Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in
Biomedical Engineering

Smart plasmonic hydrogels based on gold and silver nanoparticles for biosensing application

Yasamin Ziai[1], Chiara Rinoldi[1], Paweł Nakielski[1], Luciano De Sio[2,3] and Filippo Pierini[1]

Abstract

The importance of having a fast, accurate, and reusable track for detection has led to an increase investigation in the field of biosensing. Optical biosensing using plasmonic nanoparticles, such as gold and silver, introduces localized surface plasmon resonance (LSPR) sensors. LSPR biosensors are progressive in their sensing precision and detection limit. Also, the possibility to tune the sensing range by varying the size and shape of the particles has made them extremely useful. Hydrogels being hydrophilic 3D networks can be beneficial when used as matrices, because of a more efficient biorecognition. Stimuli-responsive hydrogels can be great candidates, as their response to a stimulus can increase recognition and detection. This article highlights recent advances in combining hydrogels as a matrix and plasmonic nanoparticles as sensing elements. The end capability and diversity of these novel biosensors in different applications in the near future are discussed.

Addresses

[1] Department of Biosystems and Soft Matter, Institute of Fundamental Technological Research, Polish Academy of Sciences, Warsaw 02-106, Poland

[2] Department of Medico-Surgical Sciences and Biotechnologies - Research Center for Biophotonics, Sapienza University of Rome Corso Della Repubblica 79, 04100 Latina, Italy

[3] CNR-Lab. Licryl, Institute NANOTEC, Arcavacata di Rende, 87036, Italy

Corresponding author: Pierini, Filippo (fpierini@ippt.pan.pl)

Current Opinion in Biomedical Engineering 2022, **24:**100413

This review comes from a themed issue on **Biomaterials: Intelligent Biomaterials**

Edited by **Seeram Ramakrishn**, **Ravin Narai**, **Himansu Sekhar Nanda**, **Masoud Mozafari** and **Gulden Camci-Unal**

Received 30 May 2022, revised 27 July 2022, accepted 24 August 2022

Available online xxx

https://doi.org/10.1016/j.cobme.2022.100413

Keywords

Smart materials, Plasmonic hydrogel, Biosensing.

Introduction

Healthcare is considered one of the most crucial issues challenging science and technology [1]. Having simple, easy-to-use diagnostic devices for the wide range of biologically significant analytes is essential for any further disease prevention and treatment [2,3]. Improving healthcare is essential in various fields, such as hygiene, drug development, food, environment, forensic, medicine, and clinical diagnoses [4]. Considering the growing release of toxic materials generated and released each year, an early detection of these materials used in all the aforementioned fields is of absolute importance, in order to prompt action to be guaranteed [5]. Biosensors were introduced in the 1960s by Clark and Lyons to meet these requirements. These devices have been developed for glucose determination and named enzyme electrodes [6].

Biosensors are defined as platforms that use specific reactions to detect the effect of electrical, thermal, or optical signals on a medium's chemical, physical, or biological characteristics [5]. Biosensors are usually based on receptors and transducers. Bio-components interact with the target analyte through the receptor; the transducer transfers the result of the reaction into a measurable signal. Bio-components, also known as bioreceptors, may include enzymes, antibodies, nucleic acids, and cells. Depending on the different types of transducers, biosensors can be electrochemical, electrical, optical (absorbance, fluorescence, and chemiluminescence), piezoelectric (also known as mass-sensitive), and thermometric [5,7].

Plasmonic biosensors, as a subgroup of optical biosensors, have been recently exploited due to the possibility of controlling light properties at a nanometric scale [8]. The plasmonic activity of these biosensors is commonly described as the resonant coupling of electromagnetic waves, resulting from the oscillations of free electrons in metals. This physical phenomenon makes it possible to constrain the light within significantly smaller wavelengths than the incident light [9]. Plasmonic biosensors are mainly categorized into two classes of detecting platforms. The first class uses thin metallic films, while the second is based on individual inorganic plasmon resonant nanostructures. In surface plasmon resonance (SPR) biosensors, the incident light is coupled with a thin metallic layer where specific conditions, such as polarization, angle, and wavelength should be met [10]. Following the advancements in nanotechnology, metal nanoparticles (NPs) have been widely explored. In the case of biosensors, these transducers confine the light within a localized surface, creating what are known as localized surface plasmon resonance (LSPR) biosensors, which allow for a more miniaturized sensing procedure [11]. LSPR-based biosensors differ in NP size, shape, and composition. The versatility of these systems makes them suitable for biological sensor devices since the wavelength can be tuned to not overlap the absorbing spectral features of the biological chromophores, thus resulting in more precise sensing and offering the possibility of multiplex detection [11]. The typical wavelength of LSPR for most noble metals lies in the range of visible to near-infrared regions. This range can vary from shorter to longer wavelengths with low (spherical) and high (rods and prisms) aspect ratios [8]. Nowadays, due to the high efficiency of the LSPR approach, the sensitivity scale of biosensing has been reduced to nano-scales, resulting in more accurate and precise biosensors [12].

Over the years, various types of LSPR biosensors based on polymer substrates have been developed for different applications. Within this framework, gold nanodots have been introduced into polymer films and used to detect biomolecules such as biotin [13]. On the other hand, a plasmonic bioink based on an organosiloxane polymer was also prepared for point-of-care (POC) biosensing [14]. Hydrogels, being a class hydrophilic of 3D-structured biomaterials, have also been used as substrates for plasmonic particles. The unique properties of hydrogels are primarily due to their high water content, which results in their soft and rubbery consistency. Their ability to swell with considerable water uptake makes their structure more similar to living tissues and mimics the extracellular matrix (ECM), which plays a vital role in tissue and organs morphogenesis, as well as cell differentiation and proliferation [15,16]. For these reasons, hydrogel has been considered beneficial in many industrial, environmental, and biomedical fields [17], including electronics [18], tissue engineering [19], drug delivery [20], and biosensing [21].

This report focuses on reviewing the recent developments in smart plasmonic biosensors in the form of hydrogel platforms. Challenges, development, and approaches for assisting in the development of these types of biosensors are the main topics of this article.

Challenges

Currently, array-based LSPR biosensors are the most commonly used in the case of detection of low amounts of molecules, where there is a need to push through the limit of detection of the system and push high throughput capabilities to the limit [22,23]. Even though LSPR-based biosensors have the advantage of detecting several molecules (i.e., number of interactions), their resulting analytical performance is very similar compared to other high-resolution SPR setups [24]. In detection systems based on conventional 2D methods, low concentration targets were difficult to detect because the exposure to continuous flow results in a limited interaction time with the sensing surface. The drawbacks of these methods can be overcome by using hydrogels, thus exploiting their ability to accommodate a large amount of water without their structure dissolving and their similarity to body tissues. From the sensing standpoint, the biorecognition of the analyte may take place more efficiently and easily when the matrix is in a hydrogel form. In addition, the sensing precision of LSPR-based sensors might be improved as the thin hydrogel can also act as a dielectric optical waveguide [25,26]. Overall, soft materials such as hydrogels can modify sensing properties when used as substrates. Due to their mechanical and structural properties, they offer more sensitive, selective, efficient, and fast sensing capabilities.

Smart biosensors based on plasmonic hydrogels

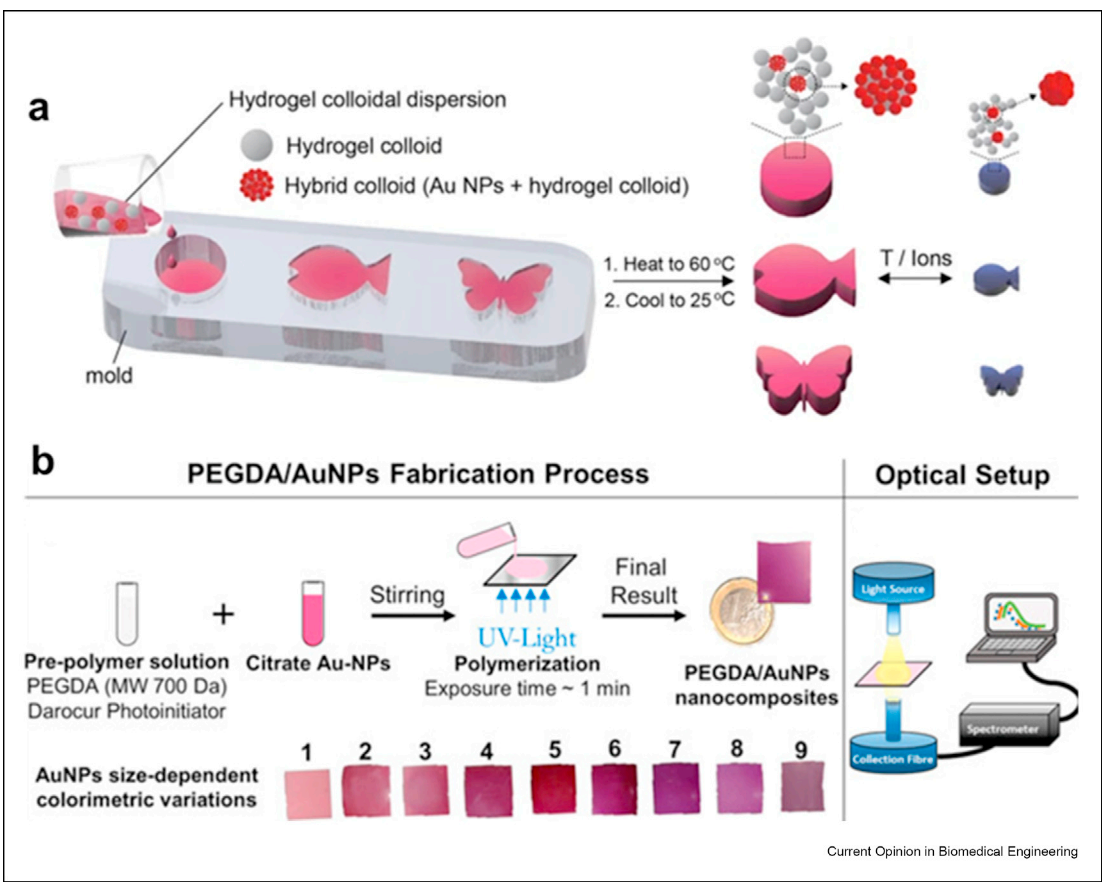
Two main transduction mechanisms have been introduced in LSPR-based biosensing platforms, including NP aggregation and the change in the refractive index of the system [27]. The first strategy provides the functionalization of plasmonic particles with binding molecules, resulting in a colorimetric variation. The indicator of this variation can be visualized in the LSPR red-shift in the absorbance spectrum, which can be detected by the naked eye. However, some limitations related to the non-specific aggregation have been reported, restricting the application of these platforms to laboratory analysis [28]. The second mechanism provides the immobilization of plasmonic particles on the surface of the substrate, making them refractive index optical sensors [27].

In order to develop LSPR-based optical enzyme biosensors, researchers have focused their attention on stimuli-responsive hydrogels [29]. The physical changes in stimuli-responsive hydrogels in response to marked variations in environmental conditions have been reported previously [30,31]. Stimuli-responsive hydrogels are water-swollen, cross-linked networks that show a reversible change in their physical characteristics in response to specific stimuli. Based on these features, the constituent hydrogels of the stimuli-responsive network can incorporate molecular recognition elements (i.e., enzymes). When the recognition elements react with specific chemical substances, the monomer units bearing the recognition elements undergo a change in either solubility or charge state. A solubility alteration can cause the swelling or shrinking of the hydrogel network. Alternatively, changes in the charge state may result in altered interactions between the charged groups and a variation in the electrolyte concentration in the hydrogel. In both cases, the described processes result in changes in the hydrogel volume. Considering these outstanding advantages, several research groups have used stimuli-responsive hydrogels to fabricate biosensors and chemical sensors for medical and environmental applications [32]. Within this framework, scientists have recognized the suitability of these materials for the production of enzyme biosensors and their further exploitation in LSPR-based biosensor development.

Gold nanoparticle-based sensors

LSPR-based biosensors, which function using noble metal nanomaterials, such as gold and silver, have been expected to achieve the highly sensitive detection of target molecules in medical applications. Gold nanoparticles (AuNPs) are widely used in sensing applications due to the visible shift in their absorption peak and high sensitivity. Moreover, AuNPs are chemically stable and have been investigated more through the years and have thus been improved in terms of surface chemistry and biocompatibility [33]. A sensor concept was demonstrated in the work of Muri et al. where they embedded AuNPs in the 3D hydrogel network of hydrogel fibers. This immobilization of the AuNPs makes the LSPR signal stronger while reducing the analyte binding to plasmonic surfaces [34]. Inspired by animals such as squid, butterflies, and chameleons, biomimetic hydrogel systems have been recently devised to alter their internal nanostructure, undergoing an optical transformation based on changes in their environment. A dual-responsive three-dimensional plasmonic hydrogel platform has been fabricated to indicate volume and color change in an aqueous surrounding. AuNPs embedded in the hydrogel colloid are responsible for the color changes caused by temperature and ion variation in the system. The fabrication process can be seen in Figure 1a, where hydrogel changes according to the temperature are also shown. The volume change as a result of temperature stimuli was best shown here [35]. A polyol-based hydrogel has been fabricated by Randriantsilefisoa et al. while AuNPs are entrapped in the system to offer a stable material to sense the influenza A virus (IAV) and indicate a color change in this medium. Bindings between the IAV and AuNPs

Figure 1



The fabrication process of hydrogel-based biosensors with AuNPs. (**a**) A schematic showing the process and its responses to temperature and ionic changes [35]. (**b**) Platform polymerization under UV light and the colorimetric variation in the platform depending on the growth step are also shown [37].

result in an aggregation of the particles, which produce an SPR-induced shift in the absorption spectra, producing a visible color change from red to blue. The reversibility of this phenomenon makes it a good detector for biomolecule quantification [36].

Moreover, an optical 3D biosensor based on poly-(ethylene glycol) diacrylate (PEGDA) hydrogel with AuNPs has been fabricated and optimized. These hydrogel patches, having spherical AuNPs, are physically retained in the network and show great stability as well as sensing capability. By optimizing the NPs size and shape, the order of detection indicates that it is a perfect candidate for small molecule (e.g., biotin) detection and can be used in wearable sensors. Figure 1b shows the polymerization process of the system in between coverslips. UV light has been used here to perform the crosslinking, and NPs with different sizes varying from 20 nm to 70 nm were used [37]. Label-free detection of biomolecules can also benefit from plasmonic hydrogels. The use of the hydrogel matrix provides an environment that resembles the perfect matrix for biomolecular interactions. The porous network with high water content improves the performance of biosensors by capturing more analyte molecules. Recently, a stimuli-responsive hydrogel based on oligo (ethylene glycol) grafted with thermo-responsive polyisocyanates was developed. The gold-coated surface of the sensor is linked to the glycol group to demonstrate the LSPR and has been used as an affinity binding system for the biosensing of biotin [38]. Proteins can also be detected using the same platforms with an LSPR-sensing method. Culver et al. have developed a biosensor to detect proteins, using poly(N-isopropylacrylamide-co-methacrylic acid) (PNM) hydrogels embedded with gold nanoshells. Hydrogels are synthesized on the surface of gold nanoshells, as they can detect changes in the concentration of lysozyme and lactoferrin — the protein biomarkers of chronic dry eye. PNM/gold nanoshells are a suitable material in this case, as the system shows a largely increased refractive index, and a strong red-shift when in contact with human tears [39]. Glucose monitoring apparatus has also been prepared using hydrogel fibers based on acrylamide-based materials, where gold AuNPs are immobilized. Volume expansion which happens as a result of the presence of glucose molecules can modulate the LSPR effect of the hydrogel fibers, allowing quantitative measurements [40].

Sensing environmental molecules, such as arsenic — crucial in the geochemical and anthropogenic fields — can be achieved by using this technique. Poly(N-isopropylacrylamide) (PNIPAAm)-based hydrogel coated on an AuNP surface can provide an LSPR sensing platform for the real-time detection of arsenic. However, this platform offers a wide range of detection potential with a simple change in the size and shape of plasmonic particles and the concentration of the monomer [41].

Silver nanoparticle-based biosensors

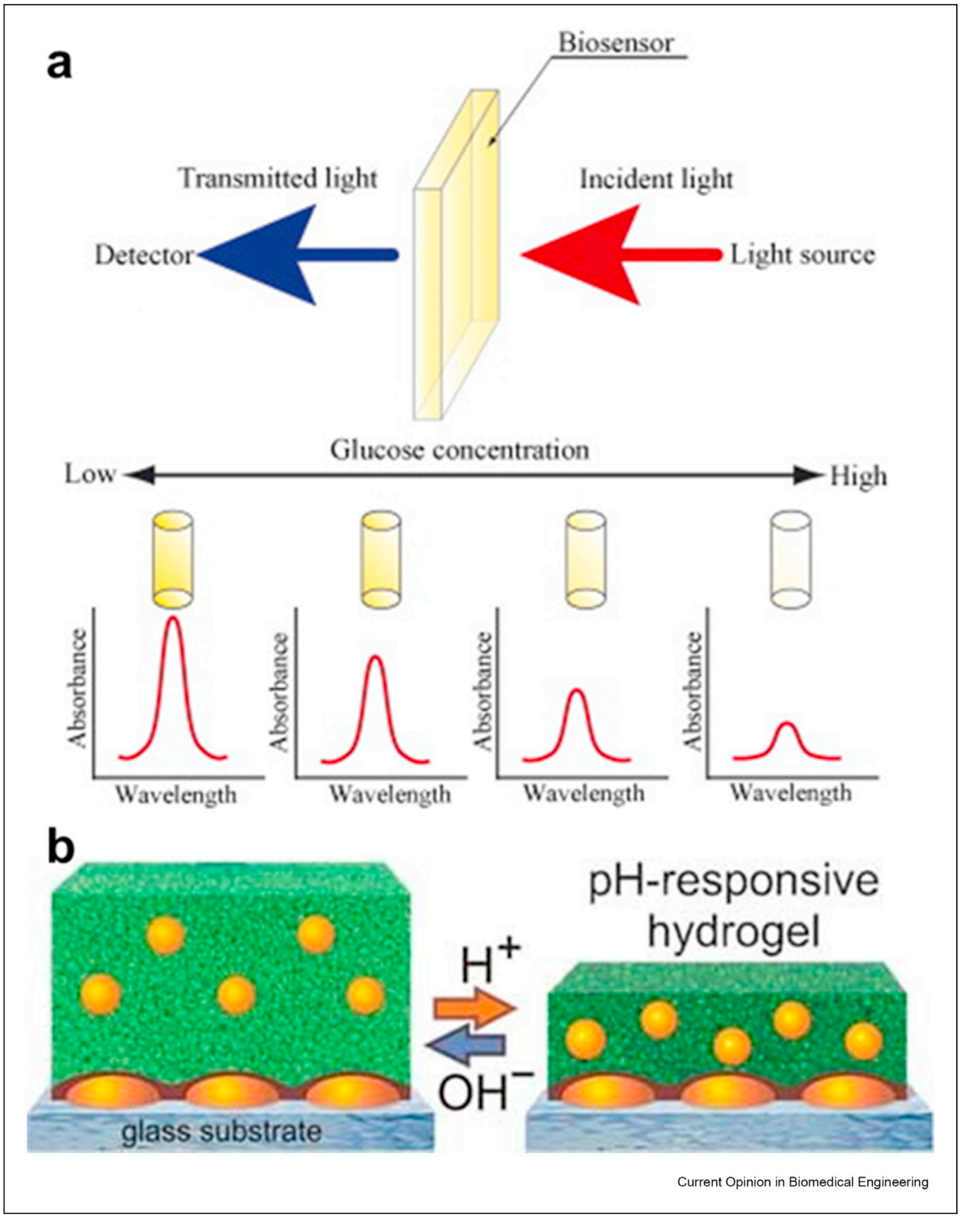
Among metallic NPs exhibiting LSPRs, although AuNPs have been studied in depth, silver NPs (AgNPs) are particularly efficient for sensing purposes [42]. Studies have shown that AgNPs demonstrate shifts in the LSPR band that are five times stronger when they are in contact with specific molecules, compared to AuNPs [43].

Hydrogen peroxide detection is of vital importance because the presence of the substance can be considered an environmental, industrial, or even clinical hazard. Filippo et al. have developed a biosensor that determines the presence of hydrogen peroxide in rainwater, which has a simplified, low-cost fabrication process, and, most importantly, is reusable [44]. This sensor is made of PVA due to its wide range of potential applications in the optical, pharmaceutical, medical, and membrane fields, as well as benefits from AgNPs for LSPR-sensing method. The strong shift in the absorption spectra and the color changing of the platform prove the LSPR sensing of the hydrogel.

Glucose is one of the most important biomolecules that requires precise detection to prevent and treat the complications associated with diabetes. Silver NPs have been widely used in this specific molecule detection. Endo et al. worked on a stimuli-responsive acrylamide-based hydrogel with polyvinylpyrrolidone (PVP) covered with silver NPs to entrap glucose molecules [45]. Stimuli-responsive hydrogels contain molecular recognition elements — such as enzymes — that specifically react with the analyte. This recognition event causes the stimuli-responsive hydrogels to swell due to an increased osmotic pressure. The swelling of stimuli-responsive hydrogels increases the average internal distance between one noble metal particle and another, thus reducing the LSPR absorbance strength [45]. Figure 2a shows the principles of the sensing platform with the use of different glucose solution concentrations. Changes in the absorption peak define the effect of surroundings on the sensing precision. Images taken of differences in the color strengths shows that the variations in AgNPs concentrations could be observed with the naked eye. Hence, AgNPs concentrations were found to affect the optical characteristics of the LSPR-based optical enzyme biosensor.

A novel glucose sensor was fabricated by Tokarev et al. as a combination of a pH-responsive hydrogel incorporated with AgNPs for two critical applications: the analysis of biomolecules (biosensing) and the probing (monitoring) of the local properties of biomaterials. Figure 2b shows the schematic of this construct under pH variation, and changes in the volume of the hydrogel can be observed. LSPR effects in noble metal NPs are observed through

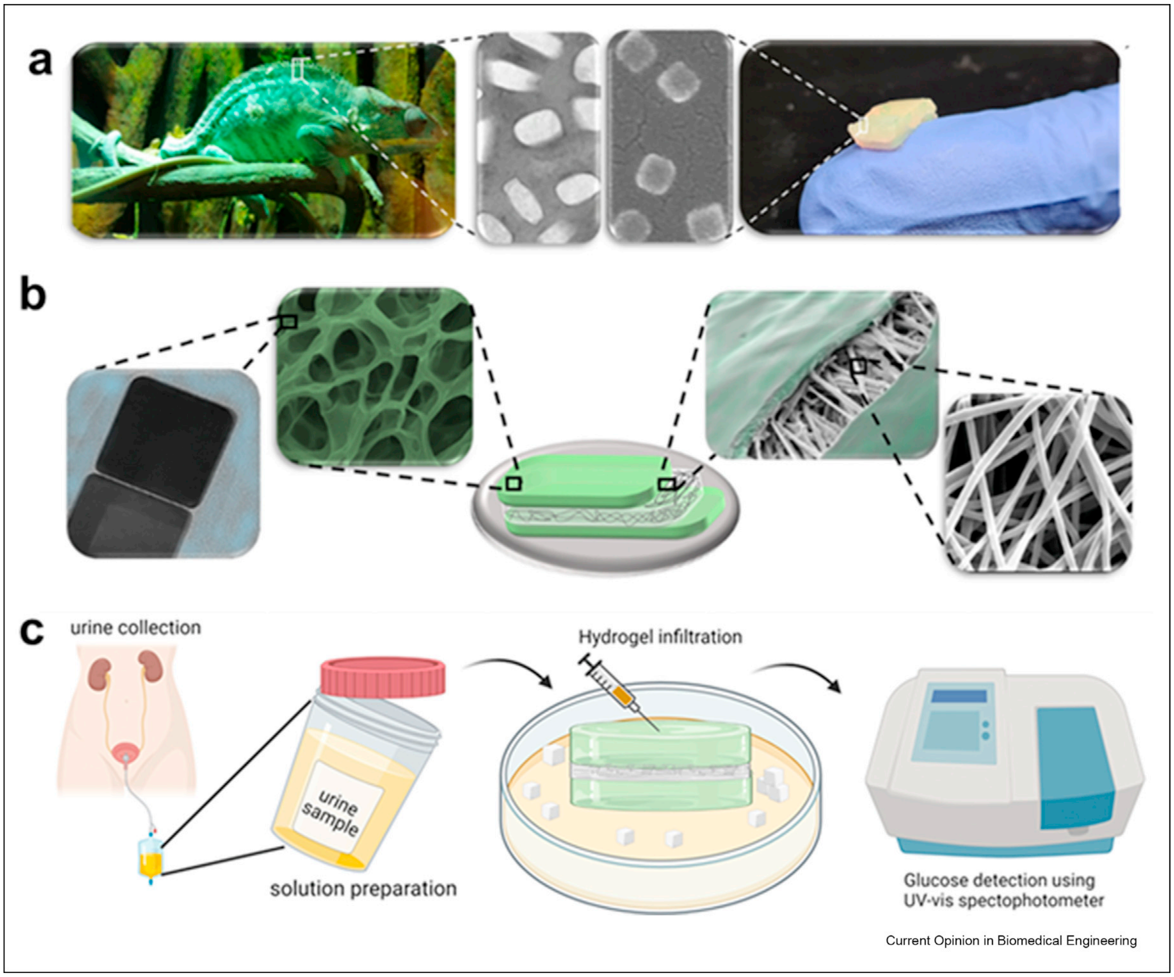
Figure 2



Stimuli-responsive hydrogel embedded with AgNPs. (**a**) Schematic illustration of detection principle of LSPR-based optical enzyme biosensor [45]. (**b**) Schematic of volume change in the construct under pH variation [46].

color variations by the naked eye or in a visible light spectrum that reveals characteristic absorbance bands. LSPR spectra are also sensitive to variations in the immediate particle environment. In particular, changes in the refractive index of the environment in the close vicinity to particle surface or in the interparticle plasmon coupling result in an alteration of the spectrum [46]. Recently, a photo-thermal responsive polymer combined with AgNPs has been investigated as a multifunctional platform to detect glucose level in urine. Ziai et al. used a poly(N-isopropylacrylamide) (PNIPAAm)-based hydrogel matrix embedded with Ag nanocubes, inspired by the unique features of chameleon skin that changes its color as a result of the light—matter interactions in the skin layers. The inspiration and the similarities between the structure of NPs can be seen in Figure 3a. Hydrogel layers were made with a layer of electrospun nanofibers. The image of the construct can be seen in Figure 3b, where each layer is shown separately, with an image from the intersection, verifying the layer-by-layer construction. Fast photothermal responsiveness and significant red-shift in the LSPR absorbance peak in the presence of different glucose concentrations are indicators of efficient sensing

Figure 3



Chameleon-inspired platform, based on AgNPs. (**a**) Inspiration from the layers of chameleon skin to choose the silver nanocubes as the plasmonic particle. (**b**) Construction based on a layer-by-layer composite, with two layers of plasmonic hydrogel and one layer of electrospun nanofibers in between them. (**c**) Application of the biosensor as a glucose detector, using urine as the body fluid [21].

features of the platform [21]. This platform was used as a biosensor to detect glucose in the urine of healthy and diabetic people, where sample solutions were infiltrated into the platform, and the absorbance peak was determined via UV–Vis (Figure 3c).

Future perspectives and conclusion

Studies on plasmonic hydrogels have upgraded the biosensing field. As a result, clinical and therapeutic detection and medication are expected to be achieved quickly, easily, and efficiently within a short time. Plasmonic particles are responsible for changes in relevant SPR frequencies when in contact with the target analyte. These changes are significantly dependent on the size and shape of NPs, thus making it possible to tune the properties to meet the requirements for different applications. The greater interest in LSPR-based biosensors compared to regular SPR sensors is mainly due to their unique features, which allow for label-free and real-time biomolecular analysis with possible detection of biomolecular interactions (antigen–antibody interaction, DNA hybridization, etc.) at low concentrations.

In addition, the simple detection mechanism of optical-based biosensors makes it possible to be integrated with different sensing platforms for lab-on-a-chip applications.

On the other hand, as 3D nanostructured materials with a considerable amount of water within their structure, hydrogels are powerful platforms for biosensor fabrication. The sensor's performance is determined mainly by the contact between the sensing receptor and the analyte. The structure of hydrogel provides an accessible environment for target molecules to be in contact with the sensing receptor. These 3D matrixes indicate high permeability for small molecules, metabolites, oxygen, and water-soluble components, making them essential for body fluid biosensors. Considering the benefits of both materials, plasmonic hydrogels are among the best candidates for biosensing applications.

Alongside the many advantages of hydrogel materials, there are aspects of the hydrogel platform which can be further improved. The use of hydrogels as 3D networks affords a greater affinity with the analyte, hence, more label-free detection possibilities. The use of stimuli-responsive materials can help us even more to have more opportunities to detect label-free biomolecules. In this way, both fabrication and detection are more accessible, while the applicability of the biosensor can be improved. Also, the use of stimuli-responsive materials will enhance the efficiency and precision of the sensor in the case of dual-responsivity, in which – in this case – there is a possibility to detect more than one target. Additionally, having a re-useable system can enhance its applicability and usability in real life. As the LSPR shift in the absorption of the plasmonic material varies with the shape and size of NPs, there is always room for improvement in terms of sensing range. Nowadays, NPs are synthesized into various shapes, such as cubes, rods, stars, wires, prisms, etc. These shapes or even different sizes of identical particles can be used in the same platform to obtain multiple sensing windows for the same material, making it more applicable for sensing molecules. Furthermore, different NPs are being prepared using both silver and gold, combined in a core–shell structure. These NPs can improve the limit of detection and the efficiency of the sensing platform compared to using single particles.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This study was supported by the First TEAM grant number POIR.04.04.00-00-5ED7/18-00, which is carried out within the framework of the First TEAM program of the Foundation for Polish Science (FNP), co-financed by the European Union under the European Regional Development Fund. The authors are also grateful for the support of this work by the National Agency for Academic Exchange (NAWA) grant no. PPI/APM/2018/1/00045/U/001. Chiara Rinoldi, Paweł Nakielski, and Filippo Pierini acknowledge the financial support from the Polish Ministry of Science and Higher Education through scholarships for outstanding young scientists. Chiara Rinoldi was partially supported by the Foundation for Polish Science (FNP).

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Turner Anthony PF: **Biosensors: sense and sensibility**. *Chem Soc Rev* 2013, **42**:3184–3196.

2. Eggins Brian R: *Biosensors: an introduction*. Springer-Verlag; 2013.

3. Kissinger Peter T: **Biosensors—a perspective**. *Biosens Bioelectron* 2005, **20**:2512–2516.

4. Rastislav Monosik, Stredansky Miroslav, Sturdik Ernest: **Biosensors—classification, characterization and new trends**. *Acta Chim Slov* 2012, **5**:109–120.

5. Alhadrami Hani A: **Biosensors: classifications, medical applications, and future prospective**. *Biotechnol Appl Biochem* 2018, **65**:497–508.

6. Scheller Frieder W, *et al.*: **Second generation biosensors**. *Biosens Bioelectron* 1991, **6**:245–253.

7. Mejía-Salazar JR, Oliveira Jr Osvaldo N: **Plasmonic biosensing: focus review**. *Chem Rev* 2018, **118**:10617–10625.

8. Hill Ryan T: **Plasmonic biosensors**. *Wiley Interdiscip Rev: Nanomed Nanobiotechnol* 2015, **7**:152–168.

9. Hardeep Kaur, Bhosale Aakash, Shrivastav Suraj: **Biosensors: classification, fundamental characterization and new trends: a review**. *Int J Health Sci Res* 2018, **8**:315–333.

10. Špačková Barbora, *et al.*: **Optical biosensors based on plasmonic nanostructures: a review**. *Proc IEEE* 2016, **104**: 2380–2408.

11. Soler, Maria, Huertas Cesar S, Lechuga Laura M: **Label-free plasmonic biosensors for point-of-care diagnostics: a review**. *Exp Rev Mol Diagnos* 2019, **19**:71–81.

12. Sannomiya Takumi, Janos Vörös: **Single plasmonic nanoparticles for biosensing**. *Trends Biotechnol* 2011, **29**: 343–351.

13. Vazquez-Mena Oscar, *et al.*: **High-resolution resistless nanopatterning on polymer and flexible substrates for plasmonic biosensing using stencil masks**. *ACS nano* 2012, **6**: 5474–5481.

14. * Yin, Ze, *et al.*: **Ultrastable plasmonic bioink for printable point-of-care biosensors**. *ACS Appl Mater Interfaces* 2020, **12**: 35977–35985.

In this paper a point-of-care, printable biosensor platform using Gold nanorods and organosiloxane polymer was synthesized and antibodies were encapsulated in the platform. This biosensor shows excellent thermal and biological properties, while the biosensing can take place in harsh conditions such as high temperature and ultrasonic agitation. The importance of this study in the present paper is the use of gold nanoparticles as a plasmonic material for biosensing applications and different platforms which can embed the particles.

15. * Rinoldi, Chiara, *et al.*: **Three-dimensional printable conductive semi-interpenetrating polymer network hydrogel for neural tissue applications**. *Biomacromolecules* 2021, **22**: 3084–3098.

This research was based on synthesizing the semi-IPN hydrogel network based on poly(N-isopropylacrylamide), incorporated with intrinsically conducting polymers. This electrically conductive platform can be used as a UV-curable ink for printing applications. Our paper noted hydrogels as a candidate platform for biosensing, and acrylamide-based hydrogels are one of the most commonly-used platforms for biosensing.

16. Yang Canhui, Suo Zhigang: **Hydrogel ionotronics**. *Nat Rev Mater* 2018, **3**:125–142.

17. Pawłowska Sylwia, *et al.*: **Ultraviolet light-assisted electrospinning of core–shell fully cross-linked P (NIPAAm-co-NIPMAAm) hydrogel-based nanofibers for thermally induced drug delivery self-regulation**. *Advanced Materials Interfaces* 2020, **7**:2000247.

18. Pardo-Yissar Vered, *et al.*: **Gold nanoparticle/hydrogel composites with solvent-switchable electronic properties**. *Adv Mater* 2001, **13**:1320–1323.

19. ** Nezhad-Mokhtari, Parinaz, Akrami-Hasan-Kohal Mohammad, Ghorbani Marjan: **An injectable chitosan-based hydrogel scaffold containing gold nanoparticles for tissue engineering applications**. *Int J Biol Macromol* 2020, **154**:198–205.

The focus of this research was to synthesize and characterize an injectable hydrogel that contains gold nanoparticles. The hydrogel is based on aldehyde-cellulose and collagen for tissue engineering purposes. The study of this paper helped us to understand more about the hydrogels embedded with plasmonic particles, their synthesis, and morphological characterization. Also, biodegradability and cell viability tests show us the potential of using this medium for bio-applications.

20. * Nakielski, Paweł, *et al.*: **Multifunctional platform based on electrospun nanofibers and plasmonic hydrogel: a smart nanostructured pillow for near-infrared light-driven biomedical applications**. *ACS Appl Mater Interfaces* 2020, **12**: 54328–54342.
A bioinspired drug delivery system was fabricated in this research, based on a composite of hydrogels embedded with gold nanoparticles and electrospun fibers. Using an acrylamide-based hydrogel with plasmonic nanoparticles shows fast photo-thermal responsivity. This nanostructure accelerates the drug release with the effect of localized temperature rise. This article helps us to understand the hydrogel performance with the presence of plasmonic nanoparticles.

21. ** Ziai, Yasamin, *et al.*: **Chameleon-inspired multifunctional plasmonic nanoplatforms for biosensing applications**. *NPG Asia Mater* 2022, **14**:1–17.
Inspired by the features of the chameleon skin, a biosensor was designed in this research article using silver nanocubes. Acrylamide-based hydrogels were used here with the support of a layer of nanofibrous mat. The glucose present in the urine can be detected using this platform with antibacterial properties. This paper is the main source to study the biosensors with plasmonic hydrogels.

22. Yu Ting, Xianyu Yunlei: **Array-Based biosensors for bacteria detection: from the perspective of recognition**. *Small* 2021, **17**: 2006230.

23. Mesch Martin, *et al.*: **Functionalized hydrogel on plasmonic nanoantennas for noninvasive glucose sensing**. *ACS Photonics* 2015, **2.4**:475–480.

24. Estevez, M-Carmen, *et al.*: **Trends and challenges of refractometric nanoplasmonic biosensors: a review**. *Anal Chim Acta* 2014, **806**:55–73.

25. Toma, Mana, *et al.*: **Active control of SPR by thermoresponsive hydrogels for biosensor applications**. *J Phys Chem C* 2013, **117**:11705–11712.

26. Andersson, Olof, *et al.*: **Gradient hydrogel matrix for microarray and biosensor applications: an imaging SPR study**. *Biomacromolecules* 2009, **10**:142–148.

27. Zhang, Zhiyang, *et al.*: **Plasmonic colorimetric sensors based on etching and growth of noble metal nanoparticles: strategies and applications**. *Biosens Bioelectron* 2018, **114**:52–65.

28. Sun, Jingwei, *et al.*: **Colorimetric sensor array based on gold nanoparticles: design principles and recent advances**. *TrAC, Trends Anal Chem* 2020, **122**:115754.

29. Diehl Fiona, *et al.*: **Plasmonic nanomaterials with responsive polymer hydrogels for sensing and actuation**. *Chem Soc Rev* 2022.

30. Koetting, Michael C, *et al.*: **Stimulus-responsive hydrogels: theory, modern advances, and applications**. *Mater Sci Eng R Rep* 2015, **93**:1–49.

31. Ryssy Joonas, *et al.*: **DNA-Engineered hydrogels with light-adaptive plasmonic responses**. *Adv Funct Mater* 2022: 2201249.

32. Sood, Nikhil, *et al.*: **Stimuli-responsive hydrogels in drug delivery and tissue engineering**. *Drug Deliv* 2016, **23**:748–770.

33. Lee, Jin-Ho, *et al.*: **Application of gold nanoparticle to plasmonic biosensors**. *Int J Mol Sci* 2018, **19**:2021.

34. Muri, Harald Ian, Andon Bano, Dag Roar Hjelme: **A single-point, multiparameter, fiber optic sensor based on a combination of interferometry and LSPR**. *J Lightwave Technol* 2018, **36**: 1159–1167.

35. Song, Eun Ji, Chul Cho Eun: **Dual-responsive and multi-functional plasmonic hydrogel valves and biomimetic architectures formed with hydrogel and gold nanocolloids**. *Sci Rep* 2016, **6**:1–10.

36. ** Randriantsilefisoa, Rotsiniaina, *et al.*: **Double trouble for viruses: a hydrogel nanocomposite catches the influenza virus while shrinking and changing color**. *Chem Commun* 2020, **56**: 3547–3550.
A hydrogel-based biosensor was presented in this paper, using gold nanoparticles. This sensor has a reversible double response, a color change, and also a change of volume. This sensor detects the influenza virus by changing the color from pink to blue by increasing the virus concentration. This research also is a very good example of the plasmonic hydrogels used for biosensing applications.

37. ** Miranda B, *et al.*: **A PEGDA hydrogel nanocomposite to improve gold nanoparticles stability for novel plasmonic sensing platforms**. *J Appl Phys* 2021, **129**:33101.
Using PEGDA and gold nanoparticles, a biosensor was fabricated and investigated. Biotin as a small molecule was used to be detected optically by this wearable biosensor. The importance of this paper, lies in the information on the effect of the size of the plasmonic particles on the sensing application, with the hydrogel medium.

38. ** Kotlarek, Daria, *et al.*: **Thin-film polyisocyanide-based hydrogels for affinity biosensors**. *J Phys Chem C* 2021, **125**: 12960–12967.
A new hydrogel platform in the shape of the thin film was fabricated and discussed in this paper. The polymeric hydrogel is based on polyisocyanide, attached to a surface plasmon resonance chip, and the sensing of biotin as a model was investigated through swelling. This paper will enlighten the horizon on the future perspectives of the biosensing platforms using plasmonic hydrogels in different shapes.

39. Culver, Heidi R, Marissa E, Wechsler, Nicholas A Peppas: **Label-free detection of tear biomarkers using hydrogel-coated gold nanoshells in a localized surface plasmon resonance-based biosensor**. *ACS Nano* 2018, **12**:9342–9354.

40. ** Guo, Jingjing, *et al.*: **Soft and plasmonic hydrogel optical probe for glucose monitoring**. *Nanophotonics* 2021, **10**: 3549–3558.

41. Liu, Chang, *et al.*: **A 3D localized surface plasmon resonance biosensor for the study of trivalent arsenic binding to the ArsA ATPase**. *Biosens Bioelectron* 2012, **38**:19–26.

42. Loiseau, Alexis, *et al.*: **Silver-based plasmonic nanoparticles for and their use in biosensing**. *Biosensors* 2019, **9**:78.

43. Lismont, Marjorie, Laurent Dreesen: **Comparative study of Ag and Au nanoparticles biosensors based on surface plasmon resonance phenomenon**. *Mater Sci Eng C* 2012, **32**: 1437–1442.

44. Filippo E, Serra A, Manno D: **Poly (vinyl alcohol) capped silver nanoparticles as localized surface plasmon resonance-based hydrogen peroxide sensor**. *Sensor Actuator B Chem* 2009, **138**: 625–630.

45. Endo, Tatsuro, *et al.*: **Stimuli-responsive hydrogel–silver nanoparticles composite for development of localized surface plasmon resonance-based optical biosensor**. *Anal Chim Acta* 2008, **611**:205–211.

46. Tokarev, Ihor, *et al.*: **Specific biochemical-to-optical signal transduction by responsive thin hydrogel films loaded with noble metal nanoparticles**. *Adv Mater* 2010, **22**:1412–1416.