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Magnetoresistance and magneto-plasmonic sensors for the detection of cancer biomarkers: A bibliometric analysis and recent advances

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ABSTRACT

The conventional approaches to diagnosing cancer are expensive, often involve exposure to radiation, and struggle to identify early-stage lung cancer. As a result, the five-year survival rate is significantly reduced. Fortunately, promising alternatives using magnetoresistance (MR) and magneto-plasmonic sensors have emerged for swiftly, accurately, and inexpensively detecting cancer in its initial phases. These sensor technologies offer numerous advantages over their counterparts, such as minimal background noise, immunity to environmental influences, compatibility with nanofabrication methods, ability to detect multiple substances simultaneously, straightforward integration, high specificity, distinctive identifying capabilities, real-time monitoring, stability, label-free detection, and remarkable sensitivity for detecting individual molecules. Nevertheless, since the use of these techniques for cancer biomarker detection is relatively new, it is essential to conduct a bibliometric analysis and review recent literature to offer guidance to both early-career and established researchers in this domain. Consequently, this study performs a scientometric evaluation of the literature related to cancer biomarker detection using MR and magneto-plasmonic methods. The objective is to pinpoint current preferred techniques and challenges by examining statistics such as publication numbers, authors, countries, journals, and research interests. Furthermore, the paper also presents the latest advancements in MR and magneto-plasmonic sensors for cancer biomarker detection, with a focus on the last decade. In addition, an overview of the ongoing research in the field of MR and magneto-plasmonic sensors for detecting cancer biomarkers is highlighted. Finally, a summary on the level of current research including the significant accomplishments, challenges, and outlooks of MR and magneto-plasmonic sensors for the detection of cancer biomarkers are highlighted.

1. Introduction

Cancer positions among the principal death causing agents globally, hindering the improvement of life expectancy [1–3]. In 2020, about 19.3 million new cancer cases (i.e. about 190 per every 100,000) and almost 10.0 million cancer deaths (nearly one in six deaths) were recorded [2]. Miserably, the cancer prevalence has been on the rise, projecting about 28.4 million cases by 2040, a 47% rise from 2020 [2,4]. WHO defines cancer as the rapid creation of abnormal cells that grow beyond their usual boundaries, and which can then invade adjoining parts of the body and spread to other organs (metastasis) and ultimately lead to death [5]. Fortunately, early identification of cancer is reported to result easier treatment/management, better chance of survival with less morbidity and cost effective treatment [5].

Conventionally, cancer is detected/diagnosed using imaging techniques such as computed tomography (CT), chest radiograph (CRG), mammography, magnetic resonance imaging (MRI), ultrasound, low-dose helical CT scan (or spiral CT scan), bone scans, positron emission

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tomography (PET), as well as a biopsy [6–12]. However, the reliance of these methods to the phenotypic properties of tumor prevents them from detecting at early stages [6,8,12]. This is in addition to the invasiveness (biopsy and then examining the tissue using cell fixation and morphology approaches to identify and detect cancer cells), expensive feature and the radiation effects associated with most of these techniques [7,13,14].

Fortunately, trace levels of biomarkers exist in the cancerous cells and by extension in the body fluid at the early stages of the cancer [6,8, 15–17]. The levels of these biomarkers associated with certain cancers can reflect cancer occurrence. Also, clinicians could be fed with relevant information enabling them to make successful treatment decisions to increase patient survival rate [18–21]. Thus, biomarkers in the body fluids such as serum or plasma, urine, saliva, sputum and tears; can provide a convenient, noninvasive, and inexpensive methods for cancer screening and diagnosis [6,22–25]. WHO has defined biomarker as any substance, structure, or process that can be measured in the body or its products and influences or predicts the incidence of outcome or disease [26]. Based on these, the detection for the biomarkers of cancer attracted significant attention. This could be reliably achieved by biosensors in a rapid, sensitive, specific, stable, cost effective and non-invasive manner [6,23]. Biosensors are chemical sensors that utilize biochemical mechanism in its recognition system [6,27–29]. IUPAC defines chemical sensor as a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal [6,30].

Biosensing platforms based on magnetoresistance (MR) sensing technique are among the most attractive means for detecting and quantifying biomarkers owing to their promising properties such as cost-effectiveness, ability to suppress background noise due to the utilization of magnetic nanoparticles (MNPs) as labels, simple operation, high compactness, and high sensitivity. The sensing technique is based on the phenomenon that the resistance of some metals or semiconductors varies with the change of applied magnetic field. Magnetic sensors therefore exploit the phenomenon by converting various magnetic fields and their quantities into electrical signal [31,32]. Overall, the MR sensing involves the utilization of magnetic labels normally comprising of magnetic nanoparticles and functional groups capable of binding appropriate biomolecules. To detect biomolecules, suitable probes need to be immobilized on the surface of the sensor and followed by letting the analyte of interest containing magnetic labels pass over the surface of the sensor. The output signal changes (reflecting analyte's concentration) can then be detected using appropriate MR sensing technique after application of external magnetic field [31]. The three types of MR sensors are anisotropic magneto resistance (AMR) sensor: Phenomenon that the resistivity of ferromagnetic materials changes with the angle between the magnetization and the current direction, giant magneto resistance (GMR sensor: Phenomenon that the resistance of magnetic films will change greatly when the bias magnetic field is applied and lastly, tunnel magneto resistance (TMR) sensor: Phenomenon that the tunneling resistance changes with the relative direction of ferromagnetic materials on both sides in ferromagnetic layer/nonmagnetic insulating layer/ferromagnetic layer (FM/I/ FM), and its mechanism is spin-dependent tunneling effect. Among MR sensors, TMR biosensors exhibit the highest MR value, implying highest sensitivity and by extension possession of a wide range of application prospects [31,33].

Historically, the development of these three (3) MR sensors has been a captivating journey spanning multiple decades. Concisely, during the early days of discoveries in the range of 1857–1980s when William Thomson (Lord Kelvin) initially noticed that certain materials experienced changes in electrical resistance when exposed to magnetic fields [34–36]. However, it wasn't until the 1980s that researchers began investigating practical applications for this phenomenon, specifically, the concept of anisotropic magnetoresistance (AMR), wherein the electrical resistance of a material changed in response to the orientation of the magnetic field concerning the material's crystallographic axes. This development led to the utilization of AMR sensors in various fields, including automotive, industrial, and consumer electronics [37,38]. In the late 1980s-1990s, A groundbreaking discovery in the late 1980s by Albert Fert and Peter Grünberg was the giant magnetoresistance (GMR) effect, revolutionizing magnetoresistance sensor technology [38,39]. GMR sensors exhibited significantly larger resistance changes when subjected to magnetic fields, making them highly sensitive and particularly well-suited for data storage applications, such as hard disk drives. Equally, within the range of late 1990s - Early 2000s, specifically in the late 1990s, Tunnel Magnetoresistance (TMR) sensors emerged, based on the quantum mechanical tunneling effect in a magnetic tunnel junction (MTJ) [40,41]. TMR sensors offered even greater sensitivity and found applications in magnetic field sensing and magnetic memory technologies. Today, magnetoresistance sensors enjoy widespread use across diverse applications, including data storage, automotive electronics, compasses, position sensors, biomedical devices, and more [42]. Continuous research drives advancements in magnetoresistance technology, exploring new materials and designs to enhance sensitivity, accuracy, and power efficiency.

However, the development of the MR sensors in biomarker detection is still hindered by their large noise and complicated fabrication process, and the need for top electrodes. Contemporary developments towards achieving ultra-sensitivity, biocompatibility and fast sensing performance are being explored using various techniques [33]. Usually, these are achieved by optimizing the sensing geometry, optimization of surface functionalization, and integrating the sensors with magnetic flux concentrators and microfluidic channels [33].

Optical sensing techniques, specifically, plasmonic sensing are promising in terms of biomarker detection due to their features such as greater sensitivity, electrical passiveness, freedom from electromagnetic interference, wide dynamic range, non-requirement of reference electrode, freedom from electrical hazards, high stability relatively, potential for higher-information content than electrical transducers, real time detection capability, label free measurement, room temperature operation and multiplexing capabilities [43–50]. However, the challenge for conventional SPR-based sensors is to extend their detection limit to lower concentrations and smaller molecules. Magneto-optic modulation techniques can be adopted to improve the performance and enhance the sensitivity [51]. Thanks to magneto-plasmonics where magnetic and plasmonic functionalities are combined to significantly realized improvement in magneto-optical activity due to the electromagnetic field enhancement associated with plasmonic resonance [52–62]. Concurrently, the plasmonic properties can be controlled by an external magnetic field, allowing for novel biosensing applications [57–62]. The combination has demonstrated promising performance in the sensing of biomolecules [58], chemical solutions [59] and gasses through detecting the ultralow refractive index changes [61]. Precisely, magneto-plasmonic sensors have potential to outperform individual magnetic field or plasmonic sensors in terms of sensitivity and detection limit, allowing their application in imaging and environmental monitoring apart from biosensing [51,52,57,60,63,64]. Historically wise, the development of magnetoplasmonic sensors started following the discovery of the concept of plasmonics in the 1950s, which involves the interaction of light with free electrons on metal surfaces [65]. Precisely, its application in sensing emerged later around the late 1990s and in early 2000s, the field of magnetoplasmonics started to gain significant attention. For example, in the early 2000s, researchers successfully developed the first magnetoplasmonic sensors [66–68]. These sensors utilized the coupling between surface plasmon resonances and magnetic materials, allowing for sensitive detection of various analytes. More importantly, the advancements in nanotechnology have been playing a crucial role in improving magnetoplasmonic sensors in the areas of nanofabrication enabling precise engineering of nanostructures for better sensor performance. Recent developments involve the deployment of the magnetoplasmonic sensors for biomedical applications, particularly in biomedicine exhibiting promising potential for the

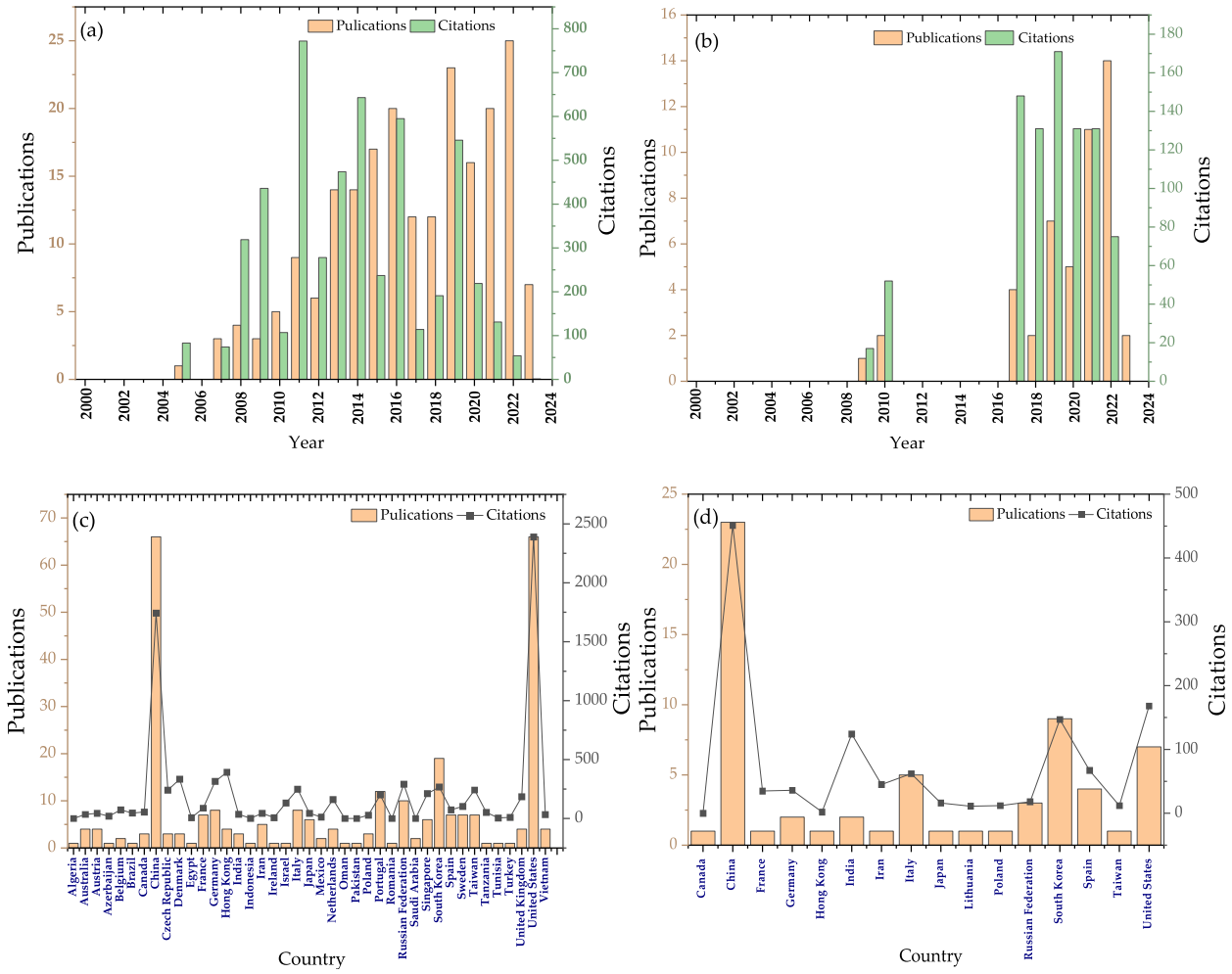

Fig. 1. Diagrams showing research trends within the range of 2000–2023 for the detection of cancer biomarkers using (a) MR sensors, (b) Magneto-Plasmonic sensors, (c) Country wise contribution for MR sensors and (d) country wise contribution for Magneto-plasmonic sensors.

detection of biomolecules, viruses, and other biomedical targets with high sensitivity and specificity [58,69–76]. This capability further promotes their utility in applications like medical diagnostics and environmental monitoring. Moreover, significant efforts have been made towards the realization of multiplexing capabilities, integration with electronics and commercialization among many others [77–80].

Despite the promising advantages of MR and magneto-plasmonic biosensors, their popularity in the detection of cancer biomarkers is still at infancy level. Thus, this work is aimed at providing a bibliometric analysis and recent advancements in MR and magneto-plasmonic biosensors for the detection of cancer biomarkers. First, a bibliometric analysis on the subject was conducted using data extracted from Scopus databases in the range of 2000–2023 in Section 2. Scopus is preferably chosen owing to its broader coverage compared to Web of Science database [81,82]. After then, a review on the recent advancements (especially in the last ten (10) years in magnetoresistance and magneto-plasmonic biosensors for the detection of different cancer biomarkers is reported in Section 3. The advancements were reviewed and reported in terms of design/geometric improvement, surface functionalization, novel plasmonic/magnetic materials and miniaturization as applied to the detection of cancer biomarkers. Finally, we conclude by highlighting the recorded achievements and existing obstacles that are hindering the deployment of the sensors for the detection of cancer biomarkers as well as possible solutions based on the bibliometric analysis and the review report. Overall, the article is expected to assist both early career and established researchers to identify the existing gaps in the fields for the ripeness cancer biomarker detection using magnetoresistance and magneto-plasmonic biosensors.

2. Bibliometric analysis of the field of magnetoresistance and magneto-plasmonic sensing of cancer biomarkers

2.1. Methodology

The data for this bibliographic study was collected on 1 April 2023 from Scopus database via its search function. The duration of the search was narrowed to the range of 2000 to present (1 April 2023) using the following formulations for the publications related to MR and magneto-plasmonic cancer biomarker sensors, respectively: ALL (magnetoresist* AND *sensor* AND for AND cancer OR tumor AND biomarker* AND detect*) AND PUBYEAR > 1999 AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "cp")) and ALL (magnetoplasmon* OR magneto-optic* AND *sensor*AND for AND cancer OR tumor AND biomarker* AND detect*) AND PUBYEAR > 1999 AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT TO (DOCTYPE, "cp")). The asterisk was added to capture all the relevant prefixes and suffixes. Initially, a total of 389 and 131 documents were obtained for the MR sensors and magneto-plasmonic sensors, respectively. After cross checking the tittles and abstracts, irrelevant research articles/conference papers, review articles, books/chapters, non-English based documents, and patents among others were excluded using the manual filter of Scopus search engine. Finally, 213 and 48 research articles and conference proceedings were acquired for

Table 1
Details of top authors with the highest number of research articles (≥ 7) related to the detection of cancer biomarkers using MR sensors.

Authors	Country	Affiliations	Documents	Citations	Total Link Strength (VOSviewer)
Wang S. X.	United States	Department of Materials Science and Engineering, Stanford University, Stanford, CA, USA Department of Electrical Engineering, Stanford University, Stanford, CA, USA	24	1351	28
Lei C.	China	Key Laboratory of Thin Film and Microfabrication (Ministry of Education), Department of Micro-Nano Electronics, School of Electronic Information and Electrical Engineering, Shanghai Jiao Tong University, Dongchuan Road 800, Shanghai, 200,240, China	14	299	20
Wang JP.	United States	Department of Chemical Engineering and Materials Science, University of Minnesota, Minneapolis, MN, 55,455 USA Department of Electrical and Computer Engineering, University of Minnesota, Minneapolis, MN, 55,455 USA Masonic Cancer Center, University of Minnesota, Minneapolis, MN, 5455 USA Institute for Engineering in Medicine, University of Minnesota, Minneapolis, MN, 55,455 USA	13	392	0
Zhou Y.	China	Key Laboratory of Thin Film and Mi-crofabrication (Ministry of Educa-tion), Department of Micro-Nano Electronics, School of Electronic In-formation and Electrical Engineering, Shanghai Jiao Tong University, Dongchuan Road 800, Shanghai, 200,240, China	13	254	19
Hall D.A.	United States	University of California – San Diego, Department of Bioengineering, La Jolla, CA, 92,093, USA University of California – San Diego, Department of Electrical and Computer Engineering, La Jolla, CA, 92,093, USA	12	1032	23
Yang Z.	China	Department of Magnetism and Magnetic Nanomaterials, Ural Federal University, 620,002 Ekaterinburg, Russia School of Physics and Electronic Engineering, Xinyang Normal University, Xinyang 464,000, China	9	212	15
Lee JR.	South Korea	Division of Mechanical and Biomedical Engineering, Ewha Womans University, Seoul, 03,760, Republic of Korea Graduate Program in Smart Factory, Ewha Womans University, Seoul, 03,760, Republic of Korea	9	137	17
Wang J.	China	Department of General Surgery at The Second Affiliated Hospital of Fujian Traditional Chinese Medical University, Collaborative Innovation Center for Rehabilitation Technology, Fujian University of Traditional Chinese Medicine, Fuzhou 350,122, Fujian, P.R. China	8	156	7
Cardoso S.	Portugal	INESC—Microsistemas e Nanotecnologias, Lisboa, Rua Alves Redol 9, 1000–049 Lisbon, Portugal Instituto Superior Tecnico (IST), Universidade de Lisboa, *Av.* Rovisco Pais, 1649–004 Lisboa, Portugal	8	52	0
Gaster R. S.	United States	Department of Bioengineering, Stanford University, Stanford, CA 94,305, USA	7	1078	15

Table 2
Details of top authors with the highest number of research articles (≥ 3) related to the detection of cancer biomarkers using MR sensors.

Authors	Country	Affiliations	Documents	Citations	Total Link Strength (VOSviewer)
Chen H.	China	Center for Molecular Recognition and Biosensing, School of Life Sciences, Shanghai University, Shanghai 200,444, P.R. China Shanghai Key Laboratory of Bio-Energy Crop, School of Life Sciences, Shanghai University, Shanghai 200,444, P.R. China	6	90	17
Lee J.	South Korea	Department of Chemistry, Chungnam National University, Daejeon 34,134, Republic of Korea	5	85	11
Chen J.	China	Center for Molecular Recognition and Biosensing, School of Life Sciences, Shanghai University, Shanghai 200,444, P.R. China School of Medicine, Shanghai University, Shanghai 200,444, China	3	25	12
Koh K.	South Korea	Institute of General Education, Pusan National University, Busan 609–735, Republic of Korea	3	66	9
Liu Y.	China	School of Medicine, Shanghai University, Shanghai 200,444, China School of Environmental and Chemical Engineering, Shanghai University, Shanghai 200,444, P.R. China	3	25	12
Wu J.	China	Eye Institute and Department of Ophthalmology, Eye & ENT Hospital, Fudan University, Shanghai 200,031, China Institutes of Brain Science, State Key Laboratory of Medical Neurobiology and MOE Frontiers Center for Brain Science, Fudan University, Shanghai 200,032, China NHC Key Laboratory of Myopia (Fudan University); Key Laboratory of Myopia, Chinese Academy of Medical Sciences; Shanghai Key Laboratory of Visual Impairment and Restoration, Shanghai 200,031, China	3	84	0
Yang M.	China	School of Opto-Electronic Engineering, Zaozhuang University, Zaozhuang, China	3	9	3
Zhang W.	China	School of Information and Engineering, Hebei University of Science and Technology, Shijiazhuang, China	3	35	2
Zhang Z.	China	Fujian Provincial Key Laboratory of Terahertz Functional Devices and Intelligent Sensing, School of Mechanical Engineering and Automation, Fuzhou University, Fuzhou 350,108, P. R. China	3	13	1
Zhao J.	China	School of Information and Engineering Hebei University of Science and Technology Shijiazhuang, China	3	34	5
Zhu H.	China	Center for Molecular Recognition and Biosensing, School of Life Sciences, Shanghai University, Shanghai 200,444, P.R. China	3	25	12

the bibliographic analysis. Equally, VOSviewer 1.6.19 software was used for the co-authorship, citation, bibliographic and co-occurrence analysis.

2.2. Result and discussions

As shown in Fig. 1(a and b), publications related to the detection of

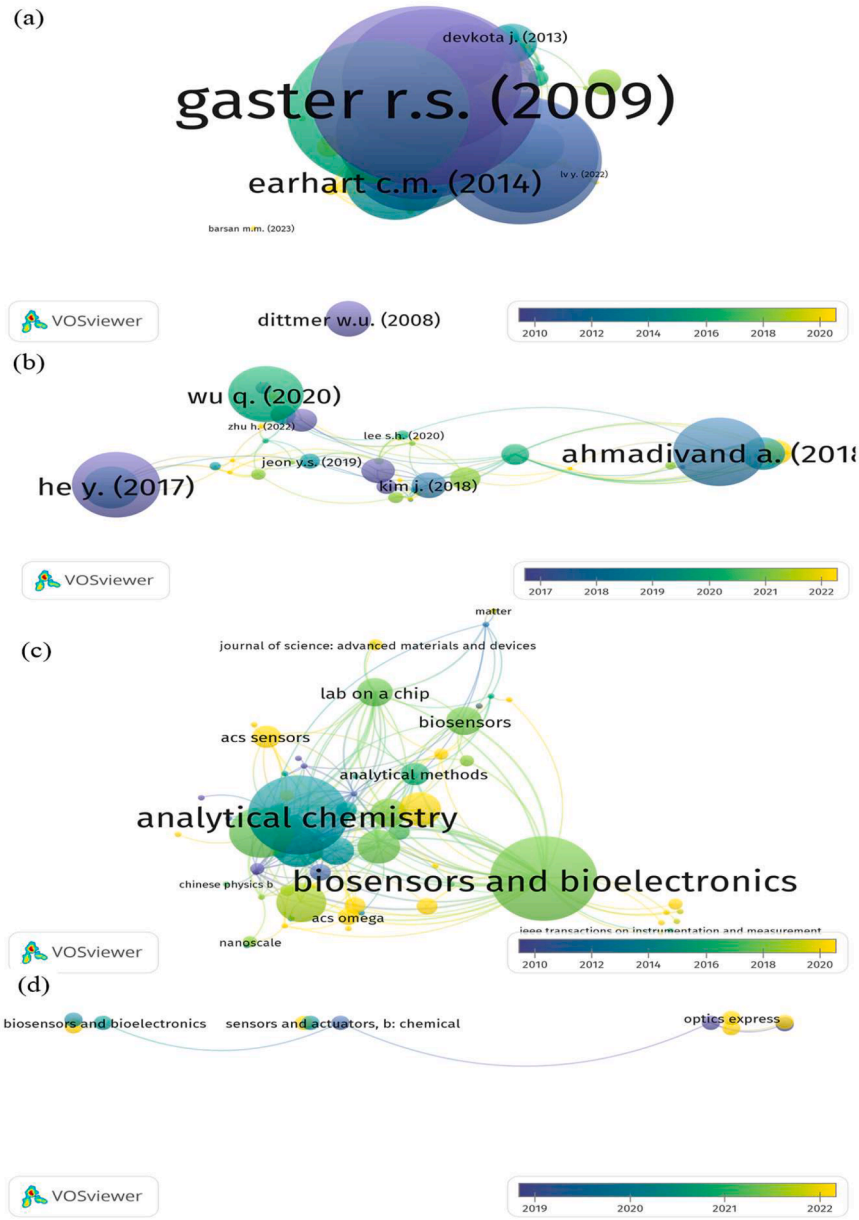

Fig. 2. Bibliographic coupling network among (a) publications for cancer biomarker-based MR sensors, (b) publications for cancer biomarker-based magneto-plasmonic sensors, (c) journals for cancer biomarker-based MR sensors and (d) journals for cancer biomarker-based magneto-plasmonic sensors.

cancer biomarkers using both the MR and magneto-plasmonic sensors are greatly lacking, especially from 2000 to 2006. However, since 2007 research publications related to MR sensors for the detection of cancer biomarkers have not missed a year. Interestingly, rapid growth signifying increased interest in these areas of research is clearly depicted from 2020 to date. This is attributed to the increased quest for non-invasive and earliest means of cancer diagnosis to curtail the alarming increase in the cancer incidence and cancer related deaths globally [2]. Moreover, Fig. 1(c,d) confirm the positions of US and China as the top countries sponsoring cancer related research due to their higher number of cancer cases globally [2,83,84]. Also, greater population in these regions could be another good reason for their success in diverse research areas [85]. Equally, the details of top researchers contributing to the development of MR and magneto-plasmonic sensors for the detection of cancer biomarkers are given in Tables 1 and 2. From the Tables, it could be observed that the top researchers for MR sensors are majorly coming from China and United States. But in the case of magneto-plasmonic sensor (Table 2), South Korea records greater output compared to the United States. This may not be unconnected with the rank of the country among the top countries with higher number cancer incidences and cancer related deaths [2]. Moreover, the Tables indicate that the top researchers have greater Total Link Strength, a parameter extracted from VOSviewer 1.6.19 software which gives idea about the degree of association/collaboration among researchers in this case [86]. This implies that a strong collaborative network is essentially required for the development of the MR and magneto-plasmonic sensors for cancer biomarker detection.

However, as shown in Fig. 2(a and c), the bibliographic coupling analysis conducted using VOSviewer software demonstrate that the links for the publications and journals related to the detection of cancer biomarkers using MR sensors are closer to each other compared to their magneto-plasmonic sensors counterpart (Fig. 2(b and d), which implies their superior relatedness [86]. Interestingly, the majority of the contributing journals are ranked in the first quarter category (Q1) by both Scopus and Web of Science databases. This indicates the reliability and reputability of the available research on the detection of cancer

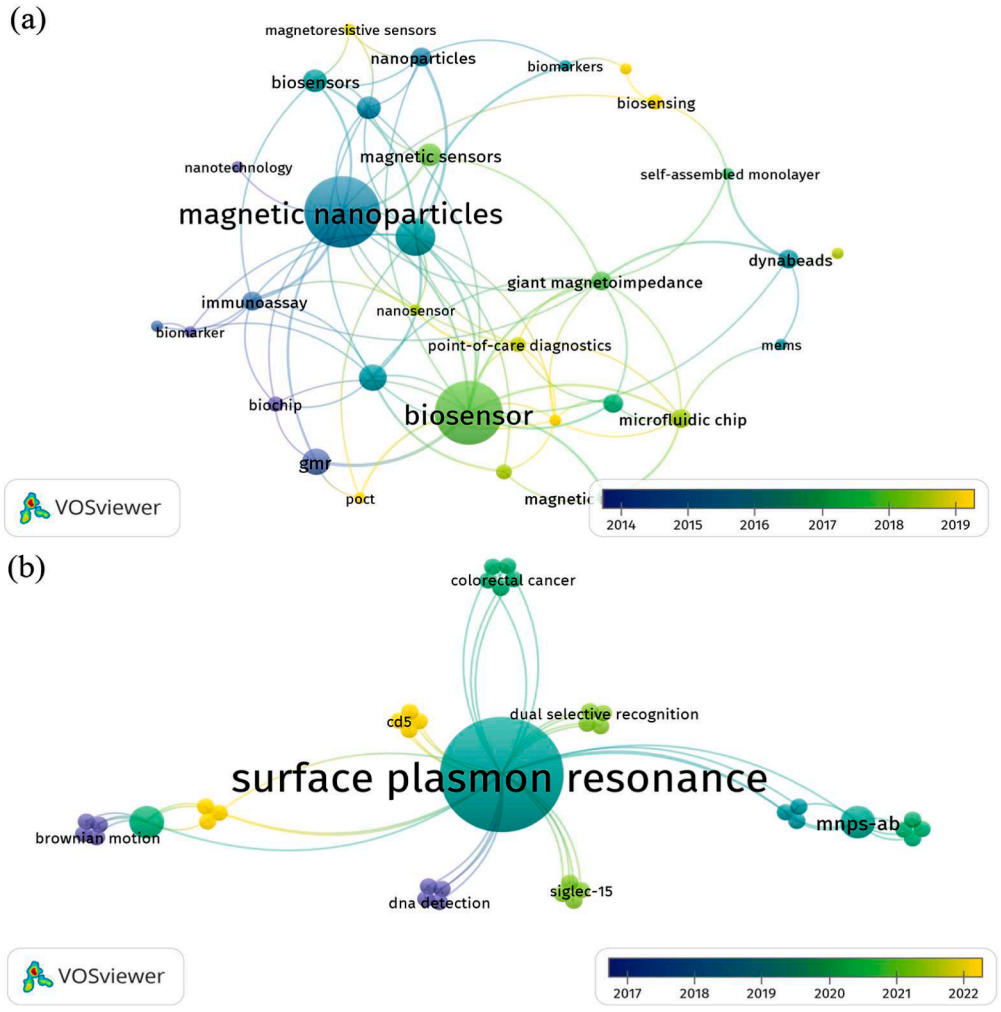

Fig. 3. Evolution of research interests from 2000 to date (April 2023) for cancer biomarker detection using (a) MR sensors (b) magneto-plasmonic sensors.

biomarkers via these two sensing techniques.

To explore the concentration and main interest of researchers in the deployment of these sensing techniques for the detection of cancer biomarkers, authors keywords were evaluated using a co-occurring module in VOSviewer. Usually, authors add keyword in a research work to reveal the direction of that work. Here, the evolution trend of the research interest is evaluated from 2000 to 2023 as shown in Fig. 3a and b for the MR and magneto-plasmonic sensors, respectively. The figures have delineated dominant areas of interest for both areas as a function of the year of investigation. For example, it could be observed that researchers have been employing GMR sensors for the detection of cancer biomarkers since before 2017. Also, recently the focus for MR sensors especially, GMR sensors has been in their deployment for the point of care testing, incorporation of magnetic beads for superior performance, miniaturization to nano scale and incorporation of microfluidic channels among others. The popularity of GMR sensors over other MR sensors is due to its moderate MR ratio, simplicity in nanofabrication process, and high linearity among others. Equally, increased interest can be observed for the magneto-plasmonic sensors in more recent years (2021-date) reporting the detection of prominent cancer biomarkers such CD5 and singlec-15 (Fig. 3b). This could be due the superior advantages of optical detection technique over other techniques. Interestingly and from the look of things, magneto-plasmonic sensing techniques will be likely dominating MR sensors in the detection of cancer biomarkers.

3. Recent advancement in MR and magneto-plasmonic sensors for the detection of cancer biomarkers

Apart from the bibliometric analysis within the period of 2000–2023, the available investigations related to the detection of cancer biomarkers using MR and magneto-plasmonic sensors in the last ten years (2012–2023) are reported and explained in the following sub-sections. Prior to that, the main preparation techniques and performance comparison for the MR and magneto-plasmonic sensors are summarized for better understanding.

3.1. Preparation techniques and performance of MR and magneto-plasmonic sensors

Magnetoresistance and magneto-plasmonic sensors as the means of detecting changes in magnetic fields are mainly prepared and fabricated using the following processes:

(a) **Magnetoresistance Sensors:** Magnetoresistance sensors exploit the phenomenon where the electrical resistance of a material changes in response to an applied magnetic field. The main steps for preparing and fabricating these MR sensors including their advantages and disadvantages are tabulated in Table 3 [87–89, 87,90]:

Table 3
Main steps for the preparation and fabrication of MR sensors.

Preparation Step	Description	Advantages	Disadvantages
Substrate Selection	Choose a suitable substrate material (often silicon or glass) for sensor fabrication.	• Provides a stable base for sensor components. • Compatibility with semiconductor processing techniques.	• Substrate cost may be high. • Limited choice of materials for specific applications.
Thin Film Deposition	Deposit thin film layers of materials with desired magnetic and electrical properties using techniques like sputtering or evaporation.	• Allows precise control over film thickness and composition. • Enables tailoring of sensor properties.	• Requires specialized equipment and controlled environment. • Deposition rates can be slow for thicker films.
Patterning	Use photolithography or other methods to define sensor geometry and pattern.	• Achieves desired sensor shape and size. • Allows miniaturization for higher sensitivity.	• Requires clean room facilities for high precision. • Process complexity increases with miniaturization.
Etching	Remove unwanted material using chemical or physical etching methods.	• Creates well-defined sensor structures. • Enables isolation of sensor elements.	• Etch rates can be difficult to control. • May introduce surface roughness or defects.
Magnetization	Apply a magnetic field to align the magnetic domains in the sensor material.	• Enhances sensor sensitivity and performance. • Enables detection of small magnetic fields.	• Requires careful calibration to achieve desired sensitivity. • External magnetic interference can affect results.
Annealing	Heat the sensor to a specific temperature to relieve stress and improve magnetic properties.	• Enhances stability and reproducibility of sensor response. • Optimizes magnetoresistive effects.	• Annealing conditions must be carefully controlled. • Risk of altering other material properties.
Passivation	Apply protective layers to prevent sensor degradation from environmental factors.	• Increases sensor lifespan and durability. • Shields against contamination and oxidation.	• Passivation layers can affect sensor performance. • May introduce additional thermal or stress issues.
Packaging	Assemble the sensor into a suitable package with electrical connections.	• Provides mechanical protection to the sensor. • Facilitates integration into larger systems.	• Packaging can affect sensor response and thermal behavior. • Challenges in maintaining consistent electrical connections.

(a) **Magneto-Plasmonic Sensors:** Magneto-plasmonic sensors combine the properties of plasmonic materials (e.g., gold or silver) with magnetism to enable sensitive detection of magnetic fields. Main fabrication steps are described in Table 4 [91–94]:

(a) Performance Comparison

The sensing performance of different magnetoresistance and magneto-plasmonic sensors for cancer diagnosis are compared based on important performance parameters as shown in Table 5 [95–99]. It could be observed that despite the promising advantages of magneto-plasmonic sensors over MR counterpart, significant efforts need to be put in place to simplify and reduce the cost of their production. Now, few companies are dedicated to manufacturing sensing devices based on magnetoresistance and magneto-plasmonic (see Table 6).

3.2. *Magnetoresistance (MR) sensors for cancer biomarkers*

The unique advantages of MR sensors have attracted the attention of numerous researchers working in diverse areas of research. Here, the recent advances in the detection of cancer biomarkers using the three (3) types of MR sensors; AMR, GMR sensor and TMR are reported especially within the last ten (10) years. Emphasis has been given to the accomplishment of ultrasensitive, selective, and reliable detection of cancer biomarkers among others. Details on the principle of the three (3) MR sensors can be found elsewhere [31,33,37,107,108].

MR sensors of different novel designs are available for the sensitive and reliable detection of various biomarkers. For example, superior performance of MR sensors has been reported with the incorporation of magnetic beads as magnetic labels for the detection of molecular recognition events. Only that, biomarker detection usually requires the surface of the MR sensors to be chemical modified for appropriate biomarker capturing. This poses problems such as contamination and damage due to chemical reactive layers. In addition, there is complexity related to the need for washing the surface of sensors as well as additional cost related to incorporation of microfluidic pumps. These issues have been addressed using a contactless prostate specific antigen (PSA) biomarker micro GMR detection system fabricated using MEMS technology [109]. Unlike traditional detection methods where the sensor is in direct contact with the sample, in this method, the sensor and PSA sample preparation are kept separate. This prevents the sensor from being contaminated or affected by the chemical solvents used in the sample preparation process. In course of the detection process, the PSA biomarker labeled with Dynabeads was captured on a small glass with an area equal to the GMR strips area. Equally, biotinylated secondary antibodies against PSA and streptavidinylated Dynabeads were used in the immunoassay process. Through the application of a DC magnetic field in the range of 50–90 Oe, the system was able to detect PSA with a detection limit as low as 0.1 ng/mL using the double-antibody sandwich assay. Furthermore, the system features other promising advantages such as easy handling, free from chemical solution damage, low power consumption, portability, cost effectiveness and immediate reusability (no need to wash). However, the sensitivity of the detection system is low compared to conventional devices due to the presence of a small gap between the sensor and sample as well as induction of weak magnetic fields by the Dynabeads to the GMR sensor [109]. Combination of multiple tumor markers detection is among reliable ways to improve sensitivity and specificity in cancer diagnosis. Also, another GMR biosensor employing similar detection process (double antibody sandwich immunoassay) was investigated and designed for the simultaneous detection of twelve (12) varieties of tumor markers (AFP, CEA, CYFRA21–1, NSE, SCC, PG I, PG II, CA19–9, total PSA, free PSA, free-β-hCG, Tg) in 15 min by integrating a GMR sensor chip, a microfluidic device and a magnetic nano-beads label (Fig. 4(a–e)) [110].

In comparison with single analyte sensors, the multi-biomarker sensor offers better benefits including cost effectiveness, reduced assay time, low reagent consumption, simplicity, and conveniency. Unfortunately, the high sensitivity of this technology restricts its application in the detection of biomarkers which needs a very high upper-limit-of-detection [110]. The appropriate detection sensitivity and early cancer diagnosis (low analyte concentration) are sometimes achieved by optimizing, amplifying or modifying only the analyte of interest. Nesvet et al. [111] reported the integration of methylation specific PCR (MSP)

Table 4
Main steps for the preparation and fabrication of magneto-plasmonic sensors.

Preparation Step	Description	Advantages	Disadvantages
Substrate Cleaning	Cleaning the sensor substrate to remove contaminants	Improves sensor surface quality	Requires careful handling to avoid surface damage
Nanoparticle Synthesis	Creating magnetic and plasmonic nanoparticles	Tailoring properties for sensor application	Precise control over nanoparticle properties can be challenging
Nanoparticle Functionalization	Coating nanoparticles for stability and specificity	Enhances stability and target binding	Chemical processes can affect nanoparticle properties
Sensor Deposition	Deposition of functionalized nanoparticles on substrate	Allows controlled placement of sensing elements	Uniform deposition may be challenging on complex surfaces
Magnetic Field Application	Applying an external magnetic field	Enhances sensitivity and selectivity	Requires additional equipment and control
Optical Measurement	Using light to measure sensor response	Non-invasive and real-time detection	Signal interpretation can be complex

Table 5
Comparison of sensing performance among magnetoresistance and magneto-plasmonic sensors.

Parameter	Magnetoresistance Sensors	Magneto-Plasmonic Sensors
Sensitivity	Moderate to High	High
Detection Limit	Low	Very Low
Specificity	Moderate to High	High
Speed	Fast	Very Fast
Cost	Relatively Low	Relatively High
Complexity	Simple design	Complex design
Multiplexing Capability	Moderate	High
Miniaturization Potential	High	Moderate to High
Stability	Generally Stable	Sensitive to environmental conditions
Biocompatibility	Generally Good	Might require surface modifications
Interference	Susceptible to external magnetic fields	Less susceptible to external factors
Applications	Medical diagnostics, lab-on-a-chip, etc.	Bio-imaging, targeted drug delivery, etc.

Table 6
Some companies that manufacture magnetoresistance and magneto-plasmonic sensors.

Company Name	Sensor Type	Website	Refs.
NVE Corporation	Magneto-Resistive	https://www.nve.com/	[100]
Crocus Technology	Magneto-Resistive	https://crocus-technology.com/	[3]
Spintronics International	Magneto-Resistive	https://www.spintronicsinc.com/	[101]
QuantumWise	Magneto-Resistive	https://quantumwise.com/	[102]
NanoSPD Technology	Magneto-Plasmonic	http://www.nanospd.com/	[103]
Plasmonics Inc.	Magneto-Plasmonic	https://www.plasmonics-inc.com/	[104]
C2Sense	Magneto-Plasmonic	https://www.c2sense.com/	[105]
BioFluidix	Magneto-Plasmonic	http://www.biofluidix.com/	[106]

to melt curve analysis (a promising technology for early detection of cancer on GMR biosensor to significantly improve the sensitivity of their DNA hybridization assay for methylation detection. An analytical limit of detection down to 0.1% methylated DNA in solution was achieved [111,112]. Another GMR sensor comprising of a 15 mm × 15 mm chip and a reaction well for the multiplex detection of ovarian cancer at its earliest state was developed and reported by Klein et al. [113]. In this work, the magnetoresistance signals of the sensor were monitored by a nearly balanced (per each sensor) Wheatstone Bridge circuit. The benchtop and hand-held versions of the GMR biosensing system were used for the multiplex detection of cancer antigen 125 (CA125 II), human epididymis protein 4 (HE4), and interleukin 6 (IL6); which are the three (3) most established biomarkers for ovarian cancer [114]. Unfortunately, the detection takes several hours due to long incubation times in the reaction well, but similar result is predicted to be acquired within the maximum of 30 min with microfluidic integration.

Also, a magneto nanosensor (MNS) with improved sensing performance and absence of cross-reactivity was reported for the multiplex detection of protein and autoantibody biomarkers for prostate cancer diagnosis [115]. In this device, 10 × 12 mm chip containing eighty MNSs were fabricated in which the GMR effect was employed to provide electrical signals related to the concentration of the analytes (autoantibody and protein biomarkers) Fig. 5(a–f).

Despite the development of GMR sensors in the detection of cancer biomarkers, commercially available portable GMR systems are still lacking. This implies the need for further improvements and discovery of various technologies to fulfill the intense need to shift from traditional laboratory tests to portable POC devices. Albuquerque et al. [116] successfully coupled GMR sensors to a portable platform for the detection of colorectal cancer using clinically relevant low concentration (nanograms per milliliter concentration level) carcinoembryonic antigen (CEA) biomarker. The chip layout used has 30 U-shaped SV sensors with dimensions 46.6 μm × 2.6 μm arranged in series of two sensors and displayed in six distinct sensing regions, with each region compromising five biological active sensors coated with a gold film (Cr 5 nm /Au 40 nm). As shown in Table 3, apart from the sensor chip, the portability was achieved with the aid of other components including magnetic labels, an electronic setup, and a reusable fluidic system [116]. A lowest detection limit (LOD) down to 4.7 ng/ml during the CEA detection was achieved which is within the clinically relevant range (3.5 ng/ml to 7.5 μg/ml) [117]. More importantly, the sensor outperformed commercially available ELISA kits (Abcam-ab99992, Thermo Fisher-EHCEA) with LOD of 250 pg/ml in addition to better dynamic range and lower reaction time.

Recently, an all-magnetic platform for the direct profiling of extracellular vesicles (EV) glycans in native clinical biofluids (brain glial cells (GLI36), lung epithelial cells (PC9), skin epithelial cells (A431) and gastric epithelial cells (MKN45)), was developed [118]. On that platform, a rationally designed polycore magnetic nanoparticles is utilized to transduce EV-bound glycans into magnetic signals quantifiable by the integrated GMR sensor which enables the direct profiling of EV glycans without the need for complex sample preparation or purification steps. This is a significant advantage as it allows for the analysis of EVs in their natural state within biofluids, such as blood or urine, which is more relevant to real-world clinical applications. Also, the platform uses rationally designed polycore magnetic nanoparticles, which selectively transduce EV-bound glycans into magnetic signals, while excluding the glycans of free-floating glycoproteins. This gives it a dual-selectivity feature which ensures that the analysis specifically targets the glycans on EVs, enhancing the accuracy of the results. Moreover, the employment of the built-in magnetoresistance sensor allows the quantification of the magnetic signals generated by the EV-bound glycans. Thus, the potentiality of the sensor to accurately measure the glycans' presence

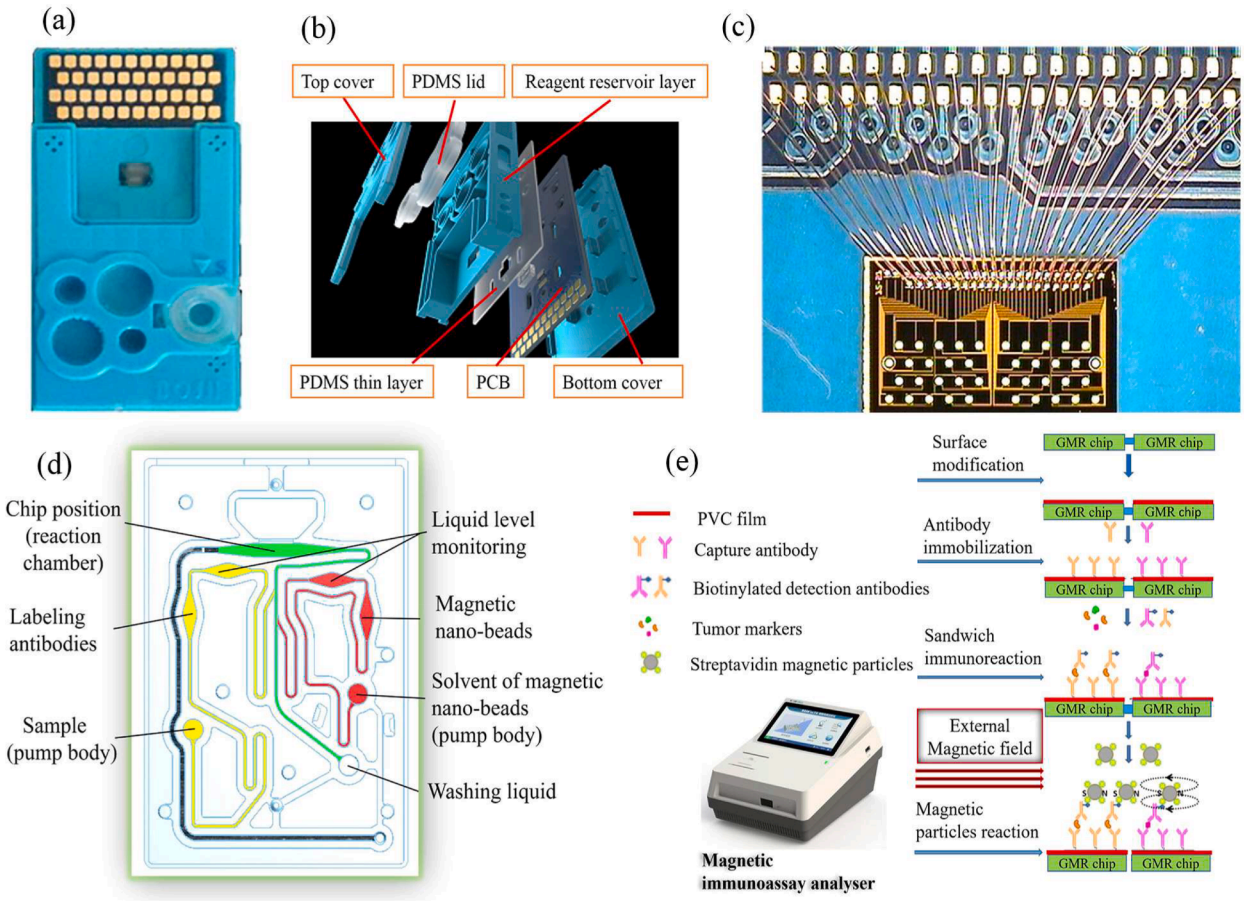

Fig. 4. (a) The test card, (b) its multilayer structure, (c) GMR chip and the connection between the GMR chip and PCB, (d) The structure of the microchannel system, (e) The reaction process of the GMR multi-biomarker immunoassay. Figs. (a)–(e) reprinted from [110], with permission from Elsevier.

and abundance, providing quantitative information about the glycome of EVs. The device has the advantages of ultra-sensitivity, rapid measurement (<30 min for the whole assay), real-time measurement and wash-free feature [118]. This approach reveals a bright future for the detection of cancer biomarkers and other diseases due to the glycosylation of most of the current clinical biomarkers.

In another recent contribution, an activity-based protease sensor was investigated and developed by immobilizing magnetic nanoparticles (MNPs) onto the surface of a giant magnetoresistive spin-valve (GMR SV) sensor using peptides (Fig. 6). The GMR SV sensor arrays can be mass-produced inexpensively and integrated into smartphone-based POC applications due to their compatibility with complementary metal-oxide-semiconductor (CMOS) technology [119,120]. More importantly, the protease samples do not contain any magnetic content which minimizes background signal (noise) and by extension enables high detection sensitivity. These are in addition to wash-free and real-time quantification. Hence, the approach is expected to set a new path towards the realization of real time quantification of biomarkers using GMR SV sensors [121].

More recently, a huge improvement in the sensitivity of GMR sensor has been recorded with the incorporation of magnetic nanowires (MNWs) as magnetic levels. Through this, a real-time, wash free and portable device is achieved in addition to the characteristic detection simplicity as well as the prevention of contamination risk during sample preparation [122].

Table 7 summarizes the recent available research on the detection of cancer biomarkers using MR sensors.

3.3. Magneto-plasmonics sensors for cancer biomarkers

As mentioned earlier, the synergic properties of magneto-optical (MO) and plasmonic materials can enable ultrasensitive detection of analytes. As such, the materials can be employed for the early detection of cancer in which the concentrations of the cancer biomarkers are extremely less. This has triggered numerous investigations. For example, investigations on the MO properties of one-dimensional magnetite nanorods containing ordered mesocages (MNOM) have been conducted and proven the exciting features of the MNOM like higher surface-to-volume ratio, better adsorption capacity and excellent electrical conductivity, simple synthesis procedure and anisotropic magnetization characteristics [123–126]. Inspired by these, few investigations were conducted associated with the detection of cancer biomarkers using magneto-plasmonic sensors (Table 4). For example, Huang et al. [127] have developed a sensitive SPR sensor integrating MNOM and a plasmonic material based on silver nanoclusters (AgNCs) for the detection of a tumor biomarker, programmed death ligand 1 (PD-L1) (Fig. 7(a and b)). AgNCs is capable of offering a substantial increase in sensitivity by electromagnetic field coupling between the localized surface plasmon resonance (LSPR) of nanoparticles (NPs) and gold film [128]. Moreover, a complex of MNOM@AgNCs was synthesized by binding AgNCs onto thiol groups functionalized MNOM through Ag–S bond by one-pot method. Through host-guest recognition and hydrophobic interaction, Anti-PD-L1 (PD-L1 Ab) could bind with pSC4 which is anchored on the gold chip. Similarly, PD-L1 specific aptamer (Apt PD-L1) is connected to the AgNCs on the magneto-optical nanocomplex. Dual recognition of PD-L1 Ab and Apt PD-L1 with PD-L1 constitutes a typical sandwich structure, enabling selective and quantitative detection of PD-L1 [127].

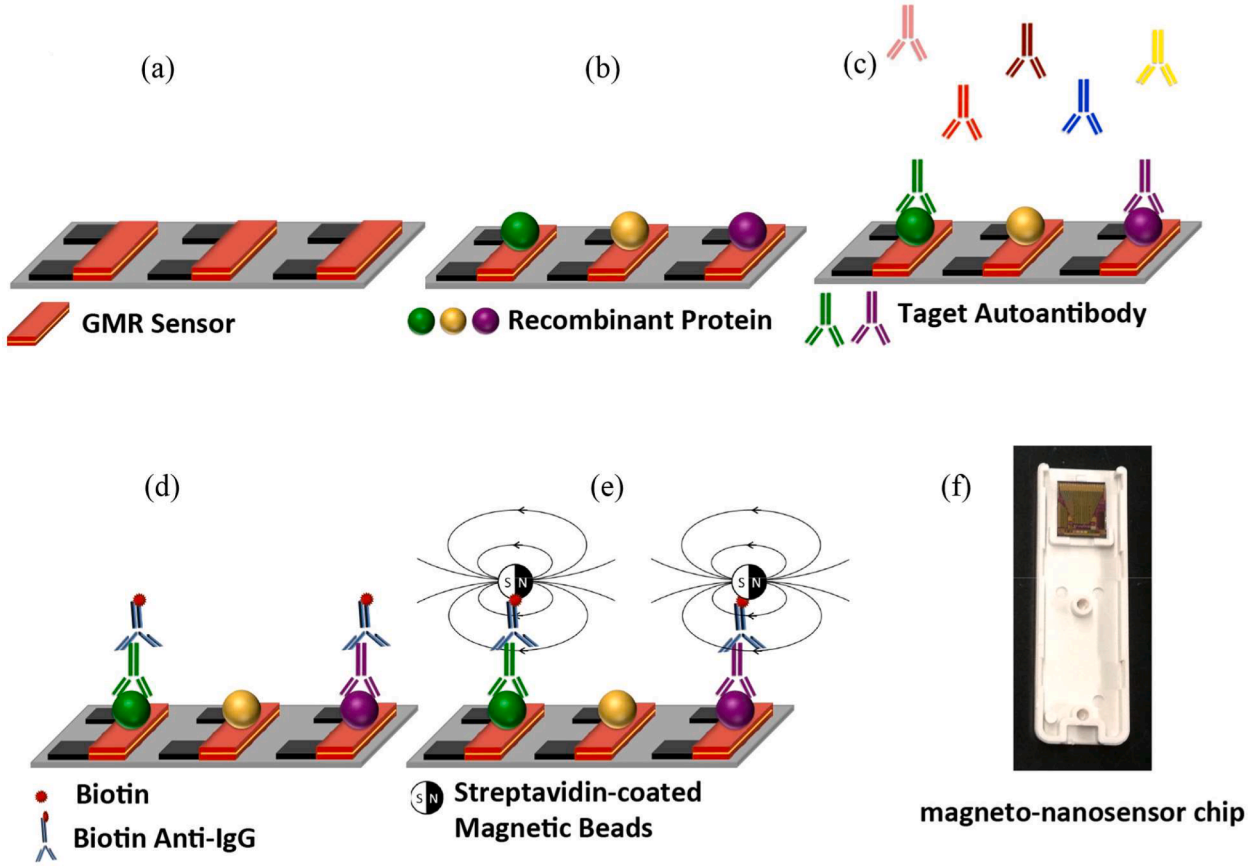

Fig. 5. (a) Diagram showing a multiplexed magnetic autoantibody immunoassay, each chip contains 80 MNSs (b) three different (colors) commercially available recombinant proteins, specific to their respective autoantibodies are immobilized on the nano-sensors as capture protein [16], (c) the serum samples spotted onto the sensors and the target autoantibodies (d) after washing away the unbound autoantibodies, biotinylated anti-human IgG antibodies are added and reacted with each of the bound autoantibodies as the detection antibody, (e) finally, the streptavidin-coated magnetic nanoparticles are added which trigger the changes in the resistance of the MNS (f) actual picture of the MNS chip (10 cm X 12 cm). Figs. (a)–(f) adapted from [115].

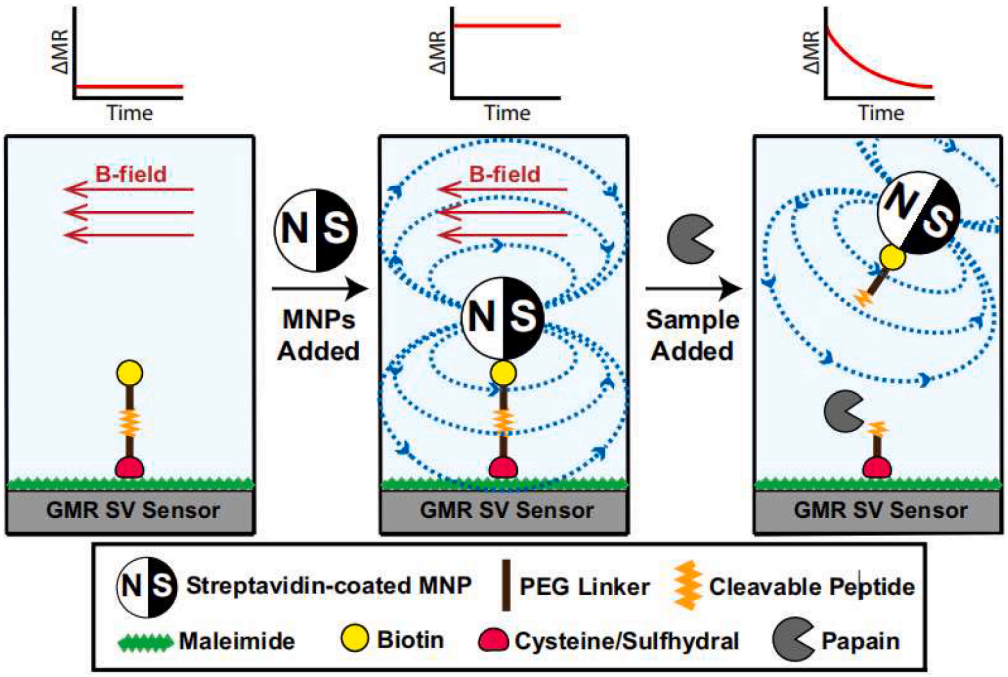

Fig. 6. View of the magnetic detection scheme for protease activity. A biotinylated peptide immobilized on the GMR SV sensors and placed in a magnetic field. Addition of streptavidin coated MNPs causes an increase in magnetoresistance (MR) as they are orientated close to the sensor surface via the streptavidin-biotin interaction. When a biofluid sample containing a protease is added, cleavage of the peptide causes a time-dependent change in the MR as the MNPs are enzymatically released from the sensor surface. Figure adapted from [121].

Table 7
A summary of MR sensors for the detection of cancer biomarkers.

Sensor	Dimension	LOD	Surface Functionalization	Labels	Biomarker [Application]	Time	Refs.
GMR	300 μm, 3 μm, stripe	PSA can be detected with a detection limit as low as 0.1 ng/mL	No functionalization	Dynabeads	Prostate specific antigen (PSA) [Prostate cancer]	–	[109]
GMR	120 μm diameter, disk shape	0.52 ng/mL 0.27 ng/mL 0.25 ng/mL 0.50 ng/mL 0.30 ng/mL 1.00 ng/mL 0.50 ng/mL 2.00 u/mL 0.02 ng/mL 0.07 ng/mL 0.30 ng/mL 1.00 ng/mL	Polyvinyl chloride (PVC)/ Capture antibodies	128 nm magnetic nano-beads	AFP CEA CYFRA21–1 NSE SCC PG I PG II CA19–9 total PSA free PSA free-β-Hcg Tg [lung cancer, liver cancer, digestive tract cancer, prostatic cancer, etc.]	15 Mins	[110]
GMR	8 × 10 array (1.2 cm × 1 cm chips)	0.1% methylated DNA in solution	Synthetic DNA probes	Streptavidin MACS (Miltenyi) magnetic nanoparticles (MNPs)	methylated plasma biomarkers (methylated DNA)	–	[112]
GMR	15 mm × 15 mm chip	3.70 U/mL 7.40 pg/mL 7.40 pg/mL	Capture antibodies or bovine serum albumin (BSA)	Ademtec 200 nm beads	125 (CA125 II) Human epididymis protein 4 (HE4) Interleukin 6 (IL6),	Several hours	[113]
GMR	10 × 12 mm, and an array of 10 × 8 MNSs	–	Capture recombinant protein	streptavidin-coated magnetic nanoparticles (Magnetic beads)	Prostate-specific antigen (PSA) Free/total PSA ratio,	–	[115]
GMR	46.6 μm × 2.6 μm	4.7 ng/mL	Mouse anti-CEA monoclonal antibody CEA rabbit anti-CEA polyclonal antibody Anti-rabbit biotinylated antibody,	Dextran and streptavidin coated magnetite	CEA [Colorectal Cancer]	Based signal (5 min)	[116]
GMR	500 mm x 3 5 mm	~104	Antibody	Polycore magnetic nanoparticles	Extracellular vesicles (EVs) [Kidney cancer cells (A498), brain glial cells (GLI36), lung epithelial cells (PC9), skin epithelial cells (A431) and gastric epithelial cells (MKN45)]	<30 min	[118]
GMR	–	Sensitivity (4 nM, 20 nM)	streptavidin coated MNPs	No label	cysteine protease, papain	3.5 mins (assay time)	[121]

Considering the variation of PD-L1 concentration with different cancer stages reaching up 25 ng/mL in cancer patients [129], different concentrations of PD-L1 in the range of 10–300 ng/mL) were measured using the magneto-plasmonic sensor. In addition to excellent sensitivity and linearity demonstrated by the sensor, a detection limit of 3.29 ng/mL which is far below the clinical requirement was achieved. More importantly, the sensor demonstrated promising clinical diagnostic applicability when tested on real samples [127].

Another work on the employment of magneto-plasmonic improved SPR sensor for the detection of Siglec-15 has been reported [130]. Siglec-15 is an important biomarker associated to numerous cancers including renal cell carcinoma [131], gastric cancer [132], nasopharyngeal carcinoma [133] and Osteosarcoma [134] among others. Through the functionalization of the SPR sensor with a novel magnetic field-aligned Fe_3O_4-coated silver magnetoplasmonic nanoparticles (Ag@MNPs) nanochain, (M-Ag@MNPs); a higher refractive index sensitivity, improved quality factor and increased detection accuracy compared to bare gold based SPR detection were realized [130] (Table 8) Fig. 8(a–f).

Gold nanoparticles (AuNPs) are another promising plasmonic material and in many cases most preferred due to their greater stability compared to silver nanoparticles (AgNPs). Recently, Kausaite-Minkstimiene et al. [135] have demonstrated the amplification of SPR response during the detection of lymphoma biomarker, CD5 (lymphocyte antigen T1) after functionalization with gold-coated magnetic nanoparticles (mAuNPs). In that case, the signal amplification strategy enabled the realization of excellent sensitivity and the detection of femtomolar concentration (8.31 fM) of CD5 biomarker [135].

In another development, a plasmonic sensing technique, surface enhanced Raman scattering (SERS) is attracting significant attention due its ultra-sensitivity, fingerprint, and single molecular detection capability enhancing quantitative analysis of substances with trace concentrations [136]. Like in SPR technique, the incorporation of plasmonic materials such as Au or Ag in magnetic nanostructures has been reported to improve SERS activity under the influence of a magnetic field substantially [137–139]. In this case, the use of the magnetic field improves the electromagnetic fields around the considered nanostructures, and ultimately increase the signal from the analyte [140]. Specifically, this has inspired various investigations related to the diagnosis of cancer at its earliest stage. For instance, Qiu et al. [139] reported a work on the SERS detection of low abundant lung cancer cell, A549 (CEA-expressed A549 cells) using a SERS substrate based on magnetic hybrids (Fe_3O_4-Au hybrids) synthesized by their team. In course of the detection, Fe_3O_4-Au hybrid nanoparticles (anti-CEA/4-ATP/Fe_3O_4-Au) was formed by incorporating a Raman reporter molecule (4-aminothiophenol (4-ATP)) and antibody of CEA (anti-CEA) on Fe_3O_4-Au hybrid nanoparticles and used as SERS tags while an anti-CEA-labeled Au NPs (anti-CEA/Au) was used as a SERS-active substrate to improve detection sensitivity. Fortunately, the detection of very low abundant CEA-expressed A549 cells (~10 cells per mL) was demonstrated by the assay. In addition to the

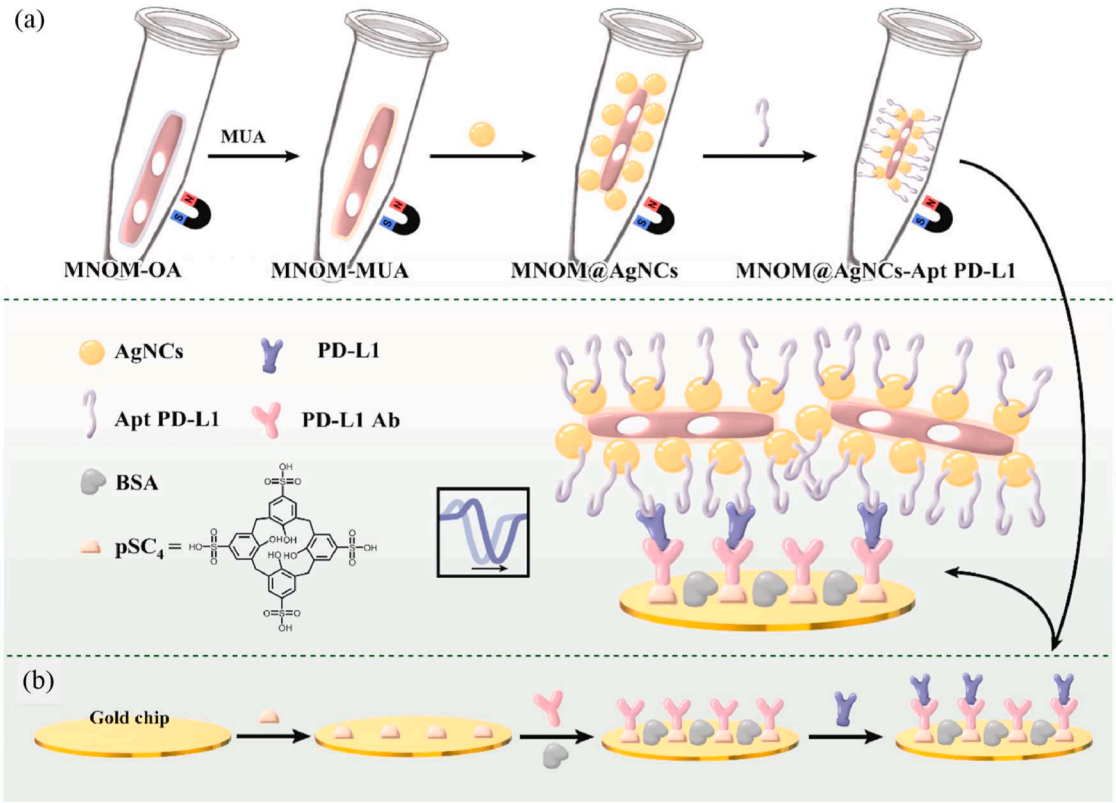

Fig. 7. (a-b) Schematic diagram of MNOM@AgNCs-Apt PD-L1 magneto-optical nanocomplex with enhanced sensitivity to detect PD-L1. Figs. (a and b) reprinted from [127], with permission from Elsevier.

Table 8
Comparisons among sensitivity (S), detection accuracy (D.A.) and quality factor (Q.F.) for different layers of the proposed sensor, which included bare gold and M-Ag@MNPs/gold. Reprinted from [130], with permission from Elsevier.

Layer in the structure	S (deg/RIU)	D.A.	Q.F. (RIU-1)
Gold	98.4950	0.5190	55.8060
M-Ag@MNPs/gold	121.5050	0.7340	78.9000

excellent sensitivity, specificity and low detection limit associated with this assay, the capability of the magnetic SERS tags to concentrate captured cells and separate them is reported to improve the efficiency of the sensor. Moreover, the detection of exosomal miRNA, a prominent cancer biomarker [141–144], using a magneto-plasmonic nanomaterial based has also demonstrated an attractive performance characteristics even though, it had not been optimized in terms of the detection of cancer specifically [145]. Table 9 summarizes the available investigations related to the detection of cancer biomarkers using magneto-plasmonic sensors.

Apart from the detection of cancer related biomarkers using magneto-plasmonic sensors/substrates, excellent performances have been reported for other applications including label-free determination of human immunoglobulin G (IgG) [146], trace analysis of furazolidone in fish feeds [147], bacteria detection [148,149] and general improvement of SERS performance [64,150]. Likewise, incorporation of magnetic materials in other optical sensing techniques demonstrated promising performance improvements [61,151–155]. This is further implying the promising capabilities of the technologies.

4. Conclusions and future prospects

The detection of cancer at its earliest stage can significantly mitigate the complications and death related to cancer. The detection of cancer related biomarkers using biosensors has been identified among the promising approaches to accomplish this early detection in an invasive, reliable, and cheap manner. Unfortunately, the concentration of these biomarkers is extremely low at the onset of cancer which imposes the requirement to utilize highly sensitive and specific techniques. MR-based sensors and magneto-plasmonic based sensors have been identified as the most appropriate sensing techniques. MR technique features high sensitivity, low background noise, wash free, low-cost components, free from environmental interference, compatibility with nano-fabrication technology, multiplex detection, and simple integration process. Likewise, magneto-plasmonic technique offers almost similar advantages in addition to excellent specificity, fingerprint capability, real-time measurement, excellent stability, label free detection, single molecular detection capability. Inspired by these, this article reports a bibliometric analysis within the range of 2000-date (April 2023) and review of the recent advancement (last ten (10) years) in the detection of various cancer biomarkers using MR and magneto-plasmonic sensors. The bibliometric analysis demonstrates that research on the detection of cancer biomarkers using these sensors is majorly dominated by countries like China, United States and South Korea. Moreover, the dominance of GMR sensors over other MR sensors is evidently observed for POCT and device miniaturization among others. Overall, these cutting-edge technologies have demonstrated their ability to detect cancer at early stages with high sensitivity and specificity. Additionally, although MR based research is currently the most prominent, there is a high tendency for magneto-plasmonic supremacy soon. In the case of the review, various contributions related to the three types of MR sensors (AMR, GMR and TMR) are available. According to the literature, each of these sensors has their pros and cons. For example, AMR biosensors are described to feature the smallest field of operation compared to GMR and TMR biosensors but have their applications hindered due to their low MR ratio and fragility at elevated temperatures. Likewise, TMR is reported to be the most promising sensing technique among the MR sensors due to

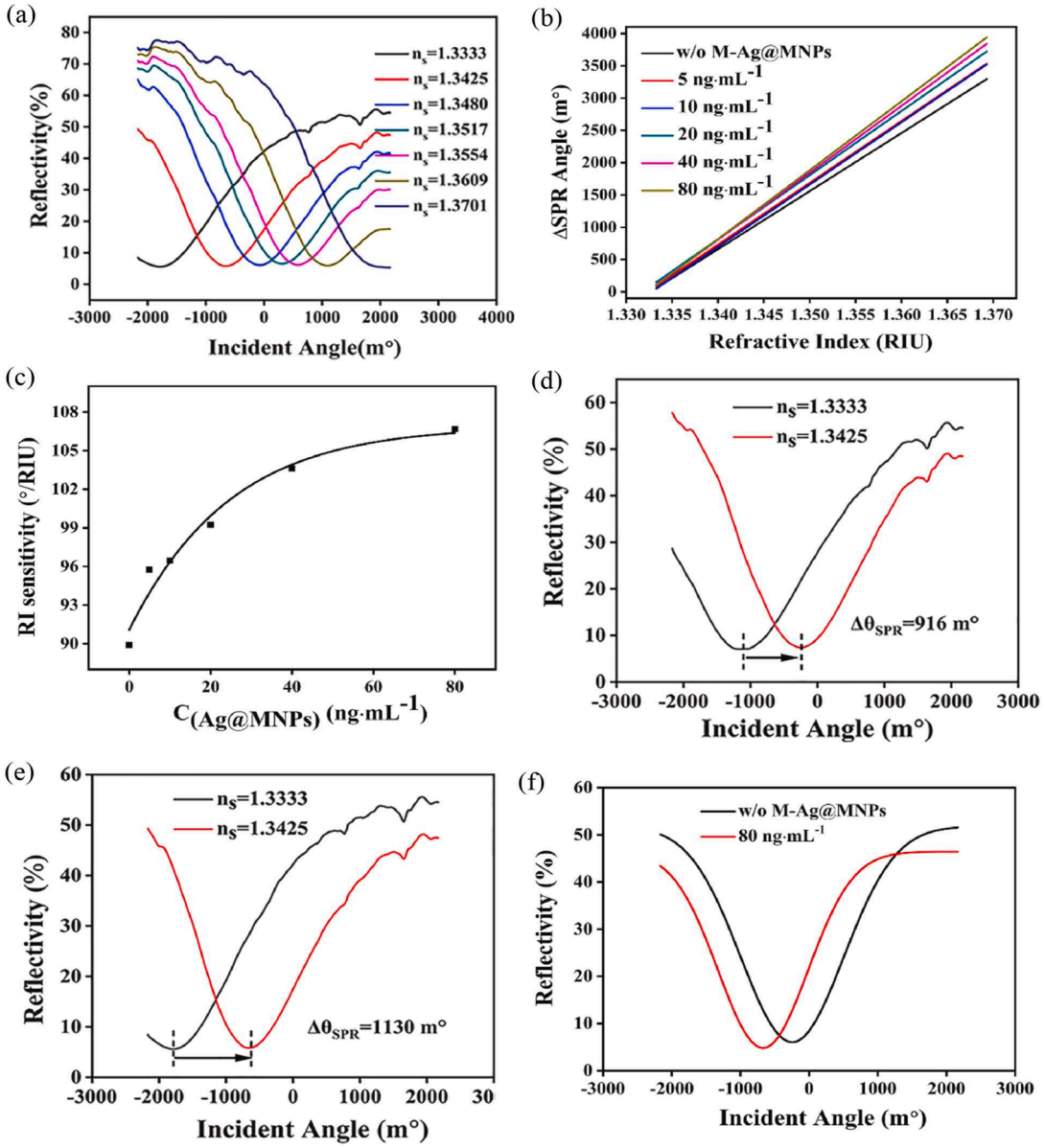

Fig. 8. (a) original SPR scan curve of 80 ng mL^{-1} M-Ag@MNPs over the range of 1.3333–1.3701, (b) Relationship between refractive index and SPR angle shifts with 0–80 ng mL^{-1} M-Ag@MNPs, (c) variation of RI sensitivity with 0–80 ng mL^{-1} M-Ag@MNPs of (b). Raw SPR curve before, (d) and after, (e) self-assembly of 80 ng mL^{-1} M-Ag@MNPs in deionized water (black) and 5% NaCl solution (RI = 1.3425) (red), (f) SPR scan curve in 5% NaCl solution (RI = 1.3425) of bare gold and M-Ag@MNPs after Gaussian simulation. Figs. (a)–(f) reprinted from [130], with permission from Elsevier.

superior MR value. Surprisingly, like AMR technique, investigations on the detection of cancer biomarkers based on TMR technique are lacking. Of all three types of MR biosensors, GMR is the only technique with available investigations on the detection of cancer biomarkers attributable to its moderate MR ratio, simplicity in nanofabrication process, and high linearity. So far, GMR sensors have achieved considerable success in the detection of biomarkers associated with various cancers including prostate cancer, melanoma, skin cancer, lung cancer etc. In this regard, various technologies, and novel ideas such as integration of magnetic flux concentrators (MFCs) and the microfluidic channels, employment of novel materials and antibodies specific to analyte of interests and utilization of cheap and simple fabrication techniques such as MEMS have been applied to various sensors and detection systems. These enabled the ultrasensitive detection of low concentration analytes of clinical interest, realization of low-cost assays, multiplex detection, contactless detection, real time measurement, realization of portable devices and attainment of excellent specificity among others.

In the future, the deployment of GMR and broadly MR sensors in POCT facilities, rapid measurement and wearable devices is highly anticipated with the improvement of surface chemical modification of the sensing devices through the deployment of adjusted versions of the prevailing sandwich, competitive and direct assays. Additionally, exploration of highly selective immobilizations as well as reinforcement of the existing assay time reduction approaches are proposed to be part of future investigation. Moreover, the successful deployment of TMR sensors for the ultrasensitive detection of low concentrations cancer biomarkers is subject to devising novel technologies that can mitigate the increased noise level resulting from the discontinuities in the tunnel barrier. More importantly, considering the increased desire to the realization of wearable devices, the direction of future research requires significant contribution towards the realization of a cost-effective way of fabricating flexible MR stacks in large-scale. Also, despite the promising performance of magneto-plasmonic sensors arising from the plasmonic properties of magneto-plasmonic nanostructures, investigations on the

Table 9
A summary of magneto-plasmonic sensors for the detection of cancer biomarkers.

Sensor	LOD	Magnetic Material/ Functionalization	Biomarker	Cancer Type	Refs.
SPR	3.29 ng/ mL	Magnetite nanorods containing ordered mesocages-silver nanoclusters (MNOM@AgNCs)	Programmed death ligand 1 (PD-L1)	Various cancer types	[127]
SPR	1.36 pg/ mL	Fe3O4-coated silver magnetoplasmonic nanoparticles (M-Ag@MNPs)	Siglec-15	Various cancer types	[130]
SPR	8.31 fM	Antibodies (anti-CD52A)-functionalized gold-coated magnetic nanoparticles (mAuNPs)	CD5, also known as lymphocyte antigen T1,	Lymphoma	[135]
SERS	~10 cells per mL	Anti-CEA/4-ATP/ Fe3O4-Au	CEA-expressed A549 cells		[139]

detection of cancers biomarkers using these sensors are extremely lacking. Thus, researchers are encouraged to explore this promising perspective especially in the areas linked to the improvement of the magneto-plasmonic nanostructures in terms of enhancement of electromagnetic fields, sensitivity, specificity, signal to noise ratio, and determination of spectral responses with application of magnetic field. Moreover, considering increased interest towards SERS sensing technique among other plasmonic techniques, incorporation of novel SERS materials capable of detecting low concentrations of cancer biomarkers with excellent sensitivity, selectivity and linearity is further expected to play a significant role toward the development of magneto-plasmonic sensors for the detection of cancer biomarkers. With tackling of the above issues and deployment of innovative ideas in the areas of micro/ nanofabrications, microfluidic technologies, point-of-care technologies, materials engineering, surface chemistry and lab-on-a-chip sensor integration among others; the application of both MR and magneto-plasmonic sensors for the detection of cancer biomarkers is anticipated to be significantly strengthened. By extension, difficulties related to the device portability, device operation, cost effectiveness, early detection/diagnosis, reliability, and general comfort will be notably mitigated. Concisely, the significance of MR and magneto-plasmonic biosensors in early cancer detection lies in their potential to revolutionize cancer diagnostics and improve patient outcomes. By enabling non-invasive, sensitive, and specific detection of cancer biomarkers, these biosensors could shift the paradigm of cancer management towards early intervention and personalized medicine. The scientific community's continued research and collaboration in this area will be critical for refining these technologies, establishing their clinical utility, and ultimately contributing to the fight against cancer on a global scale. The successful translation of MR and magneto-plasmonic biosensors into clinical practice has the potential to save countless lives and significantly reduce the burden of cancer worldwide.

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.

Data availability

Data will be made available on request.

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