that makes it possible to create incredibly intricate structures, such as arrays of nanostructures, three-dimensional structures with minute holes, and carbon Nano-tubes [192]. Our choice is meant to draw attention to the significance of self-assembly as a toolkit of procedures appropriate for designing different types of intricate hierarchical structures with inherent functioning. The development of nanofabrication by self-assembly holds great potential for improving human health and well-being along with the delicate environment of Earth, where we all must dwell. It will be interesting to see how this field plays out.

4.3 Fabrication Procedure

A recently developed, low-cost, and promising method for creating uniform and regular closed-packed arrays of GND's is used. A schematic of the fabrication procedure for ordered Au nanodisk arrays is presented in Figure 4.2. On a glass substrate, the NSL approach creates ordered arrays of gold Nano disks using self-assembled monolayers of Nano-spheres as a mask. The glass substrate was first cleaned by sonicating it for five minutes in acetone and isopropanol before covering it with gold. Before being used, the substrates were dried using nitrogen (N_2) gas. The radio frequency sputtering method is deployed to lay on a coating of gold (thickness (t_m) = 30nm) on a glass substrate. The gold surface was then covered with a self-assembled monolayer of close-packed, mono-dispersed polystyrene Nano-spheres. Third, selectively etching the area of the Au film not shielded by the Nano ellipses and transforming the densely packed polystyrene Nano sphere monolayer into arrays of separated Nano ellipses were accomplished

by using O_2 reactive ion etching. After the polystyrene residues were eliminated using toluene, the Au Nano disks remained on the substrates. It is simple to adjust the Au Nano disk's size by varying the polystyrene spheres' sizes. The successful fabrication of ordered Au nanodisk arrays has been achieved by the combination of reactive ion etching and NSL. This study shows how to pattern Au in a manageable and effective manner. The periodicity, nanoscale size, and huge edge-to-body ratio of Au nanodisk arrays make them an attractive option for a variety of electrical and spintronic production applications.

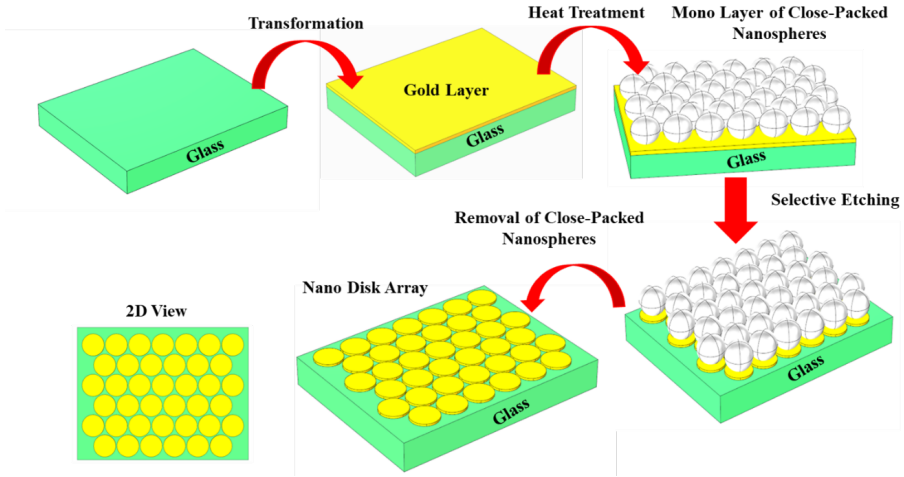


Figure 4.2. The Au nanodisk closed packed array fabrication process. Sputtering (Transformation) of gold on a glass substrate. Fabricated Sample with closed packed array of GND's with $D=757\text{nm}$, and $t_m = 30\text{nm}$. Following an hour at 70°C in piranha solution (3:1 concentrated sulfuric acid (H_2SO_4)/30% (H_2O_2)), the glass substrate was cleaned. Milli-Q water ($18.2\text{ M}\Omega\text{ cm}^{-1}$) and ethanol were then rinsed repeatedly.

The concentration of the commercial polystyrene Nano sphere suspensions (2.5% in water(H_2O)) was modified by precipitating in a micro-ultra-centrifuge and resuspending them in distinct ratios of 1:1 ethanol/water as stated by the Nano-sphere diameter. Figure 4.3 showing the fabricated samples. Here, (a) Fabricated Sample with closed packed array of GND's with $D=757\text{nm}$, and $t_m = 30\text{nm}$, and (b) Fabricated Sample with self-assembled Au monolayer and $t_m = 30\text{nm}$ for reference measurements.

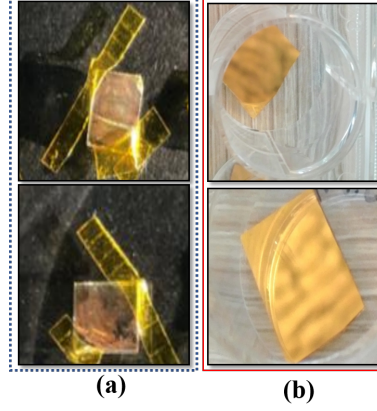


Figure 4.3. (a) Fabricated samples with closed packed array of GND's with $D=757\text{nm}$, and $t_m = 30\text{nm}$. (b) Fabricated samples with self-assembled Au monolayer and $t_m = 30\text{nm}$ for reference measurements

4.4 Metrology

An important method for characterizing nanostructures, including their topography, morphology, composition, and crystallographic details, is electron microscopy. Electron microscopes illuminate and scan an object with an electron beam to create a high-resolution image. The major reason electron microscopes are preferred over optical microscopy is that they may achieve superior resolution by using electrons with a wavelength that is far shorter than light and a deeper depth of focus. High-energy electron beams interact with samples to produce measurable signals that can be analyzed to gather the required data. These signals include transmitted electrons, characteristic X-rays, back-scatter electrons, secondary electrons, elastically and in-elastically scattered electrons, and Auger electrons.

4.4.1 Scanning Electron Microscopy (SEM)

The majority of the tiny characteristics of the plasmonic structures designed and constructed in this proposed work are below the resolution limit of optical microscopes at a size of several hundred Nanometers, therefore even at its greatest magnification, an optical microscope cannot directly examine nanoscale structures. An SEM is used instead of the electron beam because of its minuscule wavelength in order to examine and quantify the resulting nanostructure. SEMs

are a type of microscope that examines conductive materials at incredibly small sizes by utilizing interactions between an electron beam and a sample. An electron cannon fitted with a tungsten filament cathode is commonly used in an SEM to produce electrons in a high vacuum. SEM uses a concentrated electron beam to scan the sample surface rasterically. Because they are thick, the majority of samples that undergo SEM evaluation are opaque to the electron beam. A basic illustration of SEM concepts is shown in Figure 4.4. Once released, the electrons are driven downward and travel through a range of lenses and holes to form a concentrated electron beam that comes into contact with the surface of the sample. The various signals generated by electrons interacting with atoms at a few microns depth within the sample include characteristic X-rays, back-scattered electrons (BSE), and secondary electrons (SE), among others [45]. The accelerating voltage as well as the distance needed to work between the sample and the bottom lens are required for these signals to occur. The generated SE, BSE, etc., are recorded utilizing specialized detectors when a primary electron beam strikes the material. Typically, SE and BSE are employed in the creation of morphology or topography pictures in SEM. SE are low energy (50 eV) particles that are created when an incoming beam in-elastically scatters off the atomic core or valence electrons of a sample material. With energy higher than 50 eV, BSE is those that are created by elastic scattering in a significantly deeper area of the interaction volume. These are used to deliver depth information. SEMs and X-ray analyzers are often used together to determine the chemical composition of samples. This is referred to as EDS or energy-dispersive X-ray spectroscopy. Electrons are extracted from sources such as filaments using an accelerating voltage (1 to 50 KV), with beam widths varying from 1 to 10 nm subject to the source of electrons. Tungsten is the most used filament, but other options for electron beam sources include field emission guns and lanthanum hexaboride filaments. The electrons are accelerated toward the anode by the anode, which is positive concerning the filament. Condenser lenses are used to control the beam size, while objective lenses focus the electron beam into a tiny probe that controls the final image's focus. The diameter of the objective lens determines the divergence angle α of the electron beam. Spot size, depth of field, and signal quality are the three primary factors to consider while imaging nanostructures, such as disks, wires, Nano pillars, etc. In particular, cross-sectional examinations of nanopillars and wires several millimeters tall require high resolution and depth of field. High resolution and depth of field are necessary, particularly for cross-sectional studies of nanopillars and wires that are several millimeters tall. The working distance can be altered to control the spot size. With increasing working distance, image resolution decreases and is dependent on spot size. Working distance and decreasing the α can both be used to increase the depth of field. As a result, signal strength and image resolution are decreased. Therefore, a trade-off between resolution,

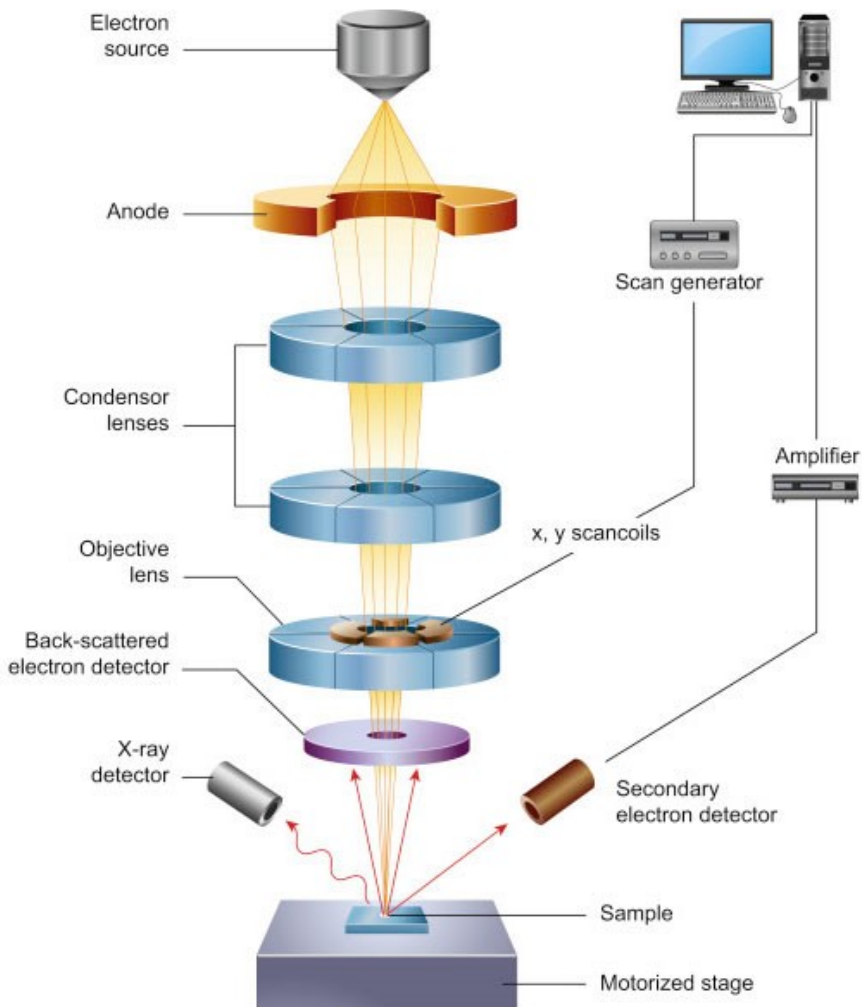


Figure 4.4. Demonstrates the essential concepts of SEM. The images displayed on the computer screen are produced by one or more detectors compiling these signals.[45]

depth of field, and signal intensity is required for imaging tall Nanostructures (pillars/wires).

The SEM analysis for our fabricated samples at CNR, Milano, Italy. The geometrical characteristics, density, and material composition of the nanostructures used in this work were all characterized using an ultra-sonic SEM. For the majority of structural and morphological characterization, an in-lens detector is employed. An operational distance range of 1.5–2.5 mm is employed along with an accelerating voltage of 1–1.8 KV. Different sorts of SE that are formed in or close to the spot center map the sample's actual surface. As electrons move through the objective lens, they can be detected very efficiently by an in-lens detector that is placed directly in the beam path and detects them directly. For EDS analysis, a SE detector is employed. When EDS analysis is performed on a sample, the optimum operational distance is 8.5 mm, and the accelerating voltage is tailored between 8–15 KV. In order to get a maximum magnification factor of $600000\times$ and a high resolution of 1.1 nm, the system may provide accelerating voltages of up to 30 KV. An SEM analysis-based image with a high voltage of 5kV and a magnification factor of $16000\times$ is shown in Figure 4.5. The excellent SEM photo makes it possible to estimate the structure's geometric size precisely, which is useful for evaluating production defects.

4.5 Deposition of Absorbed Analyte on SEIRA active substrate

To estimate the performance of the SEIRA active substrate the 4-aminothiophenol (4-ATP) monolayer is absorbed analyte. To do this, the treated SEIRA active substrate is carefully rinsed after being submerged in solvents and buffers. Next, it is coated with a self-assembled 4-ATP monolayer, which acts as a specific molecular probe layer to ascertain the substrate's achievable SEIRA activity. The substrate was meticulously cleaned with ethanol to guarantee the total removal of molecules that were not explicitly connected from the surface following the self-assembly of the 4-ATP from an ethanolic (soaked for sixteen hours in a 1mM 4-ATP (Merck-Millipore Milan, Italy)) solution. The excess unbound molecules were then rinsed out with pure ethanol, and the substrate could air dry. In this way, a uniform self-assembling monolayer of 4-ATP covalently bound to the GND's is formed on the SEIRA substrate. A self-assembled monolayer on a range of solid supports has drawn a lot of interest recently because it provides the ability to modify the surface properties by controlling the film structure at the molecular and supra-molecular levels. By using a thiol-functionalized test molecule to create a distinct mono-molecular dense layer of the test molecules on the surface, the production of a monolayer is guaranteed. Furthermore, the

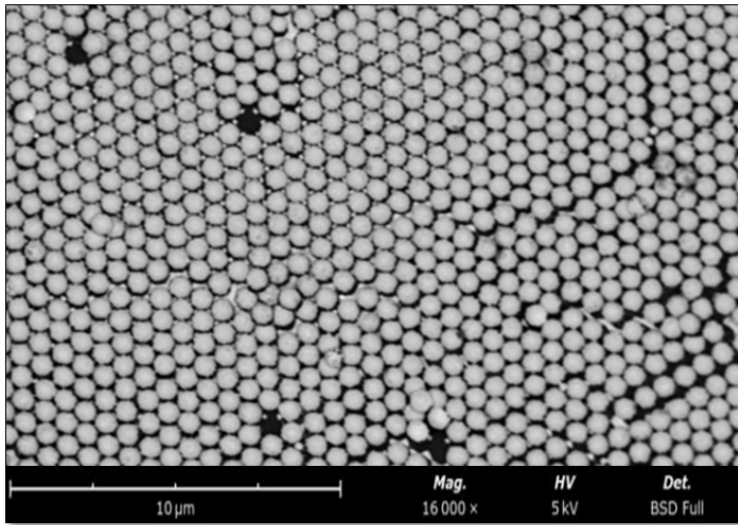


Figure 4.5. Image of a closed packed array of GND's with $D=757\text{nm}$ and $t_m = 30\text{nm}$ are proposed. SEM Image of the fabricated sample with $16000\times$ magnification factor, 5KV high voltage, and back-scattered electron detector (full).[\[45\]](#)

4-ATP does not connect to the glass substrate underneath; it only binds to the GNDs. The 4-ATP solutions' self-assembly duration's were kept minimal to prevent the solutions from altering the shape of the nanoparticles. A pristine setting is essential for producing SA monolayer of superior grade. Monolayer quality can be impacted by pollutants at even low concentrations. Steer clear of silane or poly (dimethyl siloxane) (PDMS)-treated rooms or hoods. These substances are readily able to cross-contaminate different surfaces. Iodine should also be avoided since it easily adsorbs onto gold. It is recommended to handle all thiols under a fume hood. Glass or polypropylene containers (such as centrifuge tubes, scintillation vials, and polypropylene test tubes) are used and need to be carefully cleaned to prevent solution contamination.

In conclusion, SEM is extensively utilized in our experiment for metrology in order to verify the samples' fabrication tolerance. An environmentally friendly, economical, and straightforward method of fabrication of a closed-packed array of gold Nano disks is provided by the self-assembly approach.

ATR-FTIR Characterization of SEIRA Substrate and Numerical Fitting of the Experimental Results

This chapter first describes the ATR-FTIR characterization of the proposed GND-based SEIRA substrate (as fabrication procedures explained in Chapter 4) in terms of attenuated total reflection measurement in the existence and absence of an absorbed analyte (4-ATP). To determine the sensitivity capability of our proposed GND-based SEIRA substrate, we calculated the SEIRA gain and SEIRA EF at different sample positions on the fabricated sample for repeatability and uniformity confirmation of the results. While in next we carried out a numerical fitting analysis of the experimental findings in the final segment. The comparison of experimental data with numerical predictions demonstrates a good fit. Based on the experiment and the simulated SEIRA EF, we have achieved 2.83×10^5 and 4.25×10^5 , respectively.

5.1 EM Response Characterization

We aimed to create a plasmonic Nano antenna whose resonance corresponds with the most important vibrational absorption zone, also known as the fingerprint region, in order to experimentally demonstrate the capabilities of a proposed nanoantenna that is fabricated (cost-effective method of fabrication) using

a self-assembled closed array of GNDs. The sample was fabricated on glass using GND's array-based NA with a diameter (D) ($D=757\text{nm}$) and ($t_m = 30\text{nm}$) thickness. FTIR ATR- Utilizing a reflection setup, we examined the fabricated sample's characterization using a PerkinElmer Spectrum 3 FTIR spectrometer equipped with ATR accessories, with an incident angle of 45° .

5.1.1 ATR Measurement

The fabricated sample and the ATR crystal are in contact during ATR FTIR spectroscopy. The sample on the surface in touch with the ATR crystal is impacted by the IR radiation as it passes through the crystal. Total internal reflection happens because of the two materials' different refractive indices. The "evanescent wave" that permeates the sample is produced by this reflection. The amount of IR light absorbed by the sample during evanescent wave interaction varies based on the sample's composition. This outcome is in a slight ATR. The PerkinElmer Spectrum 3 FT-IR spectrometer with universal ATR (UATR) is used to characterize fabricated samples and the highest ISO-9001 manufacturing standards were used in its construction. The UATR accessory is perfect for universal sampling for straightforward IR spectroscopic investigation since it detects the top-plate crystal, the number of reflections, and the serial number for traceability. Maximum repeatability is ensured by its special kinematic top-plate installation and electronic force gauge. Additionally, for maximum versatility, several interchangeable sample top plates are available.



Figure 5.1. (a) The PerkinElmer Spectrum 3 FT-IR spectrometer with ATR module (b) Detailed schematic of the ATR measuring system.

An essential component of the ATR measurement is the ATR crystal, which is usually an IR translucent material with a smooth surface and has a significant index of refraction, as shown in Figure 5.1. At the crystal-to-sample contact, the IR beam is fully reflected when it strikes the ATR crystal and is angled beyond the critical angle. Light has wavelike properties, therefore it travels inside the sample in close contact with the crystal and takes on the form of an evanescent wave before being instantly reflected on the border surface. Usually a few microns, the penetration depth is ascertained by the wavelength, the angle of the incoming laser beam, and the refractive indices of the ATR crystal and sample. When the IR beam interacts with the substance, it ultimately emerges from the ATR crystal and is directed toward the IR detector. In Figures 5.1(a) and 5.1(b), the PerkinElmer Spectrum 3 FT-IR spectrometer with UATR was used to characterize the chemical absorbed analytes, and the metasurface device was employed to boost the sensitivity of such ATR observations. The integrated crystal in this ATR unit is diamond, which has a refractive index range of 2.4 to 2.65 in the waveband of interest (as reported in the literature). Theoretically, the wave must impinge on the crystal with a critical angle of 33.65° to 30.25° in this situation, but in practice, the wave must inject on the diamond crystal with a 45° incident angle to ensure the production of total internal reflection. The MCT (Mercury-Cadmium-Telluride) detector is housed in the detector compartment, and the wave will only experience one entire internal reflection there. If the analytes are in liquid form, they can be dripped on the surface of the crystal or, if they are in solid form, they can be forced forcefully onto the surface by lowering the lever. Figure 5.2 Graphically Representing an experiment setup for ATR-FTIR reflection spectrum measurement. Before we start measuring SEIRA substrate,

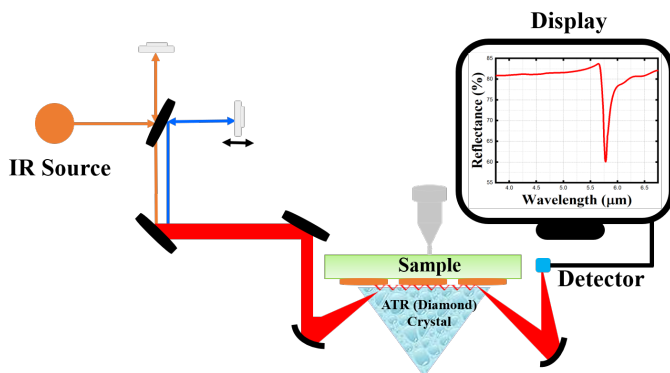


Figure 5.2. Graphically representing an experiment setup for ATR-FTIR reflection spectrum measurement.

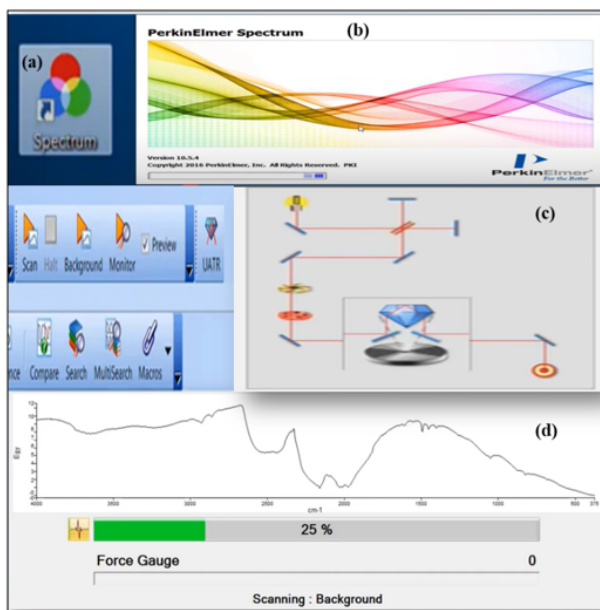


Figure 5.3. Initial ATR measurement processes illustrated graphically

Table 5.1. Reflectance Measurement Setting

Resolution	4cm^{-1}
Measurement range	$3.5\mu\text{m}$ - $6.75\mu\text{m}$
Measured	Reflectance
Accumulation	16
CO ₂ /H ₂ O settings	Yes
Apodization	Strong
Scan speed (cm/s)	Magnitude
Phase correction	0.2 cm/s

there are a few things we need to do. Turning on the Spectrum 3, pressing the back ON button, and pressing the connected computer are the first steps. We first cleaned the sample area with alcohol and put on gloves as a precaution. Next, we launched the FTIR software (Spectrum, as shown in Figure 5.3(a)) and waited for the PerkinElmer spectrum 3 FT-IR spectrometer to initialize (the interface between the software and hardware, or connection, as shown in Figure 5.3(b)). Following UATR configuration verification, the configuration icon was shown if the connection was made correctly (see Figure 5.3(c)). Next made the folder, configured the location, and carried out the background scan (see Figure 5.3(c)) for the experimental data. The initial setting used for the ATR-FTIR reflection spectrum acquired from the fabricated sample is represented here by table 5.1. The GND array-based NA with $D=757\text{nm}$ and $t_m=30\text{nm}$ was used to manufacture the sample on a glass substrate. The reflection of the ATR-FTIR is shown in Figure 5.4. We have repeated the ATR-FTIR characterization to get the reflectance spectrum from various spots to fabricated samples (such as A2 and A3) in order to ensure uniformity and repeatability. The design parameters are the same for these samples. The ATR-FTIR characterization of sample A2 reflectance spectra for four distinct spots is shown in Figure 5.5. The wavelength of the resonance peaks are such as in 5.5(a-d) $5.7834\mu\text{m}$, $5.784\mu\text{m}$, $5.785\mu\text{m}$, and $5.7864\mu\text{m}$, respectively. The only differences observed are in the reflection mismatch and its resulting fabrication flaw between different places. This result demonstrates the homogeneity (uniformity) of the resonance peak's manufactured outcomes. Figure 5.6 illustrates the reflectance spectra of sample A3, which we will repeat the ATR-FTIR characterization of for three different spots(a-c) and resonance peaks ($5.785\mu\text{m}$, $5.786\mu\text{m}$, and $5.786\mu\text{m}$). It is clear from our observations of the ATR-FTIR characterization of samples A2 and A3's reflectance spectra at various points that the results of both samples are consistent. The consistency of sample A2 and sample A3 results shows how repeatable our proposed GND-based SEIRA substrate is. Resonance peak (reflectance spectrum) of samples A2 and A3 as characterized by ATR-FTIR, with repeatability shown in Figure 5.7. We placed the bio-sample monolayer on the self-assemble fabricated sample in order to confirm the SEIRA substrate sensitivity, and we went over the bio-sample monolayer preparation in detail as it was previously covered in Chapter 4. The thickness of the monolayer is the same as the Nano antenna (GND). In this investigation, we used the SEIRA substrate to analyze biological analytes using 4-aminothiophenol (4-ATP). After 16 hours of immersion in a 1 mM 4-ATP (Merck-Millipore Milan, Italy) solution in ethanol, the SEIRA substrate was air-dried and rinsed with pure ethanol to get rid of any remaining unattached molecules. The ATR-FTIR reflection spectrum from the self-assembled fabricated sample with a 4-ATP monolayer at $t_m=30\text{ nm}$ is shown in Figure 5.8. We can see the clear absorbance dip due to the 4-ATP monolayer

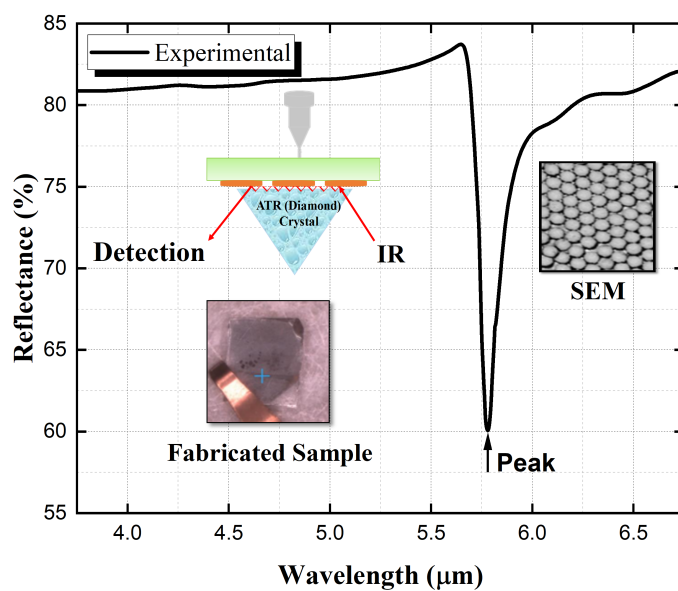


Figure 5.4. ATR-FTIR reflection spectrum obtained from the fabricated sample. Reflection peak at 5.784 μm (1728.91cm^{-1})

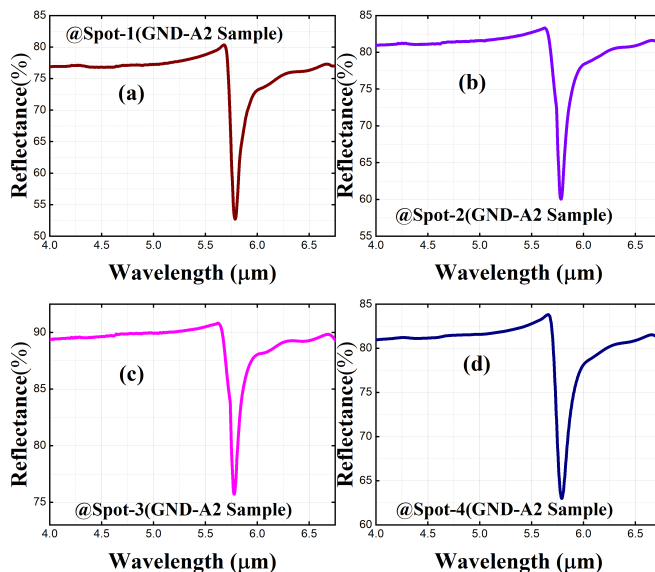


Figure 5.5. ATR-FTIR reflection spectrum obtained from the fabricated sample A2 at 4 different spots.

at 6.293 μm or (1589 cm^{-1}) and absorbance dip confirmation from the reference measurement of the 4-ATP powder on the glass (or from [193, 194]). As we see the absorbance dip due to bio-sample monolayer at 1589cm^{-1} (6293.27nm). The result in 5.8 demonstrates the SEIRA substrate has a sensitivity for 4-ATP monolayer as an absorbance dip.

5.1.2 Experimental SEIRA gain and SEIRA (EF) Findings

The SEIRA gain measures the change in reflectivity caused by the adsorbed analyte in comparison to a reference scenario in which the analyte is absent. This change in reflectivity is utilized in surface chemistry and molecular adsorption research on surfaces, among other uses, to investigate and characterize the interactions of molecules with the metal surface. To demonstrate the experimental ability of enhancement for SEIRA, the designed GNDs closed-packed array-based SEIRA substrate whose resonance matches in the fingerprint region. The definition of a SEIRA gain is a ratio of the changes in reflectivity ($\Delta R/\Delta R_0$), ΔR is changing in reflectivity for SEIRA substrate, and ΔR_0 changes in reflectivity for reference flat unstructured metallic layer in the existence and absenteeism of 4-ATP (adsorbed analyte) monolayer. For the self-assemble fabricated sample with

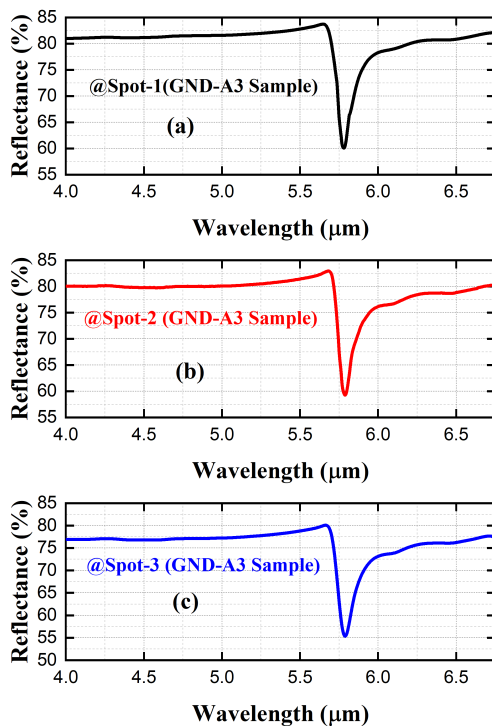


Figure 5.6. ATR-FTIR reflection spectrum obtained from the fabricated sample A3 at 3 different spots.

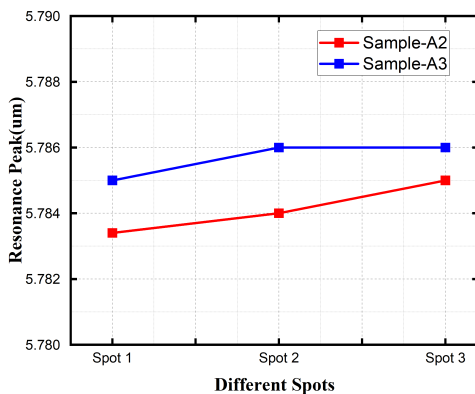


Figure 5.7. Repeatability confirmations of self-assemble fabricated sample A2 at A3 at different spots.

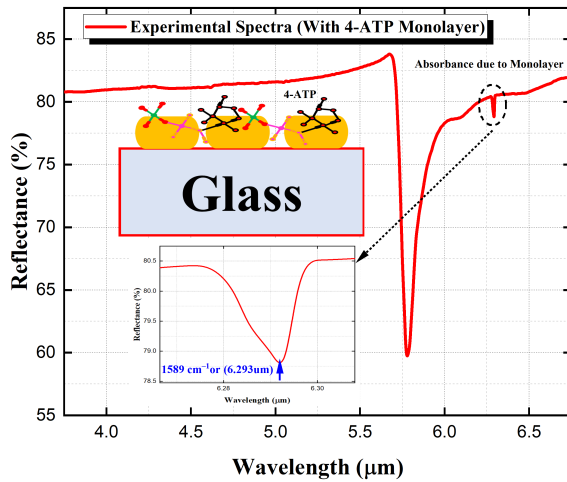


Figure 5.8. Measurement of biological analytes with SEIRA substrate. ATR-FTIR reflection spectrum obtained from the fabricated SEIRA substrate ($D = 757\text{nm}$, $t_m = 30\text{nm}$) with the 4-ATP monolayer. Change in reflection due to 4-ATP monolayer at $6.293\mu\text{m}$ (1589cm^{-1}) as absorbance dip. 4-ATP monolayer thickness was the same as the NA thickness ($t_m = 30\text{nm}$).

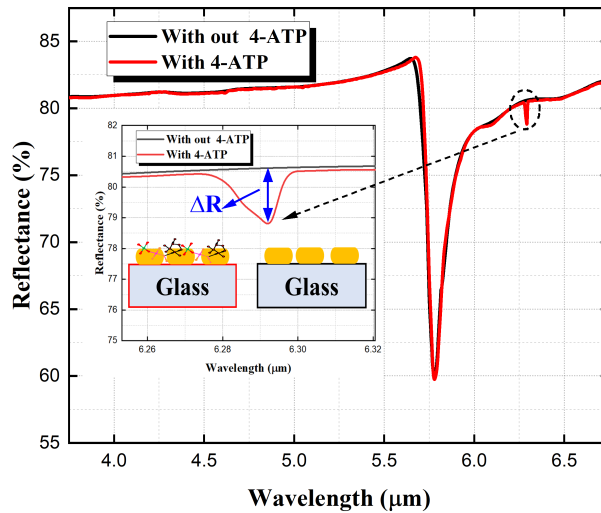


Figure 5.9. Experimental ATR-FTIR reflection spectra for a fabricated sample with NA on glass in the existence (Red) and absenteeism (Black) of a 4-ATP monolayer.

NA on glass, we calculated the ΔR for the experimental ATR-FTIR reflection spectra in the existence (Red) and absence (Black) of the 4-ATP monolayer. Figure 5.9 illustrates the variations in reflectance, which are $\Delta R=1.995$ at $6.293(1589\text{cm}^{-1})$ due to the self-assemble 4-ATP monolayer with $t_m=30\text{nm}$. Next, we characterized the reference fabricated sample using ATR-FTIR using a flat gold layer on ΔR_0 , while the flat gold layer thickness is $t_m=30\text{nm}$. We performed the ΔR_0 calculation for experimental ATR-FTIR reflection spectra from the fabricated sample flat gold on glass in the existence (Red) and absence (Black) of 4-ATP monolayer and changes in reflectance is $\Delta R_0=0.002$ at $6.293(1589\text{ cm}^{-1})$ as Figure 5.10 illustrating.

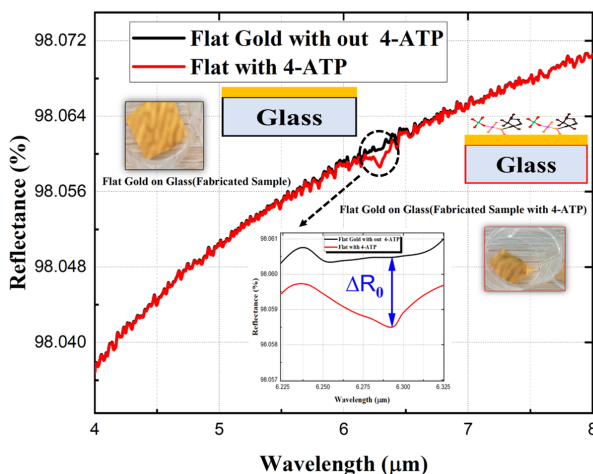


Figure 5.10. Experimental ATR-FTIR reflection spectra for a reference fabricated sample with flat gold on glass in the existence (Red) and absence (Black) of a 4-ATP monolayer.

This gain quantifies the signal strength improvement that SEIRA offers, which is particularly useful for increasing the chemical detection sensitivity of IR absorption spectroscopy. Applications of SEIRA for biosensing entail the use of this method for the detection and examination of biological molecules, including proteins, deoxyribonucleic acid (DNA), and other biomolecules. Researchers can increase the sensitivity and specificity of their biosensing investigations by adsorbing these molecules onto a metal surface and then utilizing SEIRA to augment the IR signals. This has applications in several domains where the identification of certain biomolecules is crucial, such as materials science, environmental monitoring, and medical diagnostics. To put it briefly, SEIRA gain measures the

signal augmentation that SEIRA can produce when analyzing molecular vibrations. This can be used in biosensing to more accurately identify and analyze biological components. The SEIRA gain of our proposed GNDs closed-packed array-based self-assemble SEIRA substrate is equal to 997.5. After that to evaluate the sensitivity of the self-assemble proposed SEIRA (GNDs closed array-based NA) substrate, we calculate the EF for this proposed GNDs closed packed array-based SEIRA substrate. The following is how EF is defined by the Eq.(5.1) [Ref] hat:

$$SEIRAEF = \frac{\Delta R}{\Delta R_0} \times \frac{A_0}{A_{SEIRA}} \quad (5.1)$$

As we know the ratio of $(\Delta R/\Delta R_0)$ is equal to SEIRA gain. A_0 is the total area of the unit cell (NA) exposed to light and A_{SEIRA} is an effective Area of NA where the field is localized (hot-spot).

$$A_0 = 2 \times (\sqrt{3} \times a^2); a = D + G \quad (5.2)$$

Where D is the diameter of GND, and G is the gap between the GND and $A_0 = 2.0645 \mu m^2$. In the proposed GNDs closed array-based NA, we calculate

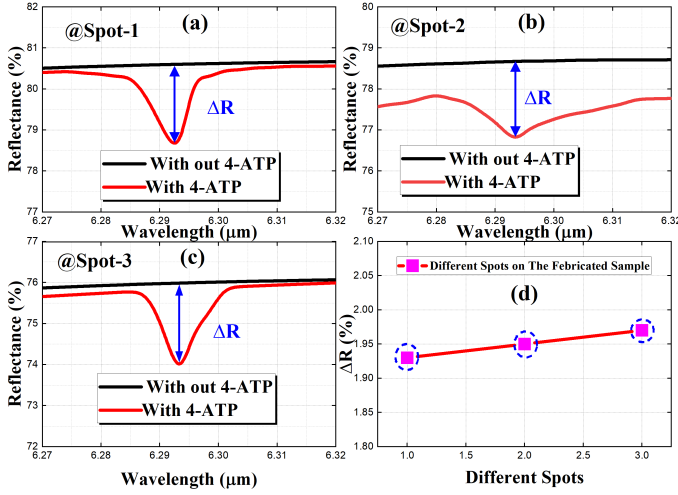


Figure 5.11. (a-c) illustrates the change in reflectance spectra ΔR calculations for our proposed GNDs closed array-based NA at three different spots in the presence of 4-ATP monolayer. (d) 2D representation of changes in reflectance is ΔR as a function of different spots.

the $A_{SEIRA} = 0.0072 \mu m^2$ and achieved $SEIRA - EF = 2.83 \times 10^5$. For unifor-

mity confirmation of the self-assembled SEIRA substrate with a self-assembled monolayer of ATP we repeated the ATR FTIR characterization for three different spots and performed the ΔR calculations at these different spots. Figure 5.11 (a-c) representing the changes in reflectance due to the self-assembled 4-ATP monolayer for three different spots, while values are $\Delta R=1.93, \Delta R=1.95$, and $\Delta R=1.97$, at $6.293\mu m (1589\text{ cm}^{-1})$ respectively. 5.11(d) is the 2D representation of changes in reflectance is ΔR as a function of three different spots. In our experimental ATR-FTIR analysis, we observed uniformity and repeatability with a minor change, which may have been caused by imperfection in the fabrication of the sample for three different spots. The experimental SEIRA gain and SEIRA EF are shown in Figure 5.12 for three distinct spots. The relevant SEIRA gain levels that can be attained are 965, 975, and 985. Meanwhile, the experimental SEIRA EF values are, in order, 2.767×10^5 , 2.795×10^5 , and 2.824×10^5 for the three distinct spots.

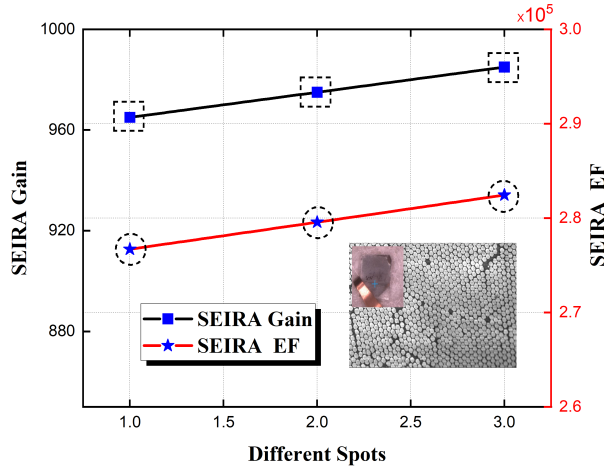


Figure 5.12. illustrates a 2D representation of SEIRA gain and SEIRA EF as a function of different spots.

5.2 Numerical Fitting of the Experimental Results

The fitting of experimental results with numerical results is demonstrated in this section. The measured ATR-FTIR reflection spectra at $5.784\mu m (1728.91\text{ cm}^{-1})$ in Figure 5.13 are fitted to simulation spectra without absorbed analyte

4-ATP monolayer. The proposed self-assembled SEIRA substrate with GNDs array-based NA with $D=757\text{nm}$ and $t_m = 30\text{nm}$. In order to obtain results that were comparable to the experimentally measured ATR-FTIR spectra characterization, we optimized the simulated design outcomes. Then, in the presence of

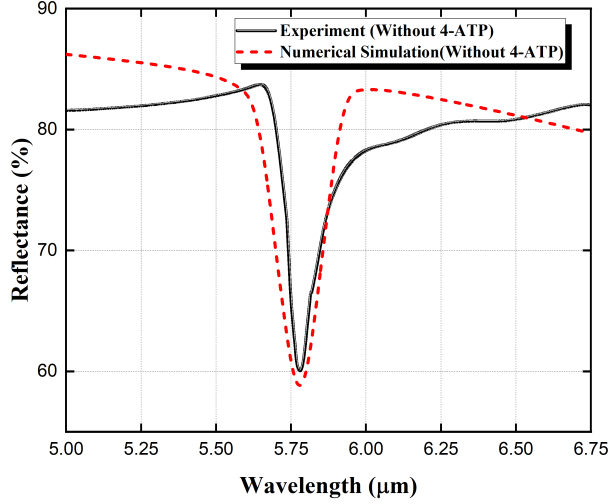


Figure 5.13. illustrates the numerical (Red) fitting of the experimental (Black) ATR-FTIR reflectance spectra in the absence of absorbed analyte such as of 4-ATP monolayer.

absorbance analyte 4-ATP monolayer, we also compared the numerically simulated spectra with the experimentally observed ATR-FTIR spectra characterization. When analyzing experimental ATR-FTIR spectra, we observed a dip in absorbance caused by absorbed analytes such as 4-ATP monolayers. However, in simulated spectra, we used an artificial absorbance analyte to test sensitivity at the same wavelength $6.293\mu\text{m}$ (1589 cm^{-1}) as shown in the experimental results. Figure 5.14 illustrates how the experimental ATR-FTIR spectra (Black) and the numerically calculated spectra (Red) were fitted when an absorbed analyte, such as a 4-ATP monolayer, was present. Where the experiment and simulated SEIRA EF are 2.83×10^5 and 4.25×10^5 , respectively. Experimental analysis of the SEIRA response demonstrates that a hierarchical approach can provide a cost-effective SEIRA substrate with superior performances with respect to the simpler single-layer configurations. ATR-FTIR was used to characterize the manufactured samples, which were discovered to be within the design tolerance. The reported numerical and experimental investigation can suggest a general way to enhance the performances of ATR FTIR combined with SEIRA for biosensing

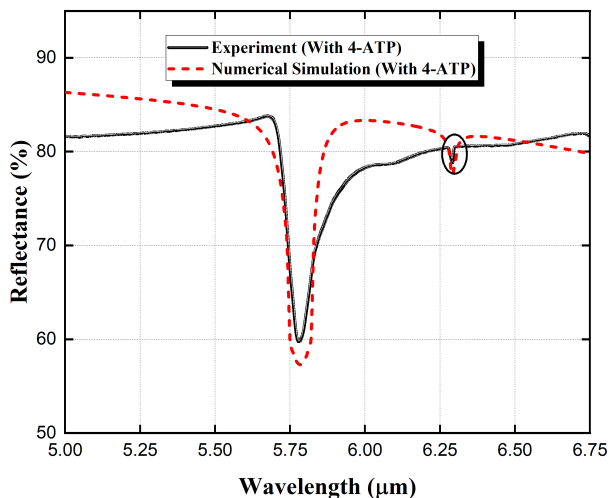


Figure 5.14. Illustrates the numerical (Red) fitting of the experimental (Black) ATR-FTIR reflectance spectra in the presence of an absorbed analyte such as of 4-ATP monolayer.

applications. The powerful SEIRA activity can easily be utilized for sensor applications with exceptional performance in combination with any traditional FTIR spectrometer. In terms of SEIRA EF, our work's findings are on par with those of cutting-edge research. According to recent advances, the SEIRA EF has an intricate design and requires costly, sophisticated manufacturing techniques. We were able to attain the SEIRA EF values 10^5 by a straightforward and economical fabrication process. A fascinating and cutting-edge field of study is the creation and engineering of SEIRA active substrates for use in ATR-FTIR spectroscopy in biosensing applications. The sensitivity of ATR-FTIR can be increased by SEIRA-active substrates, which makes it an effective tool for researching biological molecules and their molecular interactions.

Conclusions

In this work, we engineered and developed a cost-effective SEIRA-active substrate to localize and enhance the electromagnetic field distribution in a small area, thereby improving the sensitivity of detecting chemical or other biological substances. Indeed ATR-FTIR spectroscopy is a potent method for analyzing materials and surface chemical processes. By using customized substrates that can amplify the IR signal, SEIRA spectroscopy is a technique used to increase the sensitivity of ATR-FTIR. ATR-FTIR spectroscopy with SEIRA is a powerful analytical technique used in biosensing and other areas of research. Proteins, nucleic acids, and lipids are examples of biomolecules with low IR absorption, which SEIRA is very useful for identifying and analyzing. Combining ATR-FTIR and SEIRA yields various benefits for biosensing applications. The investigation of protein-ligand interactions, deoxyribonucleic acid hybridization, cell-substrate interactions, and the characterization of conformational changes in biomolecules are among the biosensing applications of ATR-FTIR with SEIRA. This method has the potential to increase our comprehension of biological processes and enhance the precision and sensitivity of biosensors, which are employed in a variety of industries such as pharmaceutical research and medical diagnostics.

Nonetheless, in order to make such a technique affordable, the SEIRA active substrate cannot require an expensive fabrication process. Therefore, We proposed the use of a self-assembly process to realize SEIRA-active substrates. By analyzing, the self-assembly processes state of the art and to fully exploit the evanescent wave interaction of the ATR-FTIR spectroscopy, we proposed to exploit an array of gold Nanodisks fabricated by Nanosphere lithography. Nanosphere lithography indeed offered a high number of degree of freedom in tailoring the nanostructures. In addition, the hot spots offered by the nanodisks are easily accessible to the evanescent probe wave of the ATR-FTIR. The SEIRA active substrate was designed using the COMSOL Multiphysics. A numerical

analysis is carried out to predict SEIRA performances and to identify the most promising geometrical configurations, thereby providing design criteria and physical insight into the conditions that affect the SEIRA response of self-assembled substrates. With the help of the COMSOL simulator, the numerical study was able to examine several aspects of the SEIRA active substrate, including the stability of the model, the influence of geometric parameters, the influence of polarization, and the influence of plasmonic and non-plasmonic materials on the performance. A parametric optimization (D (Diameter), G (Gap between GNDs), and t_m (Thickness GNDs)) was performed and the design of SEIRA active substrates was identified.

Several SEIRA substrates based on Nano disks arrays were fabricated on glass substrates. We exploited the Nano disk self-assembly lithography method as a simple and cost-efficient method for the SEIRA active substrate fabrication and after that, we performed the morphological characterization by scanning electron microscope (SEM). After that, a morphological and performance analysis is conducted using SEIRA active substrate measurements. This analysis has shown that well-ordered structures have been realized. An FTIR-ATR system was used to characterize the spectrum properties of the self-assembled SEIRA active. In particular, for measuring sensitivity, a SEIRA substrate was fabricated using the proposed design based on GNDs and a flat gold layer as a reference. To estimate the performance of the SEIRA active substrate, the 4-Aminothiophenol (4-ATP) monolayer is deposited on the as-absorbed analyte. SEIRA EF was calculated to assess the performance of the experimental SEIRA active substrate and a value of 10^5 was obtained. Repeated the ATR-FTIR characterization at several points on the designed sample for repeatability results validation of the SEIRA active substrate, and we have similar in terms of SEIRA EF. The trial findings for ATR-FTIR reflection spectra in the presence and absence of the self-assembled absorbed analyte (4-ATP monolayer) were numerically fitted in the final step. A good agreement between numerical and experimental results was also found.

Overall, experimental analysis of the SEIRA response demonstrates that the designed self-assembled SEIRA Nanodisks structures can be used as cost-effective SEIRA substrates. Using the powerful SEIRA activity in conjunction with any standard FTIR spectrometer allows for exceptional performance in sensor applications. Applications of this work may be found in analytical chemistry, materials science, and biosensing, among other domains. At the nexus of analytical chemistry, materials science, and nanotechnology, this is a cutting-edge field of study.

Bibliography

- [1] Michael Hlavatsch, Julian Haas, Robert Stach, Vjekoslav Kokoric, Andrea Teuber, Mehmet Dinc, and Boris Mizaikoff. Infrared spectroscopy—quo vadis? *Applied Sciences*, 12(15), 2022.
- [2] Elsebeth Langholz Kendix. *Transmission and Reflection (ATR) Far-Infrared Spectroscopy Applied in the Analysis of Cultural Heritage Materials*. Universita di Bologna, Italy, 2009.
- [3] Perkinelmer spectrum 3 mir std dtc kbr ld: <https://www.perkinelmer.com/product/spectrum-3-mir-std-dtc-kbr-ld-l1280133>, Accessed October 18, 2023.
- [4] Michelson interferometer: <https://www.mpoweruk.com/figs/michelson-interferometer.htm>, Accessed October 18, 2023.
- [5] Wave interference: <https://www.physics-and-radio-electronics.com/physics/waveinterference.html>, Accessed October 18, 2023.
- [6] Ernest E Angino. Far infrared (500-30 cm^{-1}) spectra of some carbonate minerals. *American Mineralogist: Journal of Earth and Planetary Materials*, 52(1-2):137–148, 1967.
- [7] Common sampling techniques of ftir spectroscopy: <https://www.edinst.com/us/blog/common-sampling-techniques-of-ftir-spectroscopy>, Accessed October 18, 2023.
- [8] Yap Wing Fen and W Mahmood Mat Yunus. Surface plasmon resonance spectroscopy as an alternative for sensing heavy metal ions: A review. *Sensor Review*, 33(4):305–314, 2013.
- [9] Yongmin Liu. Plasmonics and metasurfaces for extreme manipulation of light, Mar 2016.

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- [10] Jw. Nanobioplasmonics course, Dec 2014.
- [11] Frank Neubrech, Christian Huck, Ksenia Weber, Annemarie Pucci, and Harald Giessen. Surface-enhanced infrared spectroscopy using resonant nanoantennas. *Chemical reviews*, 117(7):5110–5145, 2017.
- [12] Andreas Tittl, Aurelian John-Herpin, Aleksandrs Leitis, Eduardo R. Arvelo, and Hatice Altug. Metasurface-based molecular biosensing aided by artificial intelligence. *Angewandte Chemie International Edition*, 58(42):14810–14822, 2019.
- [13] Ronen Adato and Hatice Altug. In-situ ultra-sensitive infrared absorption spectroscopy of biomolecule interactions in real time with plasmonic nanoantennas. *Nature communications*, 4:2154, 07 2013.
- [14] Daehan Yoo, Daniel A. Mohr, Ferran Vidal-Codina, Aurelian John-Herpin, Minsik Jo, Sunghwan Kim, Joseph Matson, Joshua D. Caldwell, Heonsu Jeon, Ngoc Cuong Nguyen, Luis Martin-Moreno, Jaime Peraire, Hatice Altug, and Sang Hyun Oh. High-contrast infrared absorption spectroscopy via mass-produced coaxial zero-mode resonators with sub-10 nm gaps. *Nano Letters*, 18(3):1930–1936, March 2018.
- [15] Daniel Rodrigo, Andreas Tittl, Nadine Ait-Bouziad, Aurelian John-Herpin, Odeta Limaj, Christopher Kelly, Daehan Yoo, Nathan Wittenberg, Sang-Hyun Oh, Hilal Lashuel, and Hatice Altug. Resolving molecule-specific information in dynamic lipid membrane processes with multi-resonant infrared metasurfaces. *Nature Communications*, 9, 06 2018.
- [16] Dordaneh Etezadi, John B. IV Warner, Hilal A. Lashuel, and Hatice Altug. Real-time in situ secondary structure analysis of protein monolayer with mid-infrared plasmonic nanoantennas. *ACS Sensors*, 3(6):1109–1117, 2018. PMID: 29845861.
- [17] Hai Hu, Xiaoxia Yang, Xiangdong Guo, Kaveh Khaliji, Sudipta Romen Biswas, Javier Garcia de Abajo, Tony Low, and Zhipei Sun. Gas identification with graphene plasmons. *Nature Communications*, 10, 03 2019.
- [18] Ronen Adato and Hatice Altug. In-situ ultra-sensitive infrared absorption spectroscopy of biomolecule interactions in real time with plasmonic nanoantennas. *Nature communications*, 4:2154, 07 2013.
- [19] Arif E. Cetin, Dordaneh Etezadi, and Hatice Altug. Accessible nearfields by nanoantennas on nanopedestals for ultrasensitive vibrational spectroscopy. *Advanced Optical Materials*, 2(9):866–872, 2014.
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-
- [20] Christian Huck, Frank Neubrech, Jochen Vogt, Andrea Toma, David Gerbert, Julia Katzmann, Thomas Härtling, and Annemarie Pucci. Surface-enhanced infrared spectroscopy using nanometer-sized gaps. *ACS Nano*, 8(5):4908–4914, 2014. PMID: 24724743.
- [21] Jochen Vogt, Christian Huck, Frank Neubrech, Andrea Toma, David Gerbert, and Annemarie Pucci. Impact of the plasmonic near- and far-field resonance-energy shift on the enhancement of infrared vibrational signals. *Phys. Chem. Chem. Phys.*, 17:21169–21175, 2015.
- [22] Lisa Brown, Xiao Yang, Ke Zhao, Bob Zheng, Peter Nordlander, and Naomi Halas. Fan-shaped gold nanoantennas above reflective substrates for surface-enhanced infrared absorption (seira). *Nano letters*, 15, 01 2015.
- [23] Benjamin Cerjan, Xiao Yang, Peter Nordlander, and Naomi Halas. Asymmetric aluminum antennas for self-calibrating surface enhanced infrared absorption spectroscopy. *ACS Photonics*, 3, 02 2016.
- [24] Jan Philip Kraack, Andres Kaeck, and Peter Hamm. Surface enhancement in ultrafast 2d atr ir spectroscopy at the metal-liquid interface. *The Journal of Physical Chemistry C*, 120(6):3350–3359, 2016.
- [25] Kai Chen, Thang Dao, and Tadaaki NAGAO. Tunable nanoantennas for surface enhanced infrared absorption spectroscopy by colloidal lithography and post-fabrication etching. *Scientific Reports*, 7:44069, 03 2017.
- [26] Liangliang Dong, Xiao Yang, Chao Zhang, Benjamin Cerjan, Linan Zhou, Ming Lun Tseng, Yu Zhang, Alessandro Alabastri, Peter Nordlander, and Naomi J. Halas. Nanogapped au antennas for ultrasensitive surface-enhanced infrared absorption spectroscopy. *Nano Letters*, 17(9):5768–5774, 2017. PMID: 28787169.
- [27] Aurelian John-Herpin, Andreas Tittl, and Hatice Altug. Quantifying the limits of detection of surface-enhanced infrared spectroscopy with grating order-coupled nanogap antennas. *ACS Photonics*, 5(10):4117–4124, 2018. PMID: 30828588.
- [28] Habibe Durmaz, Yuyu Li, and Arif E. Cetin. A multiple-band perfect absorber for seira applications. *Sensors and Actuators B: Chemical*, 275:174–179, 2018.
- [29] Jingxuan Wei, Ying Li, Yuhua Chang, Dihan Md. Nuruddin Hasan, Bowei Dong, Yiming Ma, Cheng-Wei Qiu, and Chengkuo Lee. Ultrasensitive transmissive infrared spectroscopy via loss engineering of metallic nanoantennas for compact devices. *ACS Applied Materials & Interfaces*, 11(50):47270–47278, 2019. PMID: 31769956.
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-
- [30] Cheng Shi, Callum Penrose, Jaqueline E. Pitts, Prarthana Gowda, Isaac J. Luxmoore, and Geoffrey R. Nash. Metamaterial-enhanced infrared attenuated total reflection spectroscopy. *Nanoscale Adv.*, 1:476–480, 2019.
- [31] Alice Fabas, Hasnaa El Ouazzani, Jean-Paul Hugonin, Christophe Dupuis, Riad Haidar, Jean-Jacques Greffet, and Patrick Bouchon. Dispersion-based intertwined SEIRA and SPR effect detection of 2,4-dinitrotoluene using a plasmonic metasurface. *Optics Express*, 28(26):39595–39605, December 2020.
- [32] Jikai Xu, Zhihao Ren, Bowei Dong, Xinmiao Liu, Chenxi Wang, Yanhong Tian, and Chengkuo Lee. Nanometer-scale heterogeneous interfacial sapphire wafer bonding for enabling plasmonic-enhanced nanofluidic mid-infrared spectroscopy. *ACS Nano*, 14(9):12159–12172, 2020. PMID: 32812748.
- [33] Mitchell Semple and Ashwin Iyer. Surface-enhanced mid-infrared absorption spectroscopy using miniaturized-disc metasurface. *Scientific Reports*, 11, 12 2021.
- [34] Inyong Hwang, Mingyun Kim, Jaeyeon Yu, Jihye Lee, Jun-Hyuk Choi, Su A. Park, Won Seok Chang, Jongwon Lee, and Joo-Yun Jung. Ultra-sensitive molecule detection based on infrared metamaterial absorber with vertical nanogap. *Small Methods*, 5(8):2100277, 2021.
- [35] Zhihao Ren, Zixuan Zhang, Jingxuan Wei, Bowei Dong, and Chengkuo Lee. Wavelength-multiplexed hook nanoantennas for machine learning enabled mid-infrared spectroscopy. *Nature Communications*, 13:1234567890, 07 2022.
- [36] Valentina Di Meo, Massimo Moccia, Gennaro Sanità, Alessio Crescitelli, Annalisa Lamberti, Vincenzo Galdi, Ivo Rendina, and Emanuela Esposito. Probing denaturation of protein a via surface-enhanced infrared absorption spectroscopy. *Biosensors*, 12(7), 2022.
- [37] Shuyan Zhang, Steve Wu, Yi Chen, Melissa Hum, Chi Wong, Emile Tan, Ann Lee, Jinghua Teng, Dinish U. S, and Malini Olivo. Label-free detection of mirna biomarkers using broadband multi-resonant infrared metasurfaces for early breast cancer diagnosis. *Nanoscale*, 15, 05 2023.
- [38] Laura Paggi, Alice Fabas, Hasnaa Ouazzani, Jean-Paul Hugonin, Nikos Fayard, Bardou Nathalie, Christophe Dupuis, Jean-Jacques Greffet, and Patrick Bouchon. Over-coupled resonator for broadband surface enhanced infrared absorption (seira). *Nature Communications*, 14, 08 2023.
-

-
- [39] Emilio Corcione, Diana Pfezer, Mario Hentschel, Harald Giessen, and Cristina Tarín. Machine learning methods of regression for plasmonic nanoantenna glucose sensing. *Sensors*, 22(1), 2022.
- [40] Aurelian John-Herpin, Deepthy Kavungal, Lea von Mücke, and Hatice Altug. Infrared metasurface augmented by deep learning for monitoring dynamics between all major classes of biomolecules. *Advanced Materials*, 33(14):2006054, 2021.
- [41] Aurelian John-Herpin, Andreas Tittl, Lucca Kühner, Felix Richter, Steven H. Huang, Gennady Shvets, Sang-Hyun Oh, and Hatice Altug. Metasurface-enhanced infrared spectroscopy: An abundance of materials and functionalities. *Advanced Materials*, 35(34):2110163, 2023.
- [42] Lie Wu and Xiue Jiang. *Infrared Spectroscopy for Studying Plasma Membranes*, pages 319–354. Springer Singapore, Singapore, 2018.
- [43] Yuanli Li, Weiren Cheng, Hui Su, Xu Zhao, Jingfu He, and Qinghua Liu. Operando infrared spectroscopic insights into the dynamic evolution of liquid-solid (photo)electrochemical interfaces. *Nano Energy*, 77:105121, 2020.
- [44] Ranjit Pabbati, Kondakindi Reddy, and Shaik Firdoz. *Applications of Nanomaterials in Biomedical Engineering*, pages 51–86. 03 2021.
- [45] B.J. Inkson. 2 - scanning electron microscopy (sem) and transmission electron microscopy (tem) for materials characterization. In Gerhard Hübschen, Iris Altpeter, Ralf Tschuncky, and Hans-Georg Herrmann, editors, *Materials Characterization Using Nondestructive Evaluation (NDE) Methods*, pages 17–43. Woodhead Publishing, 2016.
- [46] Peter Griffiths and James Haseth. Fourier transform infrared spectrometry, second edition. 06 2006.
- [47] W. W. Coblenz. Reminiscences of early investigations of infrared absorption spectra. *Applied Spectroscopy*, 7(3):109–111, 1953.
- [48] Pu Huang, Lijun Xu, and Yuedong Xie. Biomedical applications of electromagnetic detection: A brief review. *Biosensors*, 11(7), 2021.
- [49] Brian C Wilson, Michael Jermyn, and Frederic Leblond. Challenges and opportunities in clinical translation of biomedical optical spectroscopy and imaging. *Journal of biomedical optics*, 23(3):030901–030901, 2018.
- [50] Donald F Swinehart. The beer-lambert law. *Journal of chemical education*, 39(7):333, 1962.
-

-
- [51] Matthew Baker, Júlio Trevisan, Paul Bassan, Rohit Bhargava, Holly Butler, Konrad Dorling, Peter Fielden, Simon Fogarty, Nigel Fullwood, Kelly Heys, Caryn Hughes, Peter Lasch, Pierre Martin-Hirsch, Blessing Effiong, Ganesh Sockalingum, Josep Sulé-Suso, Rebecca Strong, Michael Walsh, Bayden Wood, and Francis Martin. Using fourier transform ir spectroscopy to analyze biological materials. *Nature protocols*, 9:1771–1791, 08 2014.
- [52] Duncan Finlayson, Christopher Rinaldi, and Matthew J. Baker. Is infrared spectroscopy ready for the clinic? *Analytical Chemistry*, 91(19):12117–12128, 2019. PMID: 31503460.
- [53] Katie Spalding, Franck Bonnier, Clément Bruno, Hélène Blasco, Ruth Board, Isabelle Benz-de Bretagne, Hugh Byrne, Holly Butler, Igor Chourpa, Pretheepan Radhakrishnan, and Matthew Baker. Enabling quantification of protein concentration in human serum biopsies using attenuated total reflectance – fourier transform infrared (atr-ftir) spectroscopy. *Vibrational Spectroscopy*, 99, 09 2018.
- [54] Allan Hynes, David Scott, Angela Man, David Singer, Michael Sowa, and Kan-Zhi Liu. Molecular mapping of periodontal tissues using infrared microspectroscopy. *BMC medical imaging*, 5:2, 06 2005.
- [55] Olivier Suys, Allison Derenne, and Erik Goormaghtigh. Atr-ftir biosensors for antibody detection and analysis. *International Journal of Molecular Sciences*, 23(19):11895, 2022.
- [56] Allan Hynes, David A Scott, Angela Man, David L Singer, Michael G Sowa, and Kan-Zhi Liu. Molecular mapping of periodontal tissues using infrared microspectroscopy. *BMC medical imaging*, 5(1):1–10, 2005.
- [57] B.C. Smith. *Fundamentals of fourier transform infrared spectroscopy, second edition*. 01 2011.
- [58] Brian C. Smith. *Fundamentals of fourier transform infrared spectroscopy*. CRC Press, 2011.
- [59] D. A. Naylor, R. T. Boreiko, and T. A. Clark. Mylar beam-splitter efficiency in far infrared interferometers: angle of incidence and absorption effects. , 17(7):1055–1058, April 1978.
- [60] D W Vidrine and C R Anderson. *Silicon Beamsplitter (rigid far-IR beam-splitter utilizing)*.
- [61] Manduca. Thermo fisher scientific, 2009.
- [62] PerkinElmer. Ft-ir spectroscopy attenuated total reflectance (atr),sample in contact with evanescent wave. https://cmdis.rpi.edu/sites/default/files/ATR_FTIR.pdf.
-

-
- [63] PedroRivasRuiz. University of reading,use of the fourier-transform infrared spectrometer. <https://www.reading.ac.uk>, 2020.
- [64] James W. Cooley and John W. Tukey. An algorithm for the machine calculation of complex fourier series. *Mathematics of Computation*, 19:297–301, 1965.
- [65] Leonard C. Afremow. High resolution spectra of inorganic pigment and extenders in the mid-infrared region from 1500 cm⁻¹ to 200 cm⁻¹. vol. 38, pag. 169-202, 1966.
- [66] E Y Jiang. Advanced FTIR spectroscopy: Principles, experiments and application. *Thermo*, 2007.
- [67] Barbara H Stuart. *Infrared Spectroscopy*. Analytical Techniques in the Sciences (AnTs). John Wiley & Sons, Chichester, England, Jun 2004.
- [68] Imali Mudunkotuwa, Alaa Alminshid, and Vicki Grassian. Atr-ftir spectroscopy as a tool to probe surface adsorption on nanoparticles at the liquid-solid interface in environmentally and biologically relevant media. *The Analyst*, 139, 12 2013.
- [69] Yeonsu Lee, Jiwon Kim, Sungmin Sim, Ignacio Llamas-Garro, and Jungmu Kim. Air-gap interrogation of surface plasmon resonance in otto configuration. *Micromachines*, 12(8):998, 2021.
- [70] R. Nuster, G. Paltauf, and P. Burgholzer. Comparison of surface plasmon resonance devices for acoustic wave detection in liquid. *Opt. Express*, 15(10):6087–6095, May 2007.
- [71] P. Drude. Zur elektronentheorie der metalle. *Annalen der Physik*, 306(3):566–613, 1900.
- [72] Lillian H. Hoddeson, G. Baym, and Nevill Francis Mott. The development of the quantum mechanical electron theory of metals: 1900-28. *Proceedings of the Royal Society of London. A. Mathematical and Physical Sciences*, 371(1744):8–23, 1980.
- [73] Arnold Sommerfeld. Ueber die fortpflanzung elektrodynamischer wellen längs eines drahtes. *Annalen der Physik*, 303:233–290.
- [74] Gustav Mie. Beiträge zur optik trüber medien, speziell kolloidaler metal-lösungen. *Annalen der Physik*, 330(3):377–445, 1908.
- [75] B Abasahl, C Santschi, T V Raziman, and O J F Martin. Fabrication of plasmonic structures with well-controlled nanometric features: a comparison between lift-off and ion beam etching. *Nanotechnology*, 32(47):475202, aug 2021.
-

-
- [76] Alexandre Aubry, Dang Yuan Lei, Antonio I. Fernández-Domínguez, Yannick Sonnefraud, Stefan A. Maier, and J. B. Pendry. Plasmonic light-harvesting devices over the whole visible spectrum. *Nano Letters*, 10(7):2574–2579, 2010. PMID: 20518545.
- [77] Grégory Barbillon. Plasmonics and its applications. *Materials*, 12:1502, 05 2019.
- [78] Juanjuan Liu, Mahsa Jalali, Sara Mahshid, and Sebastian Wachsmann-Hogiu. Are plasmonic optical biosensors ready for use in point-of-need applications? *Analyst*, 145:364–384, 2020.
- [79] Marco S. Rodrigues, Joel Borges, Cláudia Lopes, Rui M. S. Pereira, Mikhail I. Vasilevskiy, and Filipe Vaz. Gas sensors based on localized surface plasmon resonances: Synthesis of oxide films with embedded metal nanoparticles, theory and simulation, and sensitivity enhancement strategies. *Applied Sciences*, 11(12), 2021.
- [80] Xinyuan Chong, Yujing Zhang, Erwen Li, Ki-Joong Kim, Paul R. Ohodnicki, Chih-hung Chang, and Alan X. Wang. Surface-enhanced infrared absorption: Pushing the frontier for on-chip gas sensing. *ACS Sensors*, 3(1):230–238, 2018. PMID: 29262684.
- [81] Timothy Davis and Ann Roberts. Plasmonic circuits for manipulating optical information. *Nanophotonics*, 6, 10 2016.
- [82] Armando Ricciardi, Alessio Crescitelli, Patrizio Vaiano, Giuseppe Quero, Marco Consales, Marco Pisco, Emanuela Esposito, and Andrea Cusano. Lab-on-fiber technology: a new vision for chemical and biological sensing. *Analyst*, 140:8068–8079, 2015.
- [83] Naomi Halas, Surbhi Lal, Stephan Link, Wei-Shun Chang, Douglas Natelson, Jason Hafner, and Peter Nordlander. A plethora of plasmonics from the laboratory for nanophotonics at rice university. *Advanced materials (Deerfield Beach, Fla.)*, 24:4842–77, 09 2012.
- [84] A comprehensive review on plasmonic-based biosensors used in viral diagnostics. Jan 2021.
- [85] Kazuyoshi Kurihara and Koji Suzuki. Theoretical understanding of an absorption-based surface plasmon resonance sensor based on kretschmann’s theory. *Analytical chemistry*, 74:696–701, 03 2002.
- [86] Madhusudan B. Kulkarni, Narasimha H. Ayachit, and Tejraj M. Aminabhavi. Biosensors and microfluidic biosensors: From fabrication to application. *Biosensors*, 12(7), 2022.
-

-
- [87] Varnakavi. Naresh and Nohyun Lee. A review on biosensors and recent development of nanostructured materials-enabled biosensors. *Sensors*, 21(4), 2021.
- [88] A comprehensive review on plasmonic-based biosensors used in viral diagnostics. Jan 2021.
- [89] Juanjuan Liu, Mahsa Jalali, Sara Mahshid, and Sebastian Wachsmann-Hogiu. Are plasmonic optical biosensors ready for use in point-of-need applications? *The Analyst*, 2019.
- [90] Antonio Minopoli, Adriano Acunzo, Bartolomeo della ventura, and Raffaele Velotta. Nanostructured surfaces as plasmonic biosensors: A review. *Advanced Materials Interfaces*, 9, 11 2021.
- [91] Anthony G Frutos, Stephen C Weibel, and Robert M Corn. Near-infrared surface plasmon resonance measurements of ultrathin films. 2. fourier transform spr spectroscopy. *Analytical Chemistry*, 71(18):3935–3940, 1999.
- [92] Chris W. Brown, Yue Li, John A. Seelenbinder, Phillip Pivarnik, Arthur G. Rand, Stephen V. Letcher, Otto J. Gregory, and Michael J. Platek. Immunoassays based on surface-enhanced infrared absorption spectroscopy. *Analytical Chemistry*, 70(14):2991–2996, 1998. PMID: 9684546.
- [93] Amanda J. Haes, Shengli Zou, Jing Zhao, George C. Schatz, and Richard P. Van Duyne. Localized surface plasmon resonance spectroscopy near molecular resonances. *Journal of the American Chemical Society*, 128(33):10905–10914, 2006. PMID: 16910686.
- [94] Mondona Zangeneh, Nga Doan, Edward Sambriski, and Roger H. Terrill. Surface plasmon spectral fingerprinting of adsorbed magnesium phthalocyanine by angle and wavelength modulation. *Applied Spectroscopy*, 58(1):10–17, 2004. PMID: 14727715.
- [95] Joseph W. Petefish and Andrew C. Hillier. Angle-tunable enhanced infrared reflection absorption spectroscopy via grating-coupled surface plasmon resonance. *Analytical Chemistry*, 86(5):2610–2617, 2014. PMID: 24499196.
- [96] Tao Wang, Vu Hoa Nguyen, Andreas Buchenauer, Uwe Schnakenberg, and Thomas Taubner. Surface enhanced infrared spectroscopy with gold strip gratings. *Opt. Express*, 21(7):9005–9010, Apr 2013.
- [97] J.M. Chalmers and Peter Griffiths. *Handbook of Vibrational Spectroscopy*, volume 59. 01 2003.
- [98] B.H. Stuart. *Infrared Spectroscopy: Fundamentals and Applications*. Analytical Techniques in the Sciences (AnTs). Wiley, 2004.
-

-
- [99] Yanyan Chen, Caineng Zou, Maria Mastalerz, Suyun Hu, Carley Gasaway, and Xiaowan Tao. Applications of micro-fourier transform infrared spectroscopy (ftir) in the geological sciences—a review. *International Journal of Molecular Sciences*, 16(12):30223–30250, 2015.
- [100] Am Hartstein, JR Kirtley, and JC Tsang. Enhancement of the infrared absorption from molecular monolayers with thin metal overlayers. *Physical Review Letters*, 45(3):201, 1980.
- [101] Catherine Kendall, Martin Isabelle, Florian Bazant-Hegemark, Joanne Hutchings, Linda Orr, Jaspreet Babrah, Rebecca Baker, and Nicholas Stone. Vibrational spectroscopy: a clinical tool for cancer diagnostics. *Analyst*, 134:1029–1045, 2009.
- [102] Xindan Hui Hong Zhou, Dongxiao Li and Xiaojing Mu. Infrared metamaterial for surface-enhanced infrared absorption spectroscopy: pushing the frontier of ultrasensitive on-chip sensing. *International Journal of Optomechatronics*, 15(1):97–119, 2021.
- [103] Takuo Tanaka, Taka aki Yano, and Ryo Kato. Nanostructure-enhanced infrared spectroscopy. *Nanophotonics*, 11(11):2541–2561, 2022.
- [104] Dongxiao Li, Cheng Xu, Junsheng Xie, and Chengkuo Lee. Research progress in surface-enhanced infrared absorption spectroscopy: From performance optimization, sensing applications, to system integration. *Nanomaterials*, 13(16), 2023.
- [105] Karthik Reddy, Yunbo Guo, Jing Liu, Wonsuk Lee, Maung Oo, and Xudong Fan. On-chip fabry-pérot interferometric sensors for micro-gas chromatography detection. *Sensors and Actuators B-chemical - SENSOR ACTUATOR B-CHEM*, 159:60–65, 11 2011.
- [106] Jacob T. Robinson, Long Chen, and Michal Lipson. On-chip gas detection in silicon optical microcavities. *Opt. Express*, 16(6):4296–4301, Mar 2008.
- [107] Wei-Cheng Lai, Swapnajit Chakravarty, Xiaolong Wang, Cheyun Lin, and Ray T Chen. On-chip methane sensing by near-IR absorption signatures in a photonic crystal slot waveguide. *Opt Lett*, 36(6):984–986, March 2011.
- [108] Yu Chen, Hongtao Lin, Juejun Hu, and Mo Li. Heterogeneously integrated silicon photonics for the mid-infrared and spectroscopic sensing. *ACS Nano*, 8(7):6955–6961, July 2014.
- [109] Mitchell Semple and Ashwin Iyer. Surface-enhanced mid-infrared absorption spectroscopy using miniaturized-disc metasurface. *Scientific Reports*, 11, 12 2021.
-

-
- [110] Aritada Hatta, Tamio Ohshima, and Wataru Suëtaka. Observation of the enhanced infrared absorption of p-nitrobenzoate on ag island films with an atr technique. *Applied Physics A*, 29:71–75, 1982.
- [111] Heinz Wanzenboeck, Boris Mizaikoff, N. Weissenbacher, and R. Kellner. Surface enhanced infrared absorption spectroscopy (seira) using external reflection on low-cost substrates. *Fresenius Journal of Analytical Chemistry*, 362:15–20, 09 1998.
- [112] Marta Klanjšek Gunde and Matjaž Kunaver. Infrared reflection—absorption spectra of metal-effect coatings. *Applied Spectroscopy*, 57(10):1266–1272, 2003. PMID: 14639756.
- [113] Yuji Nishikawa, Tadahiro Nagasawa, Kunihiro Fujiwara, and Masatoshi Osawa. Silver island films for surface-enhanced infrared absorption spectroscopy: effect of island morphology on the absorption enhancement. *Vibrational Spectroscopy*, 6(1):43–53, 1993.
- [114] Toshimasa Wadayama, Hirochika Yano, Yusuke Sasaki, Jun ichi Takahashi, and Aritada Hatta. Infrared absorption enhancement of octadecanethiol on colloidal silver particles. *MATERIALS TRANSACTIONS*, 45(1):86–91, 2004.
- [115] Frank Neubrech, Annemarie Pucci, Thomas Cornelius, Shafqat Karim, Aitzol Garcia-Etxarri, and Javier Aizpurua. Resonant plasmonic and vibrational coupling in a tailored nanoantenna for infrared detection. *Physical review letters*, 101:157403, 11 2008.
- [116] Hui Wang, Janardan Kundu, and Naomi J Halas. Plasmonic nanoshell arrays combine surface-enhanced vibrational spectroscopies on a single substrate. *Angew. Chem. Int. Ed Engl.*, 46(47):9040–9044, 2007.
- [117] Christian Huck, Frank Neubrech, Jochen Vogt, Andrea Toma, David Gerbert, Julia Katzmann, Thomas Härtling, and Annemarie Pucci. Surface-enhanced infrared spectroscopy using nanometer-sized gaps. *ACS Nano*, 8(5):4908–4914, April 2014.
- [118] E. J. Osley, C. G. Biris, P. G. Thompson, R. R. F. Jahromi, P. A. Warburton, and N. C. Panoiu. Fano resonance resulting from a tunable interaction between molecular vibrational modes and a double continuum of a plasmonic metamolecule. *Physical Review Letters*, 110(8), feb 2013.
- [119] Yoshiaki Nishijima, Hiroki Nigorinuma, Lorenzo Rosa, and Saulius Juodkazis. Selective enhancement of infrared absorption with metal hole arrays. *Optical Materials Express*, 2:1367–1377, 10 2012.
-

-
- [120] Tao Wang, Vu Hoa Nguyen, Andreas Buchenauer, Uwe Schnakenberg, and Thomas Taubner. Surface enhanced infrared spectroscopy with gold strip gratings. *Opt. Express*, 21(7):9005–9010, April 2013.
- [121] Johannes Srajer, Andreas Schwaighofer, Georg Ramer, Stefan Rotter, Bilal Guenay, Albert Kriegner, Wolfgang Knoll, Bernhard Lendl, and Christoph Nowak. Double-layered nanoparticle stacks for surface enhanced infrared absorption spectroscopy. *Nanoscale*, 6, 11 2013.
- [122] Yongqian Li, Lei Su, Chen Shou, Chunmeng Yu, Jinjun Deng, and Yu Fang. Surface-enhanced molecular spectroscopy (sems) based on perfect-absorber metamaterials in the mid-infrared. *Scientific Reports*, 3, 2013.
- [123] Cindy Cooper, Miguel Rodriguez, Steve Blair, and Jennifer Shumaker-Parry. Mid-infrared localized plasmons through structural control of gold and silver nanocrescents. *The Journal of Physical Chemistry C*, 119:150512141939004, 05 2015.
- [124] Jón Mattis Hoffmann, Hendrik Janssen, Dmitry N. Chigrin, and Thomas Taubner. Enhanced infrared spectroscopy using small-gap antennas prepared with two-step evaporation nanosphere lithography. *Opt. Express*, 22(12):14425–14432, Jun 2014.
- [125] Joachim Heberle and Kenichi Ataka. *Surface Enhanced Infrared Absorption Spectroscopy*, pages 2528–2531. Springer Berlin Heidelberg, Berlin, Heidelberg, 2013.
- [126] Mohammed Janneh. (invited)surface enhanced infrared absorption spectroscopy using plasmonic nanostructures: Alternative ultrasensitive on-chip biosensor technique. *Results in Optics*, 6:100201, 2022.
- [127] K L Andrew Chan and Sergei G. Kazarian. Attenuated total reflection fourier-transform infrared (atr-ftir) imaging of tissues and live cells. *Chemical Society reviews*, 45 7:1850–64, 2016.
- [128] Ángela I López-Lorente and Boris Mizaikoff. Recent advances on the characterization of nanoparticles using infrared spectroscopy. *Trends in Analytical Chemistry*, 84:97–106, 2016.
- [129] Yuji. Nishikawa, Kunihiro. Fujiwara, Kenichi. Ataka, and Masatoshi. Osawa. Surface-enhanced infrared external reflection spectroscopy at low reflective surfaces and its application to surface analysis of semiconductors, glasses, and polymers. *Analytical Chemistry*, 65(5):556–562, 1993.
- [130] Ronen Adato, Ahmet Ali Yanik, Jason J. Amsden, David Lee Kaplan, Fiorenzo G. Omenetto, Mi K. Hong, Shyamsunder Erramilli, and Hatice
-

- Altug. Ultra-sensitive vibrational spectroscopy of protein monolayers with plasmonic nanoantenna arrays. *Proceedings of the National Academy of Sciences*, 106:19227 – 19232, 2009.
- [131] Kenichi Ataka, Sven Timo Stripp, and Joachim Heberle. Surface-enhanced infrared absorption spectroscopy (seiras) to probe monolayers of membrane proteins. *Biochimica et biophysica acta*, 1828 10:2283–93, 2013.
- [132] Martin Jahn, Sophie Patze, Izabella J. Hidi, Richard Knipper, Andreea I. Radu, Anna Mühlig, Sezin Yüksel, Vlastimil Peksa, Karina Weber, Thomas Mayerhöfer, Dana Cialla-May, and Jürgen Popp. Plasmonic nanostructures for surface enhanced spectroscopic methods. *Analyst*, 141:756–793, 2016.
- [133] Shahin Bagheri, Ksenia Weber, Timo Gissibl, Thomas Weiss, Frank Neubrech, and Harald Giessen. Fabrication of square-centimeter plasmonic nanoantenna arrays by femtosecond direct laser writing lithography: Effects of collective excitations on seira enhancement. *ACS Photonics*, 2:779–786, 2015.
- [134] Chihhui Wu, Alexander Khanikaev, Ronen Adato, Nihal Arju, A. Ali Yanik, Hatice Altug, and Gennady Shvets. Fano-resonant asymmetric metamaterials for ultrasensitive spectroscopy and identification of molecular monolayers. *Nature materials*, 11:69–75, 11 2011.
- [135] Tapan K. Chaudhuri and Subhankar Paul. Protein-misfolding diseases and chaperone-based therapeutic approaches. *The FEBS Journal*, 273(7):1331–1349, 2006.
- [136] Franziska Barho, Fernando González-Posada Flores, M. Milla, Mario Bomers, Laurent Cerutti, Eric Tournié, and Thierry Taliercio. Highly doped semiconductor plasmonic nanoantenna arrays for polarization selective broadband surface-enhanced infrared absorption spectroscopy of vanillin. *Nanophotonics*, 7, 11 2017.
- [137] Qian Wang, Edward T.F. Rogers, Behrad Gholipour, Chih-Ming Wang, Guanghui Yuan, Jinghua Teng, and Nikolay I. Zheludev. Optically reconfigurable metasurfaces and photonic devices based on phase change materials. *Nature Photonics*, 10:60–65, January 2016.
- [138] Cristiano D’Andrea, Jörg Bochterle, Andrea Toma, Christian Huck, Frank Neubrech, Elena Messina, Barbara Fazio, Onofrio M. Maragò, Enzo Di Fabrizio, Marc Lamy de La Chapelle, Pietro G. Gucciardi, and Annemarie Pucci. Optical nanoantennas for multiband surface-enhanced infrared and raman spectroscopy. *ACS Nano*, 7(4):3522–3531, 2013. PMID: 23530556.
-

-
- [139] Mohammed Janneh. (invited)surface enhanced infrared absorption spectroscopy using plasmonic nanostructures: Alternative ultrasensitive on-chip biosensor technique. *Results in Optics*, 6:100201, 2022.
- [140] Melissa Najem, Franck Carcenac, Luka Coutaud, Mohamed Mouhibi, Thierry Taliercio, and Fernando Gonzalez-Posada. Honeycomb-like aluminum antennas for surface-enhanced infrared absorption sensing. *Nanophotonics*, 12(12):2199–2212, 2023.
- [141] Valentina Di Meo, Andrea Caporale, Alessio Crescitelli, Mohammed Janneh, Elia Palange, Andrea De Marcellis, Marianna Portaccio, Maria Lepore, Ivo Rendina, Menotti Ruvo, and Emanuela Esposito. Metasurface based on cross-shaped plasmonic nanoantennas as chemical sensor for surface-enhanced infrared absorption spectroscopy. *Sensors and Actuators B: Chemical*, 286:600–607, 2019.
- [142] Andrea De Marcellis, Elia Palange, Mohammed Janneh, Carlo Rizza, Alessandro Ciattoni, and Sandro Mengali. Design optimisation of plasmonic metasurfaces for mid-infrared high-sensitivity chemical sensing. *Plasmonics*, 12:293–298, 04 2017.
- [143] Masatoshi Osawa. *Surface-Enhanced Infrared Absorption*, pages 163–187. Springer Berlin Heidelberg, Berlin, Heidelberg, 2001.
- [144] Jungho Mun, Dasol Lee, Sunae So, Trevon Badloe, and Junsuk Rho. Surface-enhanced spectroscopy: Toward practical analysis probe. *Applied Spectroscopy Reviews*, 54:1–34, 06 2018.
- [145] Toru Shimada, Hiroshi Nakashima, Yuta Kumagai, Yuta Ishigo, Masamichi Tsushima, Akihiko Ikari, and Yushi Suzuki. What is the key structural parameter for infrared absorption enhancement on nanostructures? *The Journal of Physical Chemistry C*, 120(1):534–541, 2016.
- [146] Jan Krajczewski, Karol Kołataj, and Andrzej Kudelski. Plasmonic nanoparticles in chemical analysis. *RSC Adv.*, 7:17559–17576, 2017.
- [147] P. Dumas, R.G. Tobin, and P.L. Richards. Study of adsorption states and interactions of co on evaporated noble metal surfaces by infrared absorption spectroscopy: II. gold and copper. *Surface Science*, 171(3):579–599, 1986.
- [148] Masatoshi Osawa and Masahiko Ikeda. Surface-enhanced infrared absorption of p-nitrobenzoic acid deposited on silver island films: contributions of electromagnetic and chemical mechanisms. *The Journal of Physical Chemistry*, 95(24):9914–9919, 1991.
-

-
- [149] B. N. J. Persson and Ansgar Liebsch. Collective vibrational modes of isotopic mixtures of co on cu(111) and cu(001). *Surface Science*, 110:356–368, 1981.
- [150] O. Krauth, G. Fahsold, and A. Pucci. Asymmetric line shapes and surface enhanced infrared absorption of CO adsorbed on thin iron films on MgO(001). *The Journal of Chemical Physics*, 110(6):3113–3117, 02 1999.
- [151] B. N. J. Persson and Roger Ryberg. Vibrational interaction between molecules adsorbed on a metal surface: The dipole-dipole interaction. *Physical Review B*, 24:6954–6970, 1981.
- [152] Annemarie Pucci, Frank Neubrech, Javier Aizpurua, Thomas Cornelius, and Marc Chapelle. *Electromagnetic Nanowire Resonances for Field-Enhanced Spectroscopy*, pages 175–215. 07 2008.
- [153] Masatoshi Osawa and Ken ichi Ataka. Electromagnetic mechanism of enhanced infrared absorption of molecules adsorbed on metal island films. *Surface Science*, 262(3):L118–L122, 1992.
- [154] Masatoshi Osawa, Ken-Ichi Ataka, Katsumasa Yoshii, and Yuji Nishikawa. Surface-enhanced infrared spectroscopy: The origin of the absorption enhancement and band selection rule in the infrared spectra of molecules adsorbed on fine metal particles. *Appl. Spectrosc.*, 47(9):1497–1502, Sep 1993.
- [155] Katherine A. Willets and Richard P. Van Duyne. Localized surface plasmon resonance spectroscopy and sensing. *Annual Review of Physical Chemistry*, 58(1):267–297, 2007. PMID: 17067281.
- [156] Joel I. Gersten and Abraham Nitzan. Electromagnetic theory of enhanced raman scattering by molecules adsorbed on rough surfaces. *Journal of Chemical Physics*, 73:3023–3037, 1980.
- [157] Alan Campion and Patanjali Kambhampati. Surface-enhanced raman scattering. *Chem. Soc. Rev.*, 27:241–250, 1998.
- [158] Nannan Li, Hang Yin, Xiaolu Zhuo, Baocheng Yang, Xiao-Ming Zhu, and Jianfang Wang. Infrared-responsive colloidal silver nanorods for surface-enhanced infrared absorption. *Advanced Optical Materials*, 6(17):1800436, 2018.
- [159] Iain A. Larmour and Duncan Graham. Surface enhanced optical spectroscopies for bioanalysis. *Analyst*, 136:3831–3853, 2011.
-

-
- [160] Xiaoxia Yang, Zhipei Sun, Tony Low, Hai Hu, Xiangdong Guo, F. Javier García de Abajo, Phaeton Avouris, and Qing Dai. Nanomaterial-based plasmon-enhanced infrared spectroscopy. *Advanced Materials*, 30(20):1704896, 2018.
- [161] Thomas G. Mayerhöfer and Jürgen Popp. Periodic array-based substrates for surface-enhanced infrared spectroscopy. *Nanophotonics*, 7(1):39–79, 2018.
- [162] Hai Hu, Xiaoxia Yang, Feng Zhai, Debo Hu, Ruina Liu, Kaihui Liu, Zhipei Sun, and Qing Dai. Far-field nanoscale infrared spectroscopy of vibrational fingerprints of molecules with graphene plasmons. *Nat Commun*, 7:12334, July 2016.
- [163] Yilei Li, Hugen Yan, Damon B Farmer, Xiang Meng, Wenjuan Zhu, Richard M Osgood, Tony F Heinz, and Phaeton Avouris. Graphene plasmon enhanced vibrational sensing of surface-adsorbed layers. *Nano Lett*, 14(3):1573–1577, February 2014.
- [164] Lauren Zundel and Alejandro Manjavacas. Spatially resolved optical sensing using graphene nanodisk arrays. *ACS Photonics*, 4(7):1831–1838, 2017.
- [165] Ricardo Aroca, Daniel Ross, and Concepción Domingo. Surface-enhanced infrared spectroscopy. *Applied spectroscopy*, 58:324A–338A, 12 2004.
- [166] Jia Chen, Zhi-Hong Mo, Xiao Yang, Hai-Ling Zhou, and Qin Gao. Exploration of organic–inorganic hybrid perovskites for surface-enhanced infrared spectroscopy of small molecules. *Chem. Commun.*, 53:6949–6952, 2017.
- [167] Ronen Adato, Serap Aksu, and Hatice Altug. Engineering mid-infrared nanoantennas for surface enhanced infrared absorption spectroscopy. *Materials Today*, 18(8):436–446, 2015.
- [168] Dominik Enders, Tadaaki Nagao, Annemarie Pucci, Tomonobu Nakayama, and Masakazu Aono. Surface-enhanced atr-ir spectroscopy with interface-grown plasmonic gold-island films near the percolation threshold. *Phys. Chem. Chem. Phys.*, 13:4935–4941, 2011.
- [169] Sang-Hyun Oh and Hatice Altug. Performance metrics and enabling technologies for nanoplasmonic biosensors. *Nature Communications*, 9, 12 2018.
- [170] Ming Li, Scott Kevin Cushing, and Nianqiang Wu. Plasmon-enhanced optical sensors: a review. *The Analyst*, 140 2:386–406, 2015.
- [171] W Suetaka and John T Yates. *Surface infrared and Raman spectroscopy: methods and applications*, volume 3. Springer Science & Business Media, 1995.
-

-
- [172] Masatoshi Osawa. Dynamic processes in electrochemical reactions studied by surface-enhanced infrared absorption spectroscopy (seiras). *Bulletin of the Chemical Society of Japan*, 70(12):2861–2880, 1997.
- [173] Atsushi Miki, Shen Ye, and Masatoshi Osawa. Surface-enhanced ir absorption on platinum nanoparticles: an application to real-time monitoring of electrocatalytic reactions. *Chemical communications*, (14):1500–1501, 2002.
- [174] Yuichi Kato, Masashi Kikugawa, and Eiichi Sudo. Attenuated total reflection surface-enhanced infrared absorption (atr seira) spectroscopy for the analysis of fatty acids on silver nanoparticles. *Applied Spectroscopy*, 71:000370281771271, 06 2017.
- [175] N. J. Harrick and K. H. Beckmann. *Internal Reflection Spectroscopy*, pages 215–245. Springer US, Boston, MA, 1974.
- [176] Wen-Jing Bao, Zhen-Dong Yan, Min Wang, Yun Zhao, Jian Li, Kang Wang, Xing-Hua Xia, and Zhen-Lin Wang. Distance-determined sensitivity in attenuated total reflection-surface enhanced infrared absorption spectroscopy: Aptamer-antigen compared to antibody-antigen. *Chemical communications (Cambridge, England)*, 50, 06 2014.
- [177] Joseph C. Hasse, Naveen Agrawal, Michael J. Janik, and Adam Holewinski. Atr-seiras investigation of the electro-oxidation mechanism of biomass-derived c5 furanics on platinum electrodes. *The Journal of Physical Chemistry C*, 126(16):7054–7065, 2022.
- [178] David S. Abraham, Ali Akbarzadeh-Sharbat, and Dennis D. Giannacopoulos. *The Finite-Element Time-Domain Method for Dispersive and Nonlinear Media*, chapter 3, pages 81–134. John Wiley Sons, Ltd, 2022.
- [179] Innovation at Work. Photonics Researchers Use Finite Element Method to Make Breakthroughs in 2020- IEEE Innovation at Work — innovationat-work.ieee.org.
- [180] O.C. Zienkiewicz, K. Morgan, and K. Morgan. *Finite Elements and Approximation*. Dover books on engineering. Dover Publications, 2006.
- [181] COMSOL Multiphysics. Introduction to comsol multiphysics®. *COMSOL Multiphysics, Burlington, MA*, accessed Feb, 9:2018, 1998.
- [182] Sujan Kasani, Kathrine Curtin, and Nianqiang Wu. A review of 2d and 3d plasmonic nanostructure array patterns: fabrication, light management and sensing applications. *Nanophotonics*, 8, 10 2019.
-

-
- [183] A. Mendoza-Galván, K. Järrendahl, A. Dmitriev, T. Pakizeh, M. Käll, and H. Arwin. Optical response of supported gold nanodisks. *Opt. Express*, 19(13):12093–12107, Jun 2011.
- [184] Niccolò Michieli, Ionut Gabriel Balasa, Boris Kalinic, Tiziana Cesca, and Giovanni Mattei. Optimal geometry for plasmonic sensing with non-interacting au nanodisk array. *Nanoscale Advances*, 2, 06 2020.
- [185] https://doc.comsol.com/5.6/doc/com.comsol.help.aco/aco_ug_pressure.
- [186] Jean-Pierre Berenger. A perfectly matched layer for the absorption of electromagnetic waves. *Journal of Computational Physics*, 114(2):185–200, 1994.
- [187] A. Otto. Excitation of nonradiative surface plasma waves in silver by method of frustrated total reflection. *European Physical Journal A*, 216:398–410, 08 1968.
- [188] Chemical Analysis, Life Sciences, and Diagnostics | Agilent — agilent.com. <https://www.agilent.com/>.
- [189] Yang Bai, Li Zhao, Dongquan Ju, Yongyuan Jiang, and Linhua Liu. Wide-angle, polarization-independent and dual-band infrared perfect absorber based on l-shaped metamaterial. *Opt. Express*, 23(7):8670–8680, Apr 2015.
- [190] Ming Li, Jianming Zhang, Savan Suri, Letha J. Sooter, Dongling Ma, and Nianqiang Wu. Detection of adenosine triphosphate with an aptamer biosensor based on surface-enhanced raman scattering. *Analytical Chemistry*, 84(6):2837–2842, 2012. PMID: 22380526.
- [191] Samer Bayda, Muhammad Adeel, Tiziano Tuccinardi, Marco Cordani, and Flavio Rizzolio. The history of nanoscience and nanotechnology: From chemical–physical applications to nanomedicine. *Molecules*, 25(1), 2020.
- [192] Ibrahim Khan, Khalid Saeed, and Idrees Khan. Nanoparticles: Properties, applications and toxicities. *Arabian Journal of Chemistry*, 12(7):908–931, 2019.
- [193] Ming Li, Jianming Zhang, Savan Suri, Letha J Sooter, Dongling Ma, and Nianqiang Wu. Detection of adenosine triphosphate with an aptamer biosensor based on surface-enhanced raman scattering. *Analytical chemistry*, 84(6):2837–2842, 2012.
- [194] Shikuan Yang, Xianming Dai, Birgitt Boschitsch Stogin, and Tak-Sing Wong. Ultrasensitive surface-enhanced raman scattering detection in common fluids. *Proceedings of the National Academy of Sciences*, 113:268 – 273, 2015.
-