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REVIEW

Advances in Metallic-Based Localized Surface Plasmon Sensors for Enhanced Tropical Disease Detection: A Comprehensive Review

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Abstract

Tropical diseases present significant challenges to global health, particularly in resource-limited regions. Early and accurate detection of these diseases is vital for effective management and control. In recent years, metallic-based LSPR sensors have emerged as promising diagnostic tools for sensitive and rapid detection of tropical diseases. This comprehensive review aims to provide an in-depth analysis of the current state of research on metallic-based LSPR sensors for the detection of various tropical diseases. In this study, we focused on the connection between neglected tropical diseases (NTDs) and its risk using metallic-based LSPR sensors to identify potential inflammatory biomarkers. We conducted a literature search using PubMed, Web of Science, and Google Scholar. Only published materials written in English were considered, resulting in the identification of ~ 220 articles. After a comprehensive evaluation, we selected 35 relevant ones. Our analysis revealed 35 links to neglected tropical diseases, providing valuable insights into their relationship using metallic-based LSPR sensors. Moreover, we explore the potential of metallic-based LSPR sensors in point-of-care testing and their integration with emerging technologies such as microfluidics and smartphone-based diagnostics. This review underscores the need for continued research efforts to develop affordable, sensitive, and user-friendly metallic-based LSPR sensors for early detection and surveillance of tropical diseases.

Keywords Metallic nanoparticles · Tropical diseases · Optical sensors · Sensitivity · Limit of detection · Localized field

Introduction

The optical properties of plasmonic nanoparticles (NPs) and their surface-plasmon resonances have garnered potential interest due to their unique characteristics. Unlike plasmons supported on bulk metal surfaces, NP plasmons present quantized electron oscillations confined to nanoscale volumes. This confinement enables manipulation of light-matter interactions while surpassing the limitations imposed by diffraction [1–3]. These properties have paved the way for diverse applications in the domain of optics [4], electronics [5], sensing [6], photonics [7], and medical diagnostics [8]. For instance, the advancement of miniaturized optical and electronic nanodevices, nanosensors, and nanophotonic circuits has been facilitated by leveraging the distinctive optical characteristics of nanoscale metals. Hence, the integration of plasmonic systems in medical diagnostics and therapeutics holds promise for improved bio-medical imaging [9], targeted drug delivery [10], and biosensing [11]. Recent theoretical advancements in NP-based plasmonics have led to valuable insights for the design and understanding of optical nanostructures. While Mie's theory of light scattering and absorption by gold (Au) nanospheres dates back over a century, modern computational frameworks and theoretical developments have enabled for the exploitation of plasmon resonances in more intricate NP architectures and assemblies [12]. In particular, plasmon hybridization theory has emerged as a powerful theoretical framework that draws parallels between plasmons in metallic nanoparticle assemblies and the behavior of electrons in quantum molecular orbitals [13, 14]. This theory predicts that plasmons on adjacent metallic nanostructures interact, mix, and hybridize, analogous to the behavior of electronic wave functions in simple atomic and molecular orbitals. The insights gained from plasmon hybridization theory hold promise for the rational assembly of plasmonic NPs into well-defined structures such

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as plasmonic molecules, polymers, and crystals. By tailoring the arrangement and properties of these plasmonic nanostructures, it becomes possible to engineer materials with customizable optical properties, opening up new horizons for advanced optical and photonic applications.

Conductive nanostructures, in particular, exhibit strong interactions with light, leading to a collective oscillations of conduction electrons, termed surface plasmon (SP) [15–18]. When the coherent collective oscillations of electrons occur under resonance conditions, it is referred as Localized Surface Plasmon Resonance (LSPR), which can outcome in highly efficient light absorption or scattering and robust field enhancement [3, 19–21]. The plasmon resonance phenomenon heavily depends on the composition [20, 22, 23], size [20, 24], and shape [3, 25, 26] of the nanostructures, as well as the surrounding environment [27–29]. Various types of materials, in a different configuration, can assist plasmons, including colloid dispersion's isotropic [30–35] and anisotropic [36–39] and anisotropic metallic NPs [40–44], metal oxide NPs [45–48], quantum dots [49–52], organized metallic nanostructures [53–56], and two-dimensional materials such as graphene [57–60].

However, nanomaterials composed of copper (Cu) [61–64], silver (Ag) [65–67], and gold (Au) [68, 68–71] have garnered special attention due to their LSPR occurring within the optical range of the electromagnetic spectrum. These materials exhibit unique optical plasmonic properties that may be harnessed for a wide range of applications.

Recently, LSPR sensors emerged as outstanding candidates for sensitive, facile, and rapid detection of tropical diseases [72–76]. LSPR sensors exploit the unique optical features of metal-based NPS, typically Au, Ag, or Cu, to detect molecular interactions at the nanoscale. By leveraging the principles of surface plasmon or localized plasmon resonances, such types of sensors enable label-free [77–79] and real-time detection [80–83] of disease-specific biomarkers with exceptional selectivity and sensitivity. The domain of LSPR sensors for tropical disease detection has witnessed significant advancements, with researchers exploring various strategies to improve detection accuracy, miniaturize sensor platforms, and integrate them with portable and point-of-care devices [72, 84–86]. These advancements have the potential to revolutionize the diagnosis and surveillance of tropical diseases, particularly in resource-constrained settings where access to centralized laboratory facilities is limited.

This review focuses on providing a detailed analysis of the current state-of-research on LSPR sensors for the detection of tropical diseases. It will delve into the underlying principles of plasmonic sensing, elucidate the advantages and challenges associated with these sensors, and underscore recent progress in their applications for the recognition of specific tropical diseases, including malaria, dengue fever, chikungunya, and others. Furthermore, this review will explore the potential of LSPR sensors in point-of-care testing and their integration with emerging technologies such as microfluidics and smartphone-based diagnostics (Fig. 1). By critically examining the progress made in this field, this review underscores the importance of ongoing research efforts in developing affordable, sensitive, and user-friendly plasmonic sensors for early detection and surveillance of tropical diseases. Ultimately, the widespread adoption of LSPR sensors has the potential to enhance disease control strategies, reduce morbidity and mortality rates, and contribute to the global effort to combat tropical diseases.

Tropical Disease

The neglected tropical diseases (NTDs) are a group of infectious diseases, predominantly affecting populations in tropical and subtropical regions. These diseases, including Leptospirosis, Chagas Disease, Dengue Fever, and others, pose significant health challenges in these areas [87–91]. NTDs are caused by various pathogens and are closely linked to environmental factors such as climate, sanitation, and disease vectors [92–94]. Socioeconomic factors like poverty, limited healthcare infrastructure, and lack of access to clean water further exacerbate the burden of NTDs, perpetuating a cycle of poverty and ill health in affected communities [95–98].

A plethora of literature highlights ongoing research efforts to improve NTD diagnosis and management. These efforts involve innovative diagnostic tools like electrochemical biosensors [99], CRISPR-based biosensors [100], and surface plasmon resonance (SPR) biosensors [101]. Additionally, researchers are exploring remote sensing technologies and terahertz (THz) sensors for disease mapping and detection [102, 103]. These studies provide valuable insights and potential solutions for the detection and understanding of NTDs.

To enhance the development of sensitive and reliable sensing platforms for NTDs, it is important to meticulously address various factors including careful material selection, surface functionalization, and consideration of factors like cross-sensitivity and selectivity among multiple analytes. Metallic-based LSPR sensors are highlighted as promising tools due to their cost-effectiveness, user-friendliness, sensitivity, and portability [104–106]. Overall, LSPR-based sensors underscore the significance of ongoing scientific research in addressing the complex challenges posed by NTDs.

Methods

Study Selection

This comprehensive review involved accessing and evaluating articles related to metallic-based sensors for the analysis

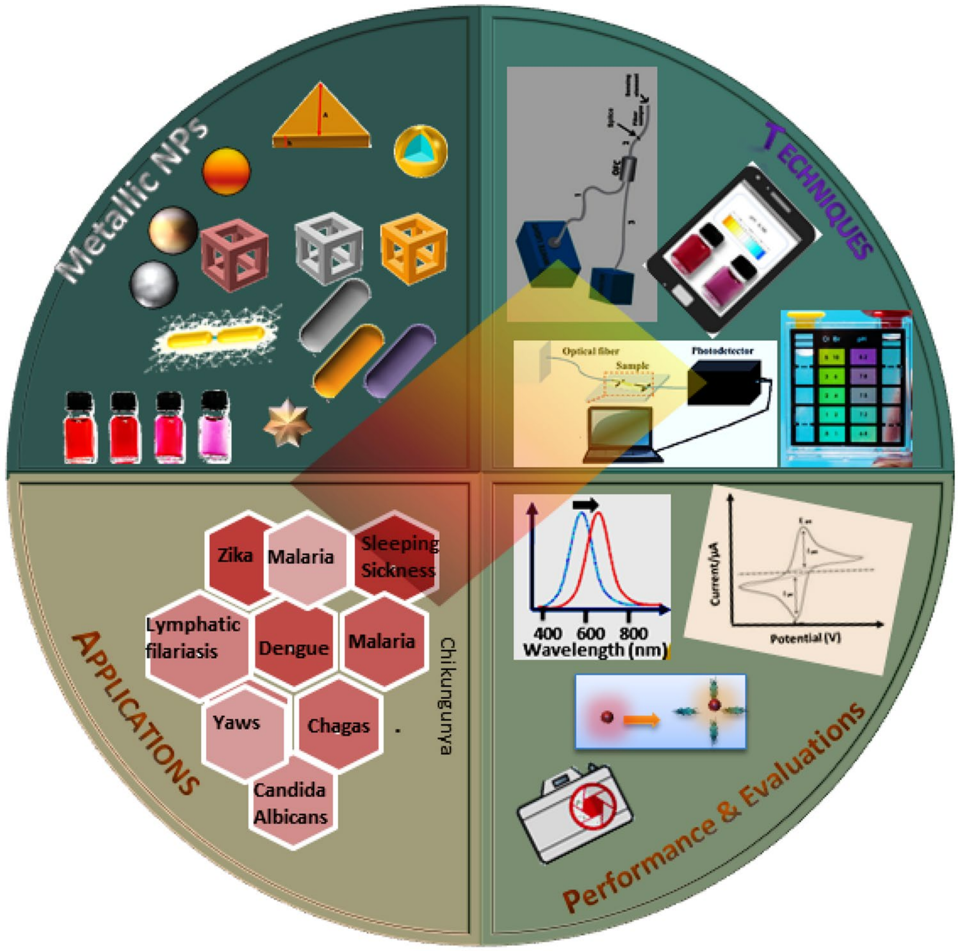

Fig. 1 Graphical representation of the metallic NPs-based on shape, size, materials composition, and spectroscopic techniques for performance evaluation to identify neglected tropical disease

of Neglected Tropical Diseases (NTDs). In 2023, we conducted three independent searches on electronic databases, including Web of Science, Google Scholar, and PubMed, using the keywords "LSPR sensors," "tropical disease," and "metallic nano-structures" to identify relevant studies for further analysis.

Data Extraction

We further narrowed down our selection to articles published within the last decade. The initial list underwent a preliminary screening, focusing on experimental studies. We specifically looked for original articles written in English while excluding review articles, conference abstracts, letters, book chapters, case studies, reports, and editorials, including method and protocol articles. To ensure thoroughness, two independent investigators evaluated the titles and abstracts for eligibility. Articles that met these criteria had their conclusions and texts reviewed to determine eligibility. We selected articles for our review if they addressed the signaling metallic-based NPs, sensitivity, Limit of Detection (LoD), and their relation to Neglected Tropical Diseases (NTDs), regardless of their methodological approaches. A visual representation of our inclusion process can be found in Fig. 2.

Principles of Plasmonic Sensing

Surface Plasmon Resonance

Ritchie and colleagues introduced the term "SPP" while studying the angle-energy distribution involved in the energy transfer process between an incident electron beam and conduction electrons within a thick metallic foil [107]. Their investigation revealed an intriguing pattern: the energy loss exhibited an inverse relationship with the film thickness. This observation showed at the potential involvement of Surface Plasmon Polaritons (SPPs) in the energy transfer process. Notably, materials like Au, Ag, and Cu have gained significant attention for studying SPPs due to their distinctive dielectric properties—characterized by highly negative real parts and relatively low positive imaginary parts (Figs. 3 and 4) [108]. A distinguishing

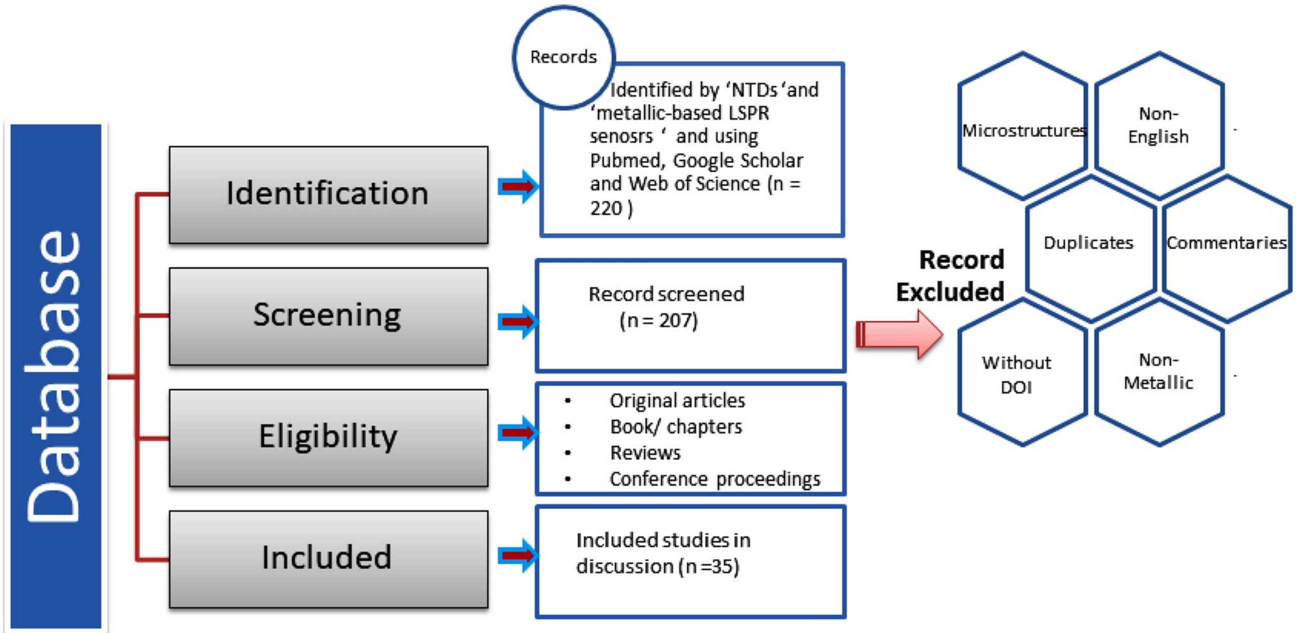

Fig. 2 Flowchart depicting the process of article identification across three independent electronic databases (Web of Science, PubMed, and Google scholar), leading to the inclusion of a total of 35 articles in the final discussion

factor setting noble metals apart from other metallic counterparts lies in their imaginary dielectric function components. As depicted in Fig. 4a, the imaginary component for Ag remains below 2 within the visible spectrum wavelength range. Similarly, Au displays a distinct minimum of around 700 nm wavelength. Particularly, intriguing is Ag's behavior, where the imaginary component stays significantly below 1 for wavelengths below 400 nm. In Fig. 4b, the red curve representing the real part of the dielectric function for Ag follows analogous patterns. It maintains a consistently negative value, dropping below −20 for wavelengths around 600 nm. This feature renders such materials exceptionally appropriate for SP coupling. Moreover, noble metals exhibit SPP coupling frequencies within the visible region of the electromagnetic spectrum, simplifying their practical application [107, 108].

Multiple techniques are available to generate SPPs in metallic thin films. These methods include using tightly focused light beams [109], employing diffraction gratings [110], or using prisms to ensure precise incidence angles

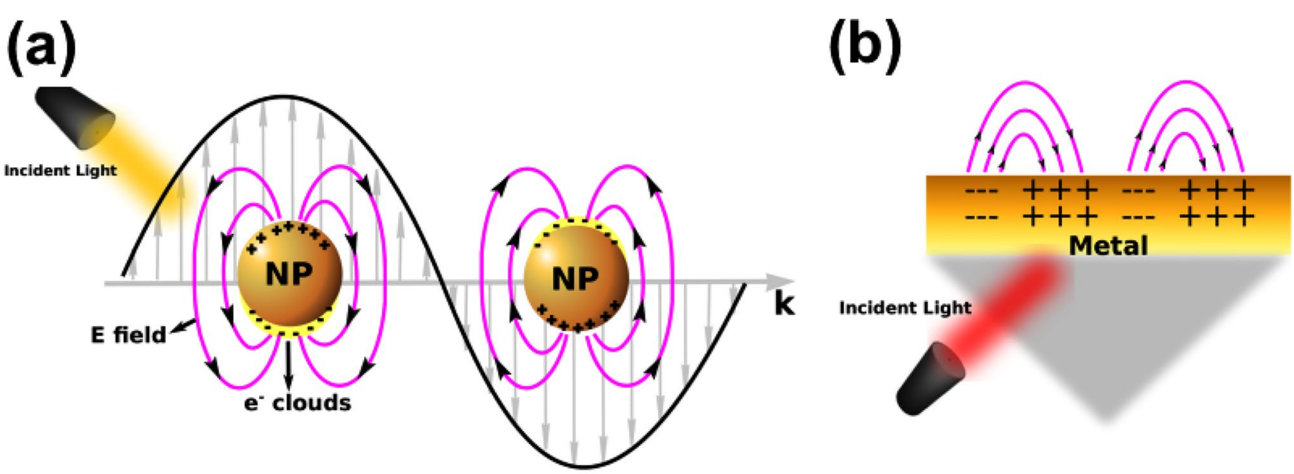

Fig. 3 Schematic diagram of the plasmonic resonance-based phenomenons in two different configurations: **a** SPR behavior and **b** LSPR phenomenon

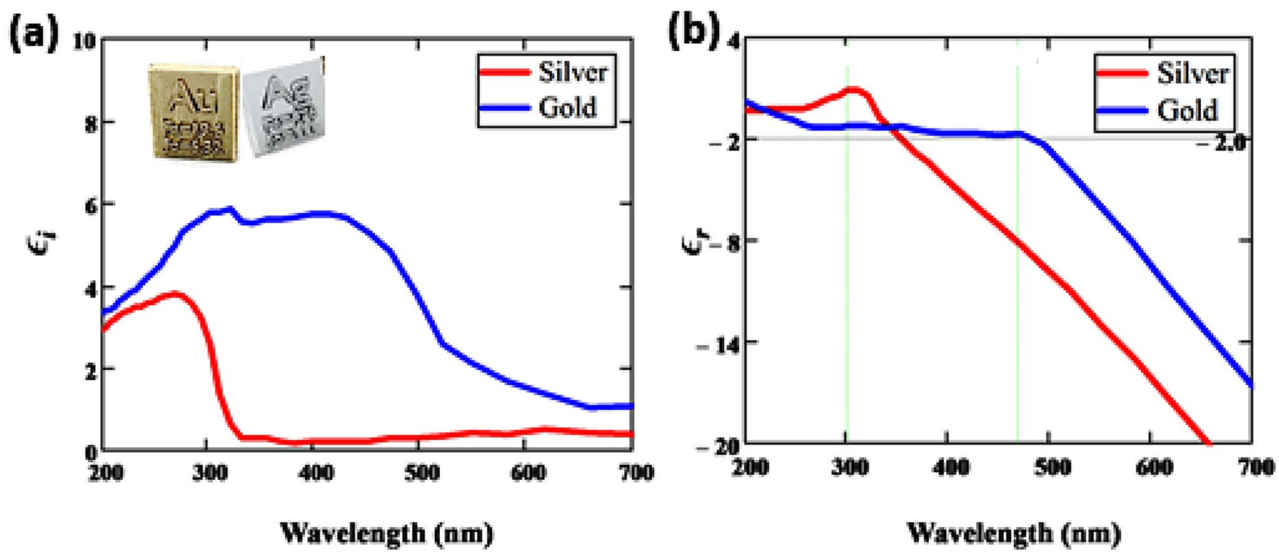

Fig. 4 **a** Imaginary and **b** real parts of the dielectric function of Ag and Au [44]

[111]. Regardless of the selected approach, a crucial prerequisite for successful SPP excitation is the alignment of the incident light beam's wavevector (k) with the SPP wavevector (k_{sp}) to assist effective coupling. Prism-based strategies can be further categorized into distinct setups, commonly known as the Kretschmann and Otto configurations. The Kretschmann configuration [112] involves positioning the metal film in direct contact with the prism's surface. Hence, the incident light beam is directed at an angle that enables a harmonious alignment of k and k_{sp}, promoting coupling between them. On the other hand, the Otto configuration [113] shares similar conditions for exciting SPPs. However, in this case, the SPP formation occurs within a gap—either filled with air or a dielectric solution—placed between the metallic film and the prism.

In both of these prism-coupling set-up configurations, the SPP is excited using a monochromatic beam, commonly employing a red laser, which is specifically well-suited for Au films. This selection of laser wavelength ensures that the value of k is defined as follows:

$$k = (\omega_0/c)\eta_0 \quad (1)$$

Here, ω_0 represents the frequency of the incident light, η_0 stands for the refractive index of the prism, and c signifies the velocity of light in a vacuum. Then, SPP wavevector is given by [114]:

$$k_{sp} = (\omega_0/c)\left[\frac{(\varepsilon_1\eta_2^2)}{(\varepsilon_1+\eta_2^2)}\right]^{1/2} \quad (2)$$

In this context, ε_1 denotes the dielectric function of the metal, $\eta_2 = \sqrt{\varepsilon_2}$ represents the refractive index (RI) of the medium situated adjacent to the metallic film (generally the analyte in sensor applications), and ε_2 relates to its respective dielectric function. The coupling phenomenon is obtained through precise adjustment of the angle of incidence of light on the metal surface, denoted as θ, ensuring that the projection of the wavevector of light onto the surface aligns with the plasmon wavevector: $k\sin\theta = k_{sp}$.

Localized Surface Plasmon Resonance

Mie [12] introduced the first theoretical analysis of the LSPR phenomenon. By solving Maxwell's equations for an electromagnetic wave that interacts with a sphere significantly smaller than the wavelength of incident light (2r << λ, where r represents the sphere's radius), Mie derived an equation to determine the particle's polarizability and subsequently, for the particle's extinction cross-section [12, 115]. The polarizability is mathematically expressed as follows:

$$\alpha = 4\pi r^3 \frac{\varepsilon_1-\varepsilon_2}{\varepsilon_1+2\varepsilon_2} \quad (3)$$

where ε_1 corresponds to the particle's dielectric function. It becomes evident that α undergoes a phenomenon of resonant enhancement when the real part of ε_1 equals $-2\varepsilon_2$, signifying the approach towards a minimum value of $|\varepsilon_1+2\varepsilon_2|$. This relationship is commonly referred to as the Fröhlich condition [115–117]. The extinction cross-section of a NP is determined by the combined effects of its absorption (σ_{abs}) and scattering (σ_{sca}) cross-sections. These characteristics rely on the particle's polarizability and can be expressed as follows:

$$\sigma_{sca} = \frac{k^4}{6\pi}|\alpha|^2, \tag{4}$$

$$\sigma_{abs} = k \ \text{Im}[\alpha]. \tag{5}$$

It's evident that the σ_{abs} and σ_{sca} exhibit distinct dependencies on the particle's radius. Consequently, the particle size plays a pivotal role in shaping its LSPR.

Factors Affecting LSPR

In the following sections, we will briefly discuss the LSPR dependence on the material composition, size, and shape.

Material-Dependent LSPR

Theoretical realization of LSPR extends to a variety of materials including metals, semiconductors, and alloys, contingent upon fulfilling the Fröhlich condition and featuring a real part of the dielectric function (Re[ε_1]) less than zero due to the presence of conduction electrons. Notably, in the realm of LSPR applications, copper (Cu), gold (Au), and silver (Ag) emerge as the most prominent metals, presenting LSPR spectral peaks within the visible spectrum. Furthermore, Al introduces a plasmon resonance in the ultraviolet region where several organic molecules exhibit light absorption [118]. Further elements like sodium (Na), lithium (Li), and gallium (Ga) also meet the Fröhlich criterion, unveiling plasmon resonance within the UV-Visible spectrum [119–122]. Nevertheless, the susceptibility of these metals to oxidation and their reactivity to the environment restricts their use as sensor platforms.

In a broad context, materials satisfying the Fröhlich criterion demonstrate a negative real part (ε_r) and a slightly positive imaginary part (ϵ_i) within the dielectric function. In the specific case of a metallic nanosphere situated in a vacuum, the Fröhlich criterion aligns with (ε_r) approximately equal to −2. This criterion is attained at wavelengths of about 350 nm for Ag, and approximately 490 nm for Au, as indicated in 4.

In the context of LSPR sensing, the preference lies with an imaginary part of the dielectric function featuring modest positive values, indicative of low electron energy loss, thus resulting in narrow LSPR linewidths. Specifically, at the point of LSPR resonance, the imaginary parts of the dielectric function are 3.81 for Au (490 nm) and 0.28 for Ag (at 350 nm), as illustrated in (Fig. 4).

Size-Dependent LSPR

The interaction between light and metallic NPs is strongly affected by the size of these structures. Reducing the size of metallic NPs amplifies the dipole contribution to the LSPR spectra. Conversely, increasing the radius of NPs introduces the potential for higher order modes, such as quadrupoles, in the case of Ag NPs, to significantly impact the particle's extinction cross-section. Notably, both σ_{sca} and σ_{abs} exhibit size-dependent behavior. Within a quasi-static approximation, the absorption cross-section of a spherical NP scales with the third power of the NP radius, while the scattering cross section relies on the sixth power of the NP's radius. Consequently, for larger metallic NPs (>50 nm), the light-NP interaction is primarily governed by scattering. In this scenario, enhancing the size of metallic NPs leads to augmented scattering cross sections [124, 125]. However, this enlargement is accompanied by a rise in radiation damping, resulting in spectral broadening and shifts [126, 127].

In the case of particles with small radii (≤ 15 nm), dipolar absorption dominates the extinction spectra. This implies that scattering, being a radiative phenomenon, is generally of lesser significance. As shown in Fig. 5, the broadening of LSPR spectrum increase as a function of size as well as the shifting of the LSPR spectra. However, Farooq et al. observed that spectral changes are more dominant for Ag NPs than for Au nanostructures [20]. Furthermore, the spectral resonance peak shift and sensitivity of different sizes of NPs can be seen in Table 1.

Shape-Dependent LSPR

Tuning the morphology of metallic NPs enables to control and fine-tune their LSPR characteristics, enabling the manipulation of plasmon peaks across a range of spectral regions. Moreover, NPs with sharper tips are contributed to exhibit LSPR at longer wavelengths compared to spherical ones. For instance, as shown in Fig. 5b. in the case of Ag NPs, nanospheres exhibit LSPR peak in the blue region, while Ag nanocubes depict an extinction peak at a green wavelength. With even more sharper tips, such as in nanotriangle structures, there's a clear shift towards longer wavelengths, resulting in a red-shifted plasmonic peak when compared to cubic nanostructures. Additionally, Chen et al. conducted a study involving Au NPs with various shapes, including nanospheres, nanorods, nanocubes, nanobranches, and nanobipyramids. The study revealed variations spanning from the visible to the near-infrared region as a function of shape [128, 129]. The plasmonic behavior and RI based sensitivity as a function of shape can be seen in Table 2.

Materials-Dependent LSPR

LSPR can be theoretically achieved in various metals, semiconductors, or alloys by fulfilling the Fröhlich condition. Among metals, Au and Ag are exclusively utilized for LSPR applications due to their negative real part and positive imaginary part of the dielectric functions. Moreover,

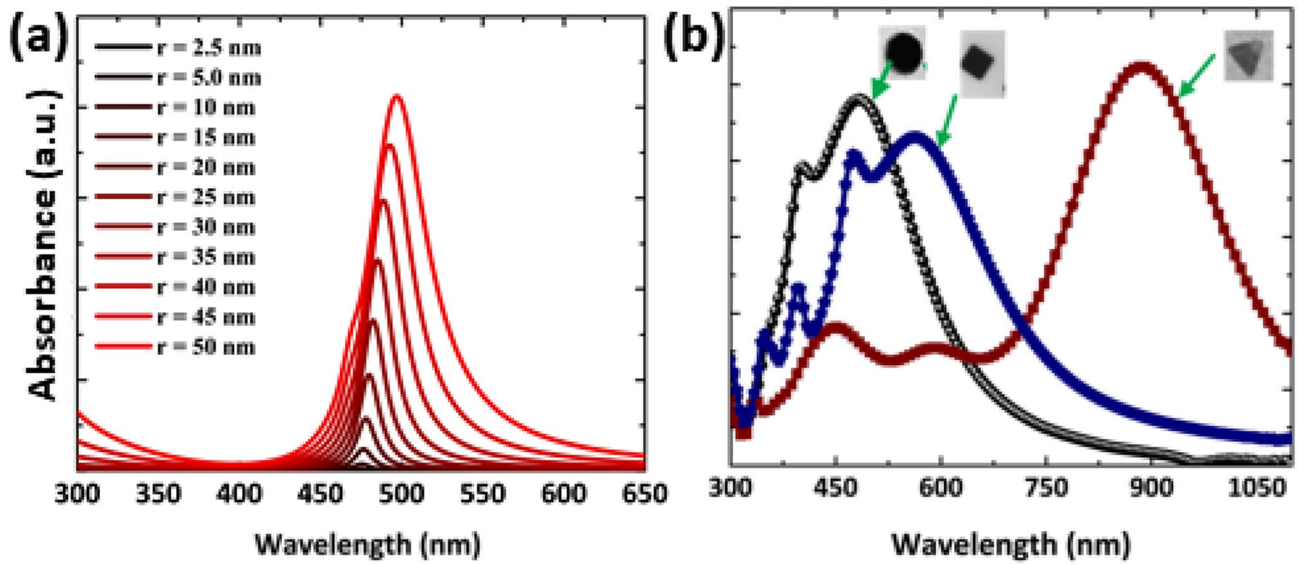

Fig. 5 **a** The optical properties of metallic NPs: **a** size dependence [5] and **b** shape dependence LSPR [123]

aluminium (Al) shows plasmon resonance in the ultraviolet region, which is impactful for light absorption by organic molecules. Copper (Cu) is another optical plasmonic metal that shows LSPR resonance, similar to Ag and Au NPs, with a narrow and intense peak. Other metals such as sodium (Na), Lithium (Li), and Gallium (Ga) may also follow the Fröhlich criterion, depicting plasmon resonance in the UV-Visible spectrum. However, their use in experiments is challenging due to their high reactivity and susceptibility to oxidation compared to Au or Ag. For Au and Ag, the LSPR can be tuned to the UV-Vis or near-IR spectrum. As shown in Fig. 4, the real parts of the dielectric functions for Au and Ag demonstrate negative values of ϵ_r, fulfilling the Fröhlich condition for a NP in air.

Localized Field Enhancement

As Fröhlich condition is satisfied, it leads to the enhancement of the localized field both inside and outside of NP. This enhancement becomes measurable through the evaluation of the electric field distributions within (E*in*) and outside (E*out*) of a NP. [130]:

$$E_{in} = \frac{3\epsilon_2}{\epsilon_1 + 2\epsilon_2} \times E_0 \tag{6}$$

$$E_{out} = E_0 + \frac{3\mathbf{n}(\mathbf{n}.\mathbf{p}) - \mathbf{p}}{\epsilon_1 + 2\epsilon_2} \times E_0 \frac{1}{r^3} \tag{7}$$

where **n** and **p** denote the unit vector normal to the surface and dipole moment, respectively.

The enhancement of the localized field (EF_F) near the surface of the NP is given as follows:

$$EF_F = \frac{|E_{max}|}{|E_0|} \tag{8}$$

where E_0 represents the incident field and E_{max} attributes the maximum field in the vicinity of NP's surface.

Increase localized field effects are more associated in non-spherical structures when they resonate plasmonically. Figure 6 represents the field enhancement across different shapes of Ag NPs – nanospheres, nanocubes, and nanotriangles – immersed in a H_2O environment. Remarkably improved EF_F values are observed, especially near the tips

Table 1 The size-dependent sensitivity and figures of merit for LSPR platfmors

Au nano spheres	Matrix type	LSPR peak (nm)	*RIS* (nmRIU^{-1})	FoM (nmRIU^{-2})	References
5 nm	Single	520	~ 44	0.5	[136]
15 nm	Ensemble	527	44	0.6	[137]
30 nm	Ensemble	530	60	-	[138]
60 nm	Ensemble	535	90	1.5	[139]
100 nm	Ensemble	552	185width at half maximum (FWHM) of the LSPR	1.9	[24]

Table 2 Diverse shapes of metallic-based LSPR sensors with their sensitivity and FoM

Nanostructure	Types	*RIS* (nm)	FoM (nm RIU^{-1})	*RIS*× FoM (nm RIU^{-2})	References
Au shell	Single	381	5.4	2057.4	[140]
Au star	Single	238	1.9	452.2	[144]
Au rattle	Single	199	3.8	756.2	[145]
Au crescent	Ensemble	596	2.4	1430.4	[146]
Au bipyramid	Ensemble	353	-	1584.0	[147]
Au dimeric NR	Single	544	12.4	6745.6	[40]

of these nanostructures. Consequently, non-spherical metallic NP posses considerable appeal for a range of plasmonic applications, including Surface-Enhanced Raman Spectroscopy (SERS) [131], fluorescence sensing [44], and imaging [132] (Fig. 7).

LSPR Sensing Mechanisms

Refractive Index Based Sensing

The relationship between the LSPR extinction spectrum and the permittivity of the surrounding medium has been a subject of thorough investigation for sensing applications. When the dielectric permittivity of the surrounding medium increases, it induces a red-shift in the plasmon resonance peak [133]. Evaluating the effectiveness of an LSPR sensor often involves the consideration of bulk sensitivity (*RIS*), quantified as the change in LSPR peak wavelength per unit alteration in the refractive index (RIU) [134, 135].

$$RIS = \frac{\Delta\lambda_{LSPR}}{\Delta n_m} \tag{9}$$

where $\Delta\lambda_{LSPR}$ represents the shift in the wavelength of the LSPR peak, and Δn_m signifies the alteration in the refractive index of the surrounding medium.

Figure of Merit

Precise shifts within the resonance peak can sometimes be challenging to discern, especially amidst a broad LSPR spectrum. For a comprehensive assessment of the sensor's efficacy, we introduce another parameter, the figure of merit (FoM). This value represents the ratio of bulk sensitivity (*RIS*) to the full width at half maximum (FWHM) of the LSPR peak (FoM = *RIS*/FWHM). Consequently, an optimal sensor must fulfill both aspects: exhibit substantial bulk sensitivity while maintaining a narrow LSPR spectrum. This criterion finds its expression in the form of RIS×FoM.

$$FoM = \frac{RIS}{FWHM} \tag{10}$$

where FWHM represents full-width half maximum of the LSPR spectrum.

A successful plasmonic sensor demands to simultaneously meeting two essential criteria: achieving high sensitivity while maintaining a distinct and narrow LSPR spectrum. Complex plasmonic structures are frequently explored for sensing purposes due to their ability to provide elevated sensitivity values. However, this pursuit of sensitivity might not consider the broader nature of the resulting LSPR peak.

Consider, for example, LSPR sensors that rely on intricate nanoparticle shapes like nanostars, nanorices, nanorods, and nanocrescents. While these sensors can demonstrate remarkable sensitivity, they might exhibit lower FoM values due to their inherently broader spectral responses. To address this trade-off, Farooq et al. [140] introduced a novel figure of merit ($RIS \times FoM$) that presents a comprehensive assessment of LSPR sensor performance by considering both sensitivity and spectral width as key factors.

Molecular Sensing

The LSPR sensor exhibits several advantageous features, making it well-suited for biomedical and biological assays. One of its key strengths is its label-free nature, enabling the detection of molecular attachments to the surface of NPs (NPs). The sensor's sensitivity is enhanced as the

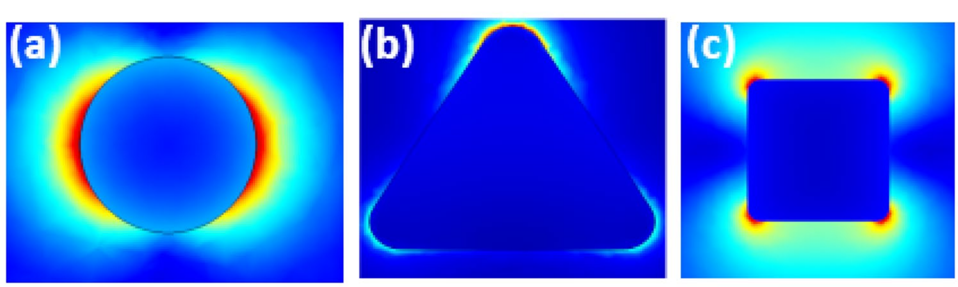

Fig. 6 Localized field enhancement of diverse shapes of Ag NPs: **a** sphere, **b** triangle, and **c** cube [123]

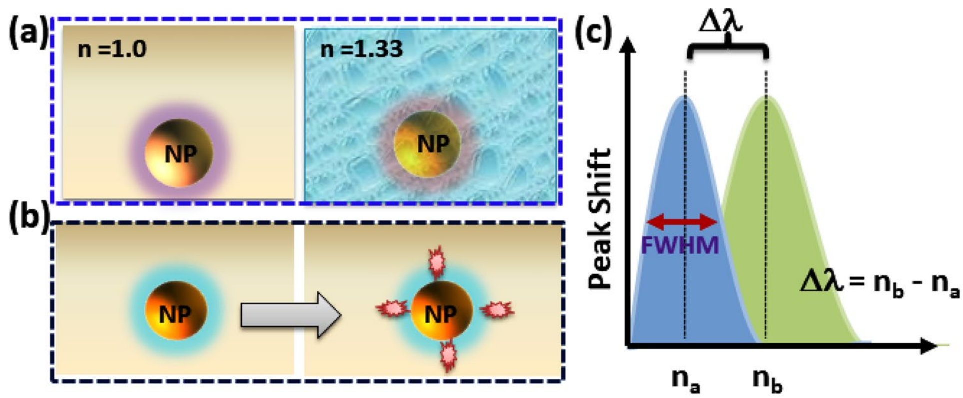

Fig. 7 A schematic diagram of LSPR sensing mechanism: **a** refractive index based sensing (RIS), **b** molecular sensing phenomenon, and **c** figure of merit

volume of analyte increases [141]. A fundamental phenomenon underlying LSPR-based molecular sensing includes self-assembled monolayer (SAM) on the surface of the NP [142]. Campbell and colleagues developed a mathematical model that elucidates plasmon resonance signals stemming from adsorbed molecular layers on nanostructures [143]. This model is explored as a valuable tool for gauging adlayer thickness on plasmonic structures, and it's relevant to both SPR and LSPR techniques. The framework of this model revolves around the interplay between the intensity of the electric field (I) and the distance (z) from the surface. The shift in the LSPR peak due to the adsorption of a molecular monolayer onto a metallic NP surface can be effectively explained by Campbell's model [143]:

$$\Delta\lambda = RIS(n_{ads} - n_m)\left(1 - e^{-2d/l_d}\right) \tag{11}$$

where l_d represents the electromagnetic field decay length around the NP, d associates to the thickness of the adsorbate layer, while n_{ads} and n_m denote the refractive indices of the adsorbate layer and the surrounding medium, respectively.

Results and Discussion

In this comprehensive review, our initial search identified a total of 250 articles from various databases, including Google Scholar, PubMed, and Web of Science (173) (see Fig. 2). After meticulously eliminating duplicate records, both manually and by employing the Bibliography Library, we were left with 220 unique articles. To ensure the relevance and specificity of our review, we excluded articles falling into several categories, including review papers, metallic nanoparticles without NTD, QDs studies, and studies focusing solely on SPR unrelated to NTDs. Additionally, literature that did not encompass tropical diseases was also removed from consideration. As a result of this rigorous screening process, we ultimately included 35 articles in our comprehensive review following a comprehensive full-text assessment.

Among the selected literature, the majority of research focused on NTDs such as DENV, ZIKV, Leishmaniasis, and Schistosomiasis in the context of tropical diseases. Interestingly, there were limited studies specifically addressing metallic-based LSPR sensors unique to NTDs, likely due to the challenges (stablity, user friendly, etc.) of metallic NPs with various other medical conditions. To provide a clear description of the distribution of selected articles, Fig. 8a offers a topic-wise classification. We also categorized these articles based on their publication year (Fig. 8b), allowing us to prioritize recent research and technological advancements. Notably, a significant proportion of the selected articles were selected before 2023, which can be attributed to the heightened demand for metallic-based sensors for NTDs. These innovations were crucial for managing tropical diseases, especially those at higher risk, in the comfort of their homes.

Conventional methods of tropical disease detection, involving microscopy, serological assays, and molecular techniques, have been foundational in public health management. However, these methods come with inherent limitations. Microscopy, while widely used, is labor-intensive and may lack the sensitivity required for early disease detection. Additionally, it relies on skilled personnel and can be time-consuming, delaying timely interventions [180, 181]. On the other hand, serological assays can provide false negatives, particularly in the case of low antibody levels, and may not discriminate between active as well as past infections. Such methods can be resource-intensive, necessitating expensive laboratory infrastructure, reagents, and skilled technicians [182, 183]. In the context of conventional studies, the novel diagnostic techniques introduced are not without their own set of limitations. CRISPR-based biosensors, while highly specific, can be complex to design and may demand optimization for diverse diseases. Additionally, these methods may not always offer the desired sensitivity for early disease detection [184, 185]. Surface plasmon resonance (SPR)

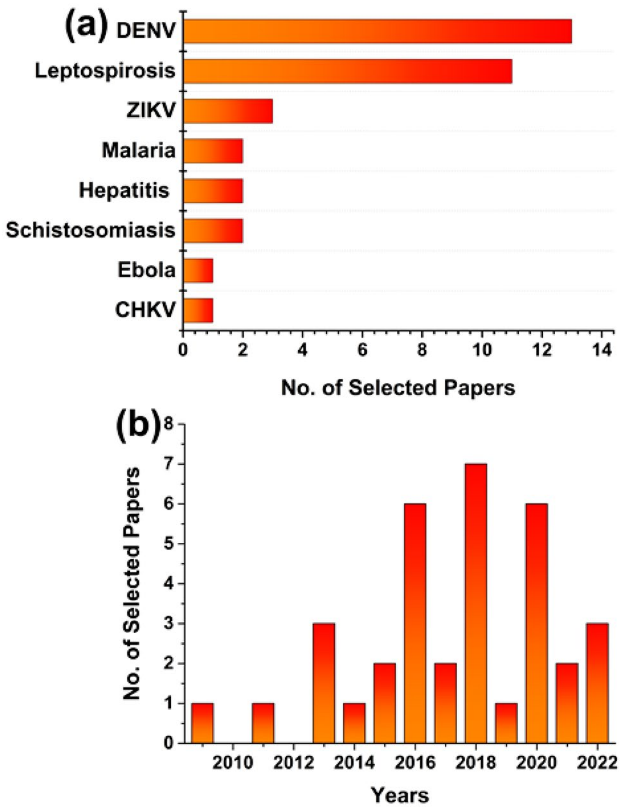

Fig. 8 The selected papers as a fucntion of classification according to **a** research topic regarding NTDs and **b** according to year of publication

biosensors and electrochemical biosensors, while promising, can be expensive to implement, and their success relies on careful material selection and functionalization [186]. Furthermore, the cost of these technologies can be a hindrance to exclusive adoption in resource-limited settings [187]. Overall, while conventional methods have been employed as the foundation for NTDs detection, they suffer from limitations attributed to sensitivity, specificity, cost, and infrastructure requirements. Convention studies, while inducting novel diagnostic methods, can limit their applications due to complexity, cost, and precision. The current research in this domain aims to provide a balance between these techniques to enhance disease sensitivity and healthcare results in regions affected by NTDs [188–190].

Plasmonic sensing platforms encompass a wide range of materials including noble metals, transition metallic nitrides, metallic chalcogenides, semiconductor nanocrystals, and metallic oxides [191]. Furthermore, these platforms can be extended to incorporate intricate multicomponent structures such as alloys and core-shell/nanoshell configurations [23, 192]. The LSPR phenomenon exhibited by these materials is finely tuned by factors such as chemical composition, shape, aspect ratio, and size, as aforementioned [193]. However, it's important to note that each material comes with its own inherent advantages and limitations, both of which hinge on the precise optimization of synthetic conditions. Achieving these optimal conditions is far from a straightforward endeavor, as they can substantially vary due to a multitude of factors extensively explored elsewhere [192, 194, 195]. These factors encompass aspects like the choice of reducing and stabilizing agents, temperature control, deposition substrate, and more. In essence, navigating the path to achieving the best possible conditions is a complex undertaking that requires careful consideration and adjustment across a diverse array of variables.

These platforms offer remarkable versatility, capable of adopting a plethora of architectural designs, all without the need for specific incidence angles, high-intensity light sources, or intricate detection systems. For instance, plasmonic NPs find utility in various formats such as suspensions [196, 197], depositions onto solid substrates like glass, semiconductors [198, 199], metallic films, polymers [200], paper [201, 202], and even fiber optics [203]. The process of illumination and detection can be executed using conventional UV-Vis spectrophotometers, harnessed through dark-field microscopy [204–206], achieved via a simple LED and a cell phone camera [201], or even through direct visual inspection [207]. In fact, these platforms deliver reliable outcomes swiftly and cost-effectively, not only within the controlled confines of a laboratory setting but also in field analyses and locations with restricted access. This adaptability and accessibility underline their significance in numerous practical applications.

The simplest LSPR platform entails utilizing suspended NPs due to its straightforward handling, enabling measurements using a conventional spectrophotometer or even unassisted visual observation [207]. A significant portion of visually interpretable LSPR colorimetric sensing platforms revolves around the aggregation of NPs, a mechanism that facilitates substantial peak shifts. Numerous research endeavors have tackled significant subjects concerning tropical diseases and diagnostic techniques rooted in the LSPR phenomenon. Kim and colleagues engineered a colorimetric rapid diagnostic test (RDT) kit with the ability to detect Zika virus (ZIKV) [208]. This innovative kit employs monoclonal antibodies in conjunction with non-structural protein-1 (NS1) conjugated to Au NPs. Further, the authors revealed that the Zika RDT presented high analytical sensitivity, with 100% identical results compared to ELISA and PCR. Additionally, the kit demonstrated remarkable selectivity, as it did not cross-react with other infected sera, involving DENV, yellow fever, and hepatitis-C virus. Similarly, Brangel and collaborators pioneered a point-of-care test employing an immunochromatographic strip and smartphone reader, which effectively detects Ebola-specific antibodies in human survivors with exceptional sensitivity and specificity [160]. The sensor also involved multiplex tests for detecting antibodies against multiple viral species, aiding in cross-reactive immunity assessment. The simple, fast, and portable system showed key potential for diagnostic procedures, therapeutic evaluation, and vaccine development in Ebola-affected regions like Uganda. In a different study, Sattarahmady et al. developed a novel diagnostic method for Leishmania major using Au NPs and a specific DNA probe [152]. The approach depends on the dispersion of Au NPs probe conjugates based on the presence of a complementary DNA-sequence, leading a sensitive shift in UV-Visible spectra as well as solution color. The method proved efficient in accurately detecting Leishmania NTD from other non-Leishmania diseases, with a detection limit of 7.0 pg μmL^{-1}. Furthermore, the PCR-free assay successfully identified genomic-DNA from, both, clinical samples and Leishmania major. This new method offers great promise for improved and efficient diagnosis of Leishmania major infections. Additionally, the researchers developed and validated a rapid and quantitative biosensor for identifying dengue virus serotypes (1-4) [162]. The biosensor uses cadmium selenide tellurium sulphide (CdSeTeS) fluorescent quantum dots (QDs) and Au NPs in combination with specific hairpin single-stranded DNA probes for each serotype. The biosensor successfully detected target virus DNA in femtomolar concentrations, demonstrating its ability for accurate serotype identification and potential point-of-care diagnostic use. Additionally, Chowdhury et al. developed a new two-way detection method using nanocomposites of Au NPs and nitrogen, sulfur codoped graphene (N, S-G) quantum dots (QDs) for DENV serotype identification and DNA quantification. The authors demonstrated efficient detection of all four DENV serotypes individually within a concentration range of $10^{-14} to 10^{-6}$ M, with a low LoD (9.4 fM). The sensing platform also depicted satisfactory performance in identifying and quantifying clinically isolated DENV DNA, leading a facile and reliable method for biomedical applications in sensitive and robust sensing probes. Moreover, Shrivas et al. developed a similar colorimetric sensing platform utilizing Au NPs to detect ampicillin in urine samples with LoD of 10 ng mL^{-1} [209]. All measurements were taken using a UV-Visible spectrophotometer of type-1800-Shimadzu-Japan, matching with a 1-cm quartz cell for the identification of ampicillin. In a separate study, Versiani and coauthors developed a sensitive diagnostic test using Au NRs coated with DENV proteins as LSPR sensors [210]. The LSPR platform detected tiny amounts of DENV antibodies and diluted DENV-positive human-sera accurately. The test differentiated the DENV from other flavivirus infections and identified the specific DENV serotype in patients using standard ELISA-plate spectrophotometers. Further, Jeon et al. established a colorimetric-based sensing platform for visual malaria diagnosis using an aptamer and Au NPS [157]. The authors employed specific aptamer pL1 and cationic polymers (PDDA and PAH) to control Au NPs color properties. In the presence of the malaria biomarker (PLDH), Au NPs turn blue due to induced fit binding, allowing detection at low concentrations and high specificity over interfering proteins in just 40 min. The study demonstrated the successful in vitro detection of DENV using a lateral flow assay based on Au NPs. The estimated detection limit achieved was 5.12×102 PFU, indicating the assay's sensitivity and potential for practical applications in virus detection [211]. Stephen et al. [212] elucidated the potential of electrochemical sensors for the detection of pathogens attributed with NTDs, evaluating the probe selection, nanomaterials, and future applications of these biosensors.

Piezoelectric systems utilize materials capable of inducing an electric-based response when subjected to mechanical oscillation. These platforms present an attractive sensing alternative for NDTs through mass response-type sensors. For instance, Pirich et al. manipulated the use of cost-effective piezoelectric devices, specifically quartz crystal microbalance (QCM) systems, for disease detection [213]. The study involved the sensors with thin films, regarding bacterial cellulose nanocrystals (CN) to enhance the sensitivity as well as specific detection of DENV protein NS1. The immunochip surface, analyzed by AFM, successfully immobilized IgG NS1. Both QCM and QCM-D (with energy dissipation monitoring) demonstrated effective detection of NS1 in serum with only a 10-fold dilution, with respective LoD of 0.1 μg mL^{-1} and 0.32 μg mL^{-1}. These findings proposed that QCM-D and QCM could be potential tool for sensitive, rapid, and low-cost diagnostic assays for DENV fever. Additionally, Ramos et al. developed a sensitive piezoelectric immunosensor for detecting anti-Leishmania antibodies in the serum of canine, crucial for diagnosing visceral leishmaniasis (VL) [214]. The sensor used re-combinant antigens immobilized on a quartz crystal electrode coated with a nafion film and Au NPs to improve stability and surface area. The immunosensor depicted an excellent linearity and low relative error at different serum dilutions, outperforming the cysteamine (Cys)-based immunosensor without Au NPs. The study findings demonstrated that the Au NP-based immunosensor held great promise as a reliable tool for VL diagnosis, especially in endemic regions and asymptomatic dog screening, crucial for disease control. In another study, they introduced a novel electrochemical immunosensor based on a one-step fabricated carbon ink graphite screen-printed electrode for detecting non-structural protein NS1 of the reemerging DENV [165]. The sensor's surface is modified using amine-functionalized (-NH2) Au NPs synthesized through a photoinduced physical method. The Au NPs improved the sensitivity of NS1 detection by square-wave-voltammetry (SWV) without the need for labeling. The immunosensor demonstrated a linear response from 0.1 to 2 $\mu g\ mL^{-1}$ NS1, with a low LoD (0.03 $\mu g\ mL^{-1}$). This facile technique showed key potential for early DENV diagnosis, facilitating in controlling its impact on global health. Overall, an in-depth investigation of LSPR based sensors for identification of NTDs can be seen in Table 3.

Responding to the increasing demand for cost-effective, portable, and user-friendly sensing platforms, glass substrates have emerged as a promising avenue for the creation of portable LSPR optical sensors [215]. In this context, Liu and colleagues employed dark-field microscopy to demonstrate that the plasmon shift of spherical gold nanoparticles immobilized on glass slides can be harnessed to quantitate the presence of 1-propanol, 1-octanol, or oil within a water droplet [216]. More recently, Farooq et al. leveraged Ag NPs on a glass substrate as a foundation for Candida albicans sensing [134]. In this study, the Ag NPs of size 10 nm were functionalized with monoclonal IgG anti-Candida antibodies for the detection of Candida albicans antigen. The practicality of the LSPR sensor was substantiated by successfully identifying C. albicans antigen concentrations as low as 50 ng mL^{-1} through the use of a spectrophotometer (Ocean Optics HR4000)[134]. In

Table 3 Selected studies for metallic-based LSPR platfmors and their performance

Sensor type	Sample type	Tropical disease	detection limit	References
Optical sensor	Au NPs	Leptospirosis	0.0077 ng/μL	[148]
Opitcal sensor	Au NPs	Leptospirosis	348 fg/mL	[149]
SERS sensor	Au NPs	Leishmaniasis	-	[150]
Electrochemical sensor	Au NPs	Leishmaniasis	200 ng/mL	[151]
Colorimetric sensor	Au NPs	Leishmaniasis	0.7 pg/μL	[152]
Optical sensor	Ag NPs	Leishmaniasis	4.2 μg/mL	[153]
Electrochemical sensor	Ag NPs	Leishmaniasis	0.07 ng/mL	[154]
Electrochemical-based sensor	Ag NPs	Leishmaniasis	0.01 pg/mL	[155]
Electrochemical-based sensor	Ag NPs	Leishmaniasis	29 ng/mL	[156]
Colorimetric-based sensor	Au NPs	Malaria	74 parasites/μL	[157]
PIT-based sensor	Au NPs	Malaria	25 μg/mL	[158]
Fluorescence-based sensor	Au NPs	Malaria	1 pgμL	[159]
Colorimetric-based sensor	Au NPs	Ebola virus	200 ng/mL	[160]
Fluorescence-based sensor	Au NPs	Ebola virus	220 fg/mL	[161]
Fluorescence-based sensor	Au NPs & QDs	DENV (1,2,3,4)	24.6, 11.4, 39.8 and 39.7 fM	[162]
Fluorescence-based sensor	N,S-G QDs & Au NPs	DENV	9.4 pM	[163]
Optical sensor	Au NPs	DENV	0.074 μg/mL	[164]
Optical sensor	Au NPs	DENV	0.07 μg/mL	[24]
Electrochemical-based sensor	Au NPs	DENV	0.03 μg/mL	[165]
Electrochemical-based sensor	Au NPs	DENV	-	[166]
Optical sensor	Au NPs	DENV	2 PFU/mL	[167]
Piezoelectric-based sensor	Au NPs	DENV	0.03 μg/mL	[165]
Electrochemical-based sensor	Au NPs	DENV	9.5×105 pfu/mL	[168]
Electrochemical-based sensor	Au NPs	DENV	-	[169]
Optical sensor	Au NPs	DENV	0.07 μg/mL	[136]
Optical sensor	Ag NPs	CANDV	50 ng/mL	[134]
Optical sensor	Ag NPs	CANDV	50 ng/mL	[170]
Optical sensor	Ag NPs	CANDV	102 CFU m/L	[171]
Geno-sensor	Au NPs	ZIKV	0.2 and 33 fM ng/mL	[172]
Fluorescence-based sensor	Au NPs, QDs	ZIKV	2.9 copies/mL	[173]
Fluorescence sensor	Au NPs, QDs	ZIKV	35.0 copies/mL	[174]
Electrochemical-based sensor	Au NPs	ZIKV	0.82 pmol/L	[175]
SERS-based sensor	Au NPs	ZIKV	10 ng/mL	[176]
Electrochemical-based sensor	Au NPs	ZIKV	10 pM to 1 nM	[177]
Geno-sensor	Au NPs	Schistosomiasis	0.685 pg/mL	[178]
Geno-sensor	Au NPs	Schistosomiasis	0.6 pg/mL	[179]

another study, the enzymatic-like activity of Au NPs, akin to that of enzymes, is intricately influenced by factors such as their aggregation state, surface ligands, and morphology. By harnessing chromogenic substrates, colorimetric sensing platform that capitalizes on the peroxidase-mimicking capacity of Au NPs can be proficiently employed for the purpose of pathogen detection [217]. Additionally, a new diagnostic method was developed by Camara et al. for dengue fever in the acute phase of infection[164]. The method applies on an all-optical fiber sensor based on LSPR and specular reflection from Au NPs to detect NS1 antigen at different concentrations. The optical fiber-based sensor holds promise as a potential tool for DENV diagnosis with LoD of 0.074 μg/mL due to its rapid, reliable, and user-friendly simple operation. In an alternative approach, the researchers introduced novel label-free LSPR immunosensors based on Au NPs for DENV sensing. By optimizing spherical-shaped Au NPs size, the platforms show high molecular sensitivity, a sharp spectral resonance peak, and a high figure of merit (FoM). Further, the their platforms demonstrate successful identification of dengue NS1 antigens with a low limit of detection, presenting promise for engineering efficient immunosensor platforms [24, 136]. Notably, the advantages and disadvantages of LSPR based sensors can be found in Table 4.

An alternative strategy for enhancing both robust LSPR shift and sensing specificity involves employing a "sandwich assay" with an additional antigen or antibody molecule. Recently, Deroco et al. [73] showcased the use of a sandwich-immunoassay LSPR sensing platform to diagnose NTDs. A new assay using lambda exonuclease (λ -exonuclease) and SERS was introduced for fast detection of three bacterial meningitis pathogens in cerebral spinal fluid. The assay showed high sensitivity, multiplexing capability, and quantification of individual pathogens using unique SERS signals merged with partial least squares (PLS) regression. This innovative SERS assay offers significant advantages over current fluorescent-based methods and presents promising opportunities for future advancement in healthcare management, ensuring timely and effective diagnosis of bacterial meningitis [218]. A colorimetric sensing method using dual amplification was employed for detecting thrombin. The assay involved two aptamers (TBA1 and TBA2) in a sandwich configuration with Au NPs [219]. The transition from a red to purple hue upon thrombin binding to TBA1, coupled with the redshift observed in the absorption peak due to the integration of TBA2 with Au NPs, assisted the naked-eye identification of thrombin concentrations at an ultralow level of 3 $\mu g\ mL^{-1}$. Employing UV-Vis analysis, LoD was rigorously determined to be 1.33 $\mu g\ mL^{-1}$. Impressively, the sensing platform displayed exceptional discernment even in the presence of intricate interferents, yielding a remarkable recovery rate of 97.4% when assessed with authentic biological human serum samples. The application, furthermore, of the sandwich-immunoassay LSPR technique was extended to the detection of the hepatitis-B virus surface antigen (HBsAg). In a novel study, Kim et al. established a glass substrate featuring Au NPs coupled with an anti-HBsAg antibody, enabling for the detection of HBsAg through the development of a sandwich immunoassay involving an additional layer of Au NPs functionalized with anti-HBsAg antibodies. This innovative approach,

Table 4 Advantages and disadvantages of sensors, biosensors, and conventional methods with limitations

Aspect	Sensors	Biosensors	Conventional methods
Advantages	- High sensitivity	- High specificity	- Established methods
	- Real-time monitoring	- Rapid detection	- Widely availability
	- Low sample volume	- Quantitative data	- Established expertise
	- Minimal sample handling	- Minimal sample preparation	- Well-recognized
	- Potential for automation	- Potential for miniaturization	- Cost-effective
		- Integrated with electronics	
Disadvantages	- Specific to target analytes	- Design complexity	- Limited sensitivity
	- Limited specificity	- Cost of bio-receptors	- Limited specificity
	- Cost of instrumentation	- Stability of bioreceptors	- Labor-intensive
	- Expertise required	- Potential for false positives	- Long turnaround time
	- Limited multiplexing	- Limited multiplexing	- Expensive equipment
Limitations	- Interference from matrix	- Stability of recognition	- Sensitivity challenges
	- Calibration requirements	- Potential cross-reactivity	- Lack of specificity
	- Biological fouling	- Shelf life of bioreceptors	- Sample variability
	- Complex signal analysis	- Sensitivity to environmental	- Infrastructure challenges
		- conditions	
		- Limited target range	

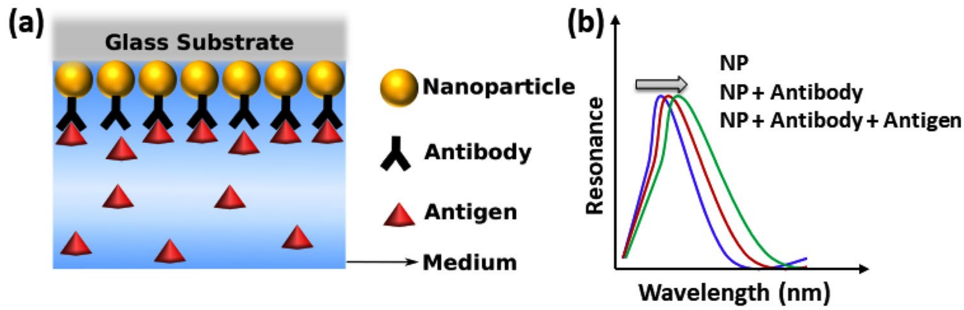

Fig. 9 **a** The schematic diagram of the LSPR sensing platform used for molecular detection. **b** The plasmonic spectral peak of NPs as a function of molecular interaction with NPs, i.e., antibody and antigen [123].

as detailed by Kim et al. [220], effectively enhanced the platform's LoD.

In another exceptional techniques for sensing, Nasrin et al. introduced a new dual-mode detection platform for recombinant of CHIKV E1 protein using NPs. The system integrated both fluorescence and electrochemical signals for detection [221]. This method included immobilizing NPs with methylene blue (MB) inside liposomes, and after adding CHIKV, the sandwich structure was magnetically isolated using antibodies and modified Fe_3O_4 NPs. By releasing the nanoconjugates and monitoring the fluorescence and electrochemical signals, CHIKV was detected at a low concentration, with a LoD of 32 fg mL^{-1}. Such devices explore changes in plasmonic resonance peaks due to the adsorption of specific molecules or biomarkers (Fig. 9). Importantly, this biosensor obtains a selective LoD of 100 $pg\ mL^{-1}$, showing exceptional potential for affordable, portable diagnostics across critical diseases.

Challenges and Limitations

Stability

The stability of plasmonic nanoparticles (NPs) is crucial for their effective utilization in various sensing applications, as their high surface-to-volume ratio makes them prone to aggregation, leading to a loss of their unique properties. Researchers employ surface modification techniques, such as the use of stabilizing agents, to prevent aggregation and enhance the potential of these NPs in fields like nanomedicine and catalysis. In the realm of molecular diagnostics, plasmonic NPs have been extensively studied for LSPR colorimetric assays [207]; however, the risk of NP aggregation due to non-target factors like ionic strength, pH, solvent composition, and temperature can result in false-negative or false-positive outcomes. Strategies to mitigate aggregation include exploiting the selectivity of aggregation induced by specific factors, such as mercury ions. Additionally, techniques like laser ablation are employed to avoid aggregation during NP synthesis, providing NPs with a negative zeta potential that enhances their stability even at room temperatures. For instance, TiN NPs synthesized through laser ablation in colloids have shown promise for long-term colloidal stability due to their negative charge, contributing to extended electrostatic stabilization of the solutions [222].

Reproducibility

The reproducibility of NPs poses a huge challenge in optical sensing applications. The synthesis of NPs in suspension includes complex chemical reactions in thermodynamically and kinetically controlled conditions, and small variations in reaction conditions can lead to differences in shape, size, as well as compositions of the NPs, exploiting their characteristics and behavior. Consequently, NPs' high surface area can result in agglomeration and sedimentation, further impacting their reproducibility [223]. Diverse characterization techniques, such as SEM, TEM, and DLS, could yield slightly different outcomes, contributing to variability in reported properties [224]. On large-scale production, providing consistent quality and reproducibility across huge batches is challenging due to manufacturing processes, fluctuations in raw materials, or equipment. Additionally, the surface chemistry and properties of NPs could be sensitive to environmental conditions and interactions with other molecules, enabling to variations in their performance. Over time, NPs may also exhibit changes in size, shape, or aggregation, adding to the complexity of achieving reproducible results. Fortunately, achieving this goal is entirely feasible and within reach. Addressing these challenges demands standardized protocols, careful experimental design, and thorough characterization to ensure reliable and reproducible NP synthesis. Evaluating these several interfaces ensures the advancement of predictive relations between structure and activity, determined by nanomaterial features like shape, size, roughness, surface chemistry, as well as surface coatings. This type of knowledge is fruitful regarding safe use of nanomaterials. Further, integrated efforts and open data sharing are the key components among researchers, can support validation, and establish strong guidelines for NP production and characterization, leading to broad reproducibility in this dynamic field [225].

Nanomaterials' Effects on Ecosystem

The broad range of use of NPs across multiple applications has alarmed about their adverse effects on the environment, and living organisms, including humans. A plethora of research has shown that prolonged exposure to these NPs may exhibit to both short and long-term toxicity [226–228]. Even in non-toxic form, Ag NPs can be harmful to humans, damaging cell membranes, mitochondria, and DNA, resulting in structural malfunctions and apoptosis [229, 230]. Furthermore, inhalation of NPs can lead to their deposition in the nasopharyngeal vein, providing a pathway for them to reach the cerebellum via olfactory nerves. Because of their small size, these NPs can penetrate the blood-brain barrier and result in neurotoxicity and dopamine depletion in brain cells, potentially affecting brain physiology and function [231]. These findings show the importance of understanding and addressing the potential risks attributed to the use of NPs in various applications.

Quantification

While the LSPR sensor design has advanced significantly, the practical application of SERS detection in areas requiring high accuracy, like sensing and medical diagnosis, remains limited due to the huge challenge of quantification [232]. The SERS offers remarkable signal enhancement, enabling single-molecule-level detection, it faces limitations related to specificity and reliability due to the variability of enhancement factors (EF_{SERS}) for different analytes and NPs. Particularly at ultra-low analyte concentrations ($< 10^{-7} molL^{-1}$), the probability of achieving significant SERS enhancement is low, leading to temporal fluctuations in intensity and spectral position, known as 'blinking', which poses challenges for molecular recognition [233]. Researchers have proposed mechanisms such as adsorption, molecular diffusion cycles, and changes in hotspot configuration as potential causes of these instabilities.

Future Directions

The future of LSPR biosensors for NTDs promises to revolutionize disease detection, diagnosis, and healthcare management. Researchers are focused on improving sensitivity and selectivity, aiming to identify specific biomarkers associated with tropical diseases accurately. Through nanostructure engineering and functionalization optimization, these advancements will enable precise and reliable disease diagnosis, even at low analyte concentrations. Additionally, the development of multiplexing capabilities allows for the simultaneous detection of multiple disease indicators in a single sample, expediting diagnosis and identifying co-infections prevalent in tropical regions.

The future of LSPR biosensors also entails the creation of field-deployable and robust designs, essential for regions with limited access to modern laboratory facilities. Portable, user-friendly point-of-care diagnostic devices will bring diagnostics closer to patients, particularly in resource-limited tropical areas, enabling quicker intervention and alleviating the burden on healthcare infrastructure. Furthermore, the affordability and accessibility of LSPR biosensors will facilitate large-scale disease monitoring and surveillance in tropical settings, empowering public health officials to implement targeted interventions effectively.

Integration with emerging technologies, such as microfluidics, machine learning algorithms, and smartphone connectivity, is anticipated to enhance biosensor performance, streamline data processing, and enable remote monitoring capabilities. Collaborative research efforts and international partnerships are essential for accelerating progress in this field, enabling transformative solutions to combat tropical diseases and improve global health outcomes. Overall, the future of LSPR biosensors for tropical illnesses aims to enhance accessibility, efficiency, and impact in the fight against infectious diseases prevalent in tropical regions, ultimately benefiting vulnerable populations.

Conclusion

In conclusion, this study underscores the pivotal role of metallic-based LSPR sensors in tropical disease detection, particularly in the context of Neglected Tropical Diseases (NTDs). These sensors offer high sensitivity and label-free detection, making them valuable tools for swift and accurate diagnosis. The integration of LSPR sensors with smartphone technology enhances point-of-care testing, providing cost-effective solutions that are particularly beneficial in regions with limited healthcare infrastructure.

Recent research has demonstrated the potential of metallic-based LSPR sensors in detecting a range of tropical illnesses, including Chagas disease, leishmaniasis, dengue fever, Zika virus infection, and sleeping sickness. These sensors have the capacity to significantly improve disease diagnosis and treatment. Furthermore, their adaptability to complex biological environments and the ability to provide rapid results make them promising contributors to global health initiatives aimed at combating NTDs.

Overall, metallic-based LSPR sensors demonstrate a transformative technology in the diagnosis and monitoring of tropical diseases. Their exceptional attributes, such as high sensitivity and portability, make them invaluable tools for enhancing healthcare accessibility and improving overall healthcare outcomes in regions burdened by tropical illnesses. The integration of LSPR sensors into healthcare systems holds the potential to drive earlier detection and more effective treatment, making a substantial impact on global efforts to combat NTDs.

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Data Availability The data is available on request from the corresponding author.

Declarations

Conflict of Interest The authors declare no competing interests.

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