Principle and Application of Biophotonic Chips

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Abstract. Contemporarily, biophotonic chips have garnered significant attention from researchers due to their strong immunity to electromagnetic interference, high sensitivity, rapid response rate, and relatively simple structural design. They have found extensive applications in fields such as medical diagnosis, food quality and safety testing, environmental monitoring, and national security. This article provides an overview of the development history, fundamental principles, applications, and fabrication processes of biophotonic chips. The earliest development of biophotonic chips can be traced back to the end of the 20th century. The basic principle involves the interaction of light, utilizing technologies like photonic crystals, surface plasmon resonance, and fluorescence spectroscopy to achieve the detection and analysis of biological molecules. The article briefly describes the fabrication process of biophotonic chips, which involves intricate techniques such as photolithography and electron beam exposure. Furthermore, it analyzes and discusses their widespread applications in medical diagnosis, drug development, and environmental monitoring, among other fields. Lastly, the study evaluates the key challenges present in biophotonic chips and provides an analysis of their future development prospects.

Keywords: Biophotonic chips; photolithography; medical diagnosis.

1. Introduction

Biophotonic chips, also known as biochips or photonic biochips, represent a significant advancement in the field of biotechnology and photonics. These chips integrate photonic and biological components on a single platform, enabling the manipulation and analysis of biological samples using light-based techniques. The development of biophotonic chips has a rich history that spans several decades. In a sense, the very concept of a biochip was made possible by the work of Fred Sanger and Walter Gilbert, who were awarded a Nobel Prize in 1980 for their pioneering DNA sequencing approach that is widely used today [1]. Early research focused on the integration of optical components, such as waveguides and sensors, with biological systems. Over time, advancements in nanofabrication techniques and materials science allowed for the miniaturization and mass production of biochips, leading to their widespread adoption in various applications, such as, Digital-micro udic biochips (DMFBs) are revolutionizing laboratory procedures for point-of-care clinical diagnostics, environmental monitoring, and drug discovery [2]. The research significance of biophotonic chips lies in their ability to revolutionize several areas of biotechnology and healthcare. These chips offer precise control over light-matter interactions, enabling enhanced sensing, imaging, and analysis of biological samples. They are revolutionizing laboratory procedures for point-of-care clinical diagnostics, environmental monitoring, and drug discovery [3]. By providing high sensitivity, specificity, and speed, biophotonic chips can significantly improve the accuracy and efficiency of biomedical research and clinical diagnostics. Furthermore, biophotonic chips hold promise for personalized medicine, point-of-care testing, and environmental monitoring. Their compact size, portability, and potential for integration with other technologies make them versatile tools for various applications. Ongoing research focuses on optimizing the performance of biochips, exploring new functionalities, and developing novel manufacturing techniques to further advance their capabilities.

Biophotonic chips have a wide range of applications in various fields. Here are some notable applications: High-throughput DNA sequencing, Cole Trapnell and et discuss the use of a biophotonic chip-based DNA sequencing platform for high-throughput sequencing of a viral genome [4]. The biophotonic chip enables the detection of individual DNA molecules in real-time, allowing for rapid and accurate sequencing. Label-free protein analysis, H. Bayley and et describe the application of a

biophotonic chip-based nanopore system for label-free analysis of protein-protein interactions. The biophotonic chip with nanopores allows for the direct detection and characterization of individual proteins, enabling the study of protein binding kinetics and conformational changes. Cellular assays for drug screening and highlight the use of a biophotonic chip-based high-content imaging system for cellular assays in drug screening [5]. The biophotonic chip enables the visualization analysis of cell viability and cell death in multicellular tumor spheroids, facilitating the evaluation of drug efficacy.

The field of biophotonics has witnessed remarkable advancements in recent years, driven by the integration of optics and photonics with biology and medicine. Among the various innovative technologies that have emerged, biophotonic chips hold tremendous potential for revolutionizing diagnostics, therapeutics, and biomedical research. With their ability to manipulate and analyze light at the nanoscale, biophotonic chips offer unprecedented opportunities for high-throughput, label-free, and real-time detection and analysis of biomolecules and cellular processes. This review aims to provide a comprehensive overview of the principles and applications of biophotonic chips, highlighting their significance and impact in various fields. We will discuss the Basic description of biophotonic chips, the Principle and Mechanism of biophotonic chips, the Fabrication and performances of biophotonic chips, the Applications of biophotonic chips and finally Limitations and Future outlooks of biophotonic chips in this article.

2. Basic Description

Biophotonic chips represent a revolutionary technology that merges the fields of optics and biology, enabling precise manipulation and analysis of light at the nanoscale. These microscale devices incorporate both optical components and biological elements to create a platform for high-throughput, label-free, and real-time detection and analysis of biomolecules and cellular processes. By harnessing the power of light, biophotonic chips offer tremendous potential for advancements in various fields, including biomedical diagnostics, therapeutics, and bioengineering. At the core of biophotonic chips are the optical components that enable the control and manipulation of light. These components include waveguides, microresonators, photonic crystals, and plasmonic structures. Waveguides are structures that guide light along a specific path, allowing for efficient light-matter interactions. Microresonators, on the other hand, confine light within a small volume, enhancing the sensitivity and detection limits of the chip. Photonic crystals and plasmonic structures provide unique optical properties, such as enhanced light-matter interactions and localized surface plasmon resonance, which allow for precise control over the interaction of light with biological samples.

In addition to the optical components, biophotonic chips incorporate biological elements that enable specific molecular recognition and interaction with biological samples. These biological elements can include DNA probes, antibodies, enzymes, and cells. They are either immobilized onto the chip surface or integrated within the chip structure. This integration of optics and biology creates a synergistic platform that enables precise and sensitive detection and analysis of biomolecules, cells, and cellular processes. The applications of biophotonic chips are vast and hold great promise in various fields. In biomedical diagnostics [5], biophotonic chips offer rapid and sensitive detection of biomarkers for disease diagnosis. They enable high-throughput DNA sequencing, facilitating the identification of genetic mutations associated with diseases. Additionally, biophotonic chips integrated with nanopores allow label-free analysis of protein-protein interactions, providing insights into disease pathways and drug targets [6].

Biophotonic chips also play a crucial role in therapeutics and drug discovery. By offering a high-content imaging system, these chips enable the analysis of cellular responses to drugs, facilitating the evaluation of drug efficacy [7]. They also allow for precise control over drug delivery and monitoring of cellular responses in real-time, enabling targeted therapies and personalized medicine. Moreover, biophotonic chips have significant implications in biotechnology and bioengineering. They enable advancements in areas such as synthetic biology and tissue engineering by providing precise control over light-mediated cellular processes. By integrating optogenetic tools, biophotonic chips allow for

spatiotemporal control over cellular behavior, which can be harnessed in tissue engineering and regenerative medicine. Furthermore, these chips integrated with microfluidic systems enable high-throughput analysis of cellular functions and metabolic pathways, facilitating the development of bioengineered systems for bioproduction and bioremediation.

In conclusion, biophotonic chips represent a cutting-edge technology that combines the power of optics and biology. By integrating optical components and biological elements, these chips enable high-throughput, label-free, and real-time detection and analysis of biomolecules and cellular processes. With applications ranging from biomedical diagnostics to therapeutics and bioengineering, these chips have the potential to revolutionize various fields, ultimately leading to advancements in healthcare, personalized medicine, and bioengineering.

3. Principle

Contemporarily, as people's concerns regarding food quality testing, medical diagnostics, environmental quality monitoring, and national security have increased, there has been a growing demand for analytical techniques that offer low concentrations, high precision, rapidity, and stability. This has led to greater expectations and requirements for the development of advanced analysis methods. Among these methods, the field of biosensors has garnered significant anticipation. Biosensors consist of bacteria, proteins, DNA, and related biomolecules that, upon contact with the sensor's transducer, initiate biochemical reactions. These reactions generate corresponding molecular information, which, after undergoing signal processing, can be converted into light, sound, electrical, or other signals. By aggregating and processing this information, it becomes possible to obtain details about the concentration and status of the target substance [8]. Over the past few years, bio-photonic chip technology has gained substantial attention and development compared to other biosensors. This is due to its superior resistance to interference, high sensitivity, and simplified structure, making it a promising avenue for research and advancement. A bio-photonic chip is typically used to directly interface with chemical solutions or biological media such as DNA, proteins, bacteria, and other biomaterials in order to facilitate biochemical reactions and obtain qualitative or quantitative data results. During the process of biochemical reactions, light interacts with target substances, resulting in changes in the phase, frequency, and intensity of light. By analyzing these changes in optical data, the system conducts backend data processing to extract relevant information about the target substances. Currently, based on variations in sensing principles, bio-photonic chips can be categorized into the following types: Bio-photonic chips based on spectral detection technology [9], bio-photonic chips utilizing optical fiber sensing technology [10], bio-photonic chips utilizing surface plasmon resonance technology [11], bio-photonic chips based on photonic crystal technology [12], bio-photonic chips based on microresonator ring technology [13] and bio-photonic chips employing Mach-Zehnder interferometry technology [14].

A sensor based on fluorescence spectroscopy utilizes the characteristics of fluorescent molecules to detect and analyze biological molecules [9]. Fluorescent molecules are excited to higher energy levels by absorbing light energy and subsequently emit fluorescence when returning to lower energy levels. The fluorescence properties of these molecules are influenced by molecular structure and environment, enabling them to be employed for detecting the presence, concentration, and interactions of molecules. The target biological molecule or analyte is combined with fluorescent molecules as labels to reflect the presence of the target substance in the fluorescence signal. Upon excitation by laser or other light sources, the fluorescent labeled molecules absorb light energy and transition to higher energy levels. When transitioning back to lower energy levels, the fluorescent labeled molecules emit fluorescence photons. The energy and wavelength of these fluorescence photons are associated with the molecular structure. The photons are detected by a spectrometer, and their intensity, lifetime, or frequency is measured through spectral analysis. Changes in the fluorescence signal are used to infer the presence and concentration of the target molecule.

Biophotonic chips based on fiber optic sensing technology primarily operate under two principles: transmission fiber optic sensing and reflection fiber optic sensing [10]. Transmission Fiber Optic Sensing: In transmission fiber optic sensing, light signals pass from a light source through a sample or a biological molecule recognition element, and then enter the fiber optic sensor for detection. The presence of the target molecule causes changes in the propagation characteristics of light within the fiber optic, such as attenuation, phase variation, or wavelength shift. These changes are detected and recorded by the sensor, and then inferred through spectral analysis or interference measurement to determine the presence and concentration of the target molecule. Reflection Fiber Optic Sensing: In reflection fiber optic sensing, light signals pass from a light source through a sample or a biological molecule recognition element, and then undergo reflection within the fiber optic sensor before returning to the detector. The presence of the target molecule also leads to changes in the propagation characteristics of light within the fiber optic, which are detected and analyzed through parameters such as amplitude, phase, or frequency within the reflected signal.

A biophotonic chip based on surface plasmon resonance (SPR) technology is a highly sensitive sensor used for real-time monitoring of interactions between biological molecules [11]. SPR sensors utilize the phenomenon of surface plasmon resonance on a metal surface (typically gold or silver). When incident light passes through a metal film on glass or metal surfaces, it interacts with the free electrons in the metal, leading to coupling of the electromagnetic field. When the incident light angle reaches a specific value known as the resonance angle, surface plasmon resonance occurs, resulting in the formation of a localized electric field enhancement region on the metal surface, generating a resonance absorption peak. This technology, based on the phenomenon of surface plasmon resonance at the metal-dielectric interface, enables the detection and analysis of biological molecules by monitoring changes in optical signals induced by resonance.

A biophotonic chip based on photonic crystal is a highly sensitive sensor that utilizes the periodic optical structure of a photonic crystal to achieve detection and analysis of biological molecules [12]. The periodic structure of the photonic crystal guides light waves of specific wavelengths to undergo Bragg diffraction within the lattice, preventing their propagation within the photonic bandgap (forbidden band) and leading to the formation of a photonic bandgap. When target biological molecules interact with the bio-molecular recognition elements (antibodies, oligonucleotides, etc.) on the surface of the photonic crystal, changes in refractive index alter the Bragg diffraction conditions of the photonic crystal, thereby altering the position and properties of the photonic bandgap.

4. Fabrication and Performances

The fabrication and performance of biophotonic chips involve the integration of optical components with biological materials to enable various applications in biomedicine, biochemical sensing, and healthcare [13, 14]. These chips utilize light to interact with biological samples and provide valuable information about their composition and behavior. The fabrication process of biophotonic chips typically involves several step [15]:

Design: The chip's design is created using computer-aided design (CAD) software, taking into account the desired functionality and the specific requirements of the application.

Substrate preparation: A suitable substrate, such as silicon or glass, is prepared by cleaning and deposition of necessary layers, such as an insulating layer.

Photolithography: Photoresist, a photosensitive material, is applied to the substrate, followed by exposure to UV light through a photomask. This process defines the patterns for subsequent steps.

Etching: Etching techniques are used to selectively remove material from the substrate, according to the defined patterns from photolithography. This creates features like waveguides and microfluidic channels.

Deposition and integration: Various materials, such as polymers, metals, and biomolecules, are deposited onto the substrate using techniques like physical vapor deposition (PVD), chemical vapor deposition (CVD), or spin-coating. These materials are crucial for achieving the desired functionality.

Characterization and testing: The fabricated chip is then characterized and tested to ensure its performance meets the design specifications.

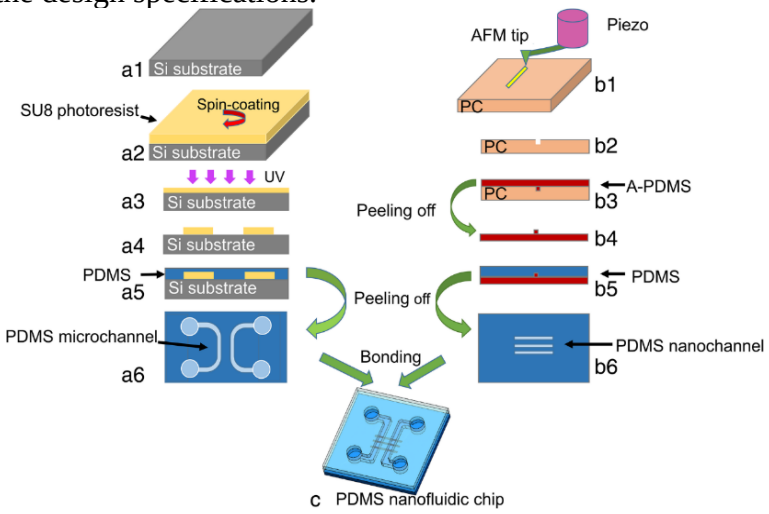


Fig. 1 Flowchart of nanofluidic chip fabrication

Biophotonic chips offer several key performances:

High sensitivity: A photonic crystal is a periodic dielectric nanostructure designed to allow or block the propagation of electromagnetic waves of certain wavelengths, making it an attractive optical material for controlling and manipulating light. They can detect extremely low concentrations of biological analytes, enabling highly sensitive measurements [16].

Real-time monitoring: Real-time monitoring of biophotonic chips involves the continuous and instant measurement of various parameters within the chip. This monitoring process helps in understanding the chip's performance, optimizing its functionality, and ensuring its reliability. These chips can provide real-time monitoring of biological samples, allowing for dynamic analysis of biological processes and reactions [17].

Multiplexing capability: The multiplexing capability of a biophotonic chip refers to its ability to perform multiple operations or measurements simultaneously. In the context of biophotonics, multiplexing is particularly valuable as it allows for efficient and parallel analysis of various biological samples or processes. Biophotonic chips can be designed to simultaneously analyze multiple analytes, providing efficient and parallel analysis [18].

Miniaturization: The miniaturization of biophotonic chips is a crucial aspect in the field of biophotonics as it enables compact and portable devices for various applications in healthcare, diagnostics, and life sciences. These chips are typically compact, allowing for integration into portable devices, handheld instruments, or lab-on-a-chip systems [19].

Biocompatibility: The biocompatibility of a biophotonic chip refers to its ability to interact safely and effectively with biological systems without causing any adverse effects. This is an important consideration when developing and using such chips for applications in biology, medicine, and biotechnology. The materials used in biophotonic chips are often biocompatible, enabling their use in biological environments without causing adverse effects [20].

The field of biophotonics is rapidly advancing, and the fabrication techniques and performances of biophotonic chips continue to evolve to enable new applications in healthcare, diagnostics, and biological research.

5. Applications

In recent decades, the maturation of CMOS technology has significantly advanced the development of biophotonic chips. Unlike traditional chips that rely on carriers for information transport, photonic chips use light as their transmission medium, enabling signal transmission in the terahertz spectrum. As a result, biophotonic chips have emerged as highly efficient platforms for

biosensing, medical diagnostics, drug screening, and bio-microfluidics. Biophotonic chips interact with biomolecules, cells, or tissues, granting researchers the capability to detect and analyze specific biomolecules or biochemical reactions. Such chips have applications ranging from DNA sequencing and protein analysis to disease detection. Although there are various technologies for preparing biosensors, silicon-integrated circuits stand out due to their maturity. Consequently, integrated circuits based on biosilicon photonic detectors are among the most promising technologies today [21]. Silicon photon detectors, in particular, are esteemed for their real-time response to infrared light signals between the tested sample and the receptor molecule. Their notable sensitivity and reliability make them ideal for continuous, quantitative, label-free biosensing. Technologies like Mach–Zehnder interferometers (MZIs) [22], Microring resonators (MRRs) [23], Microdisk resonators (MDRs) [24], Bragg grating resonators [25], and one-dimensional (1D) or two-dimensional (2D) photonic crystals (PhCs) [26] have long been staples in the biosensing and diagnostic arenas (Fig. 2).

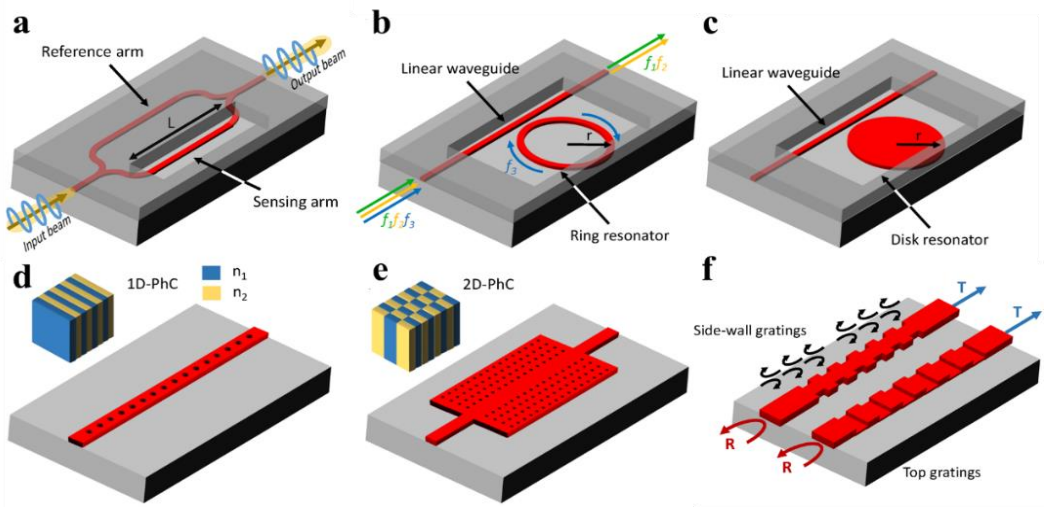


Fig. 2 (a) Illustration of a typical Mach-Zundel interferometer. The light is split into two arms (the sensing arm and the reference arm) and recombined at the output through an on-chip Y-junction. The degree of interference is proportional to the change in RI occurring in the sensing arm. (b) Diagram of a conventional micro ring resonator (MRR) sensor. By using a bus waveguide, light is guided to couple into the resonator at a frequency corresponding to the resonant condition. (c) Diagram of a microdisk resonator sensor. (d) 1D conformation of a photonic crystal; (e) 2D conformation of a photonic crystal. Inset: schematic diagrams of each format showing periodic arrangements, with different colors representing materials with different indices. (f) Illustration of two types of Bragg grating devices with sidewall or top gratings. r and t are reflections and transmissions from the grating. 180° arrows represent large reflections across the grating.

MZIs stand as paramount optical instruments, adept at manipulating light waves to produce intricate interference patterns [27]. Their predominant adoption in the biosensing sphere can be attributed to their unparalleled proficiency in discerning infinitesimal variances in refractive indices or phases stemming from biomolecular interactions. In a groundbreaking 2016 study, Qin et al. unveiled a state-of-the-art label-free MZI optical biosensor [28]. Impressively, its numerically simulated sensitivity reached a staggering 115,000 rad/RIU-cm within a 16 μm-long slow-light domain, an enhancement by a factor of seven when juxtaposed with conventional MZI biosensors that possess millimeter-length sensing precincts. Concomitantly, Song B. et al. introduced an innovative label-free DNA biosensor anchored in a microfiber-assisted MZI, pioneering in situ real-time monitoring of DNA hybridization kinetics [29]. Intriguingly, the microfibers underwent meticulous alterations through the sequential deposition of a polylysine (PLL) monolayer and single-stranded DNA (ssDNA) probes. This intricate process facilitated the creation of ultra-sensitive surfaces tailored to bind specifically with complementary ssDNA. An astoundingly low detection threshold of 0.0001 pmol/μL was achieved using a U-shaped microcavity spanning 176.88 μm. Given its diminutive form factor, seamless integrative potential, and pronounced sensitivity towards DNA

hybridization, this biosensor exhibits prodigious promise as an indispensable tool in arenas like medical diagnostics, oncological screenings, and comprehensive medical assessments. The diverse applications of MZIs in biosensing undeniably leave an indelible mark on pivotal sectors, including medical diagnostics, pharmacological explorations, molecular biology, and environmental scrutiny. These sophisticated instruments persistently underscore their cardinal role in facilitating the precise, real-time elucidation of intricate biomolecular interactions.

Microring resonators stand as intricate optical contrivances, intricately designed with a resonant cavity structure encapsulated within a circular waveguide. Their operational mechanism hinges on the nuanced shifts in resonant wavelengths instigated by alterations in the refractive index of the ambient medium. Their emergence in the biosensing domain has been met with considerable acclaim, a sentiment stemming from their sterling sensitivity, diminutive stature, and prowess in rendering real-time snapshots of biomolecular interactions. In a seminal 2018 paper, Tan et al. unveiled a groundbreaking technique of box spectroscopy, employing an ultra-miniaturized silicon MRR. This feat was achieved by ingeniously integrating a bending directional coupler, resulting in a staggering free spectral range (FSR) exceeding 30 nm [30]. Fast forward to 2020, Ali advanced a pioneering silicon photonic MRR tailored for the meticulous detection of malign cells coursing through the bloodstream [31]. This biosensor, with its impressive sensitivity exceeding 200 nm/RIU and a Q-factor reaching 1200, opens a new frontier for the hyper-selective identification of unlabeled neoplastic cells. The gamut of applications for microring resonators in the realm of biosensing traverses an expansive landscape, encapsulating sectors like medical diagnostics, molecular biology, pharmacological innovation, and environmental surveillance. Their supreme sensitivity, capability for real-time surveillance, and propensity for further miniaturization underscore their invaluable contribution in propelling our comprehension of biomolecular interactions and catalyzing the genesis of avant-garde sensing technologies.

Microdisk resonators, colloquially known as microdisk cavities or microdisk resonant cavities, epitomize compact optical marvels that adeptly trap light within a disk-like resonant cavity. With their distinguished high Q factor, they have been instrumental across a pantheon of applications, notably in biosensing. In an avant-garde study, Sun et al. showcased a miniaturized spectrometer anchored on a singular tunable MDR [32]. Remarkably, its unique design, leveraging a lone MDR, ensures an exclusive channel for all spectral constituents. Its diminutive stature strikes an optimal equilibrium among spectral resolution, spectral breadth, and dynamic range, boasting an impressive resolution of 0.01 nm across a 20 nm spectral ambit. These sensors, with their heightened sensitivity, compact design, and affinity with microfabrication techniques, are pivotal in bolstering advancements in medical diagnostics, molecular biology, and environmental monitoring.

Bragg grating resonators, conceptualized on the bedrock of Bragg gratings, are state-of-the-art devices. They exploit periodic fluctuations in refractive indices to selectively mirror specific light wavelengths. A trailblazing endeavor by Chen et al. led to the development of a fiber-optic biosensing paradigm tailored for nuanced biomolecular detection, harnessing a high-reflectivity fiber Bragg grating (FBG) [33]. This robust platform utilized optical fibers exuding ultra-narrow band cladding mode resonance while ensuring the integrity of the fiber gratings, amplifying its longevity. Its superior Q-factor metrics, alongside its label-free disposition and GO coating, culminated in a detection limit plummeting to an impressive 32 pM for IgG. With its stellar detection prowess, this platform is poised to be a frontrunner in biomolecular detection. The integration of Bragg grating resonator with microarray platforms can potentially usher in an era of simultaneous multi-biomolecular interactions monitoring, setting the stage for high-throughput analyses spanning protein binding to DNA hybridization.

1D and 2D photonic crystals manifest as structured lattices, characterized by periodic refractive index perturbations on micro or nano scales, skillfully governing light propagation. These intricate architectures have catalyzed paradigm shifts in biological research, courtesy of their precision-driven interaction with light. In a pioneering study, Abderrahmane A. et al. delved into a 1D photonic crystal design utilizing multilayers of 2D gallium sulfide and a 2D dolomite [GaS/Mica]ND[GaS/Mica]N

and multilayers of 2D gallium sulfide [GaS/G]ND[GaS/G]N [34]. They investigated the performance of this photonic crystal as a biosensor using glucose concentration. The sensor showed a high sensitivity of 832 nm/RIU, a high quality factor of 1.46 × 105 RIU-1, a Q-factor of more than 105, and a minimum detection limit of 3.4 × 10-7 RIU. Similarly, in 2020, Li Q et al conceived a biomimetic sensing chip tailored for miRNA-21 detection, employing photonic crystals and yielding miRNA-21 detection sensitivities spanning 1 pM to 10 nM, signifying its monumental potential in preemptive oncological diagnostics [35]. These endeavors underscore the multifaceted utility of 1D and 2D photonic crystals in biological research. As we charter the waters of burgeoning photonics, the scientific fraternity remains poised to unearth pioneering avenues, leveraging photonic crystals, and furthering our understanding and technological prowess in life sciences.

6. Limitations & Prospects

Contemporary biophotonic chips stand poised as quintessential platforms, underpinning a myriad of applications ranging from pharmaceutical development and environmental surveillance to health prognostication and clinical diagnostics. By harnessing the sophistication of the established CMOS technology, silicon-centric biophotonic chips have the potential to attain elevated levels of integration, diminutive sizes, economic feasibility, and aptitude for large-scale fabrication and deployment. While the existing iteration of biophotonic chips proffers an amalgamation of multifarious sensor functionalities, their evolution is not without impediments. Foremost among these is the intricate orchestration of diverse optical and biological constituents upon a unified substrate, which necessitates the meticulous alignment of light emitters, detectors, waveguides, and specimen management systems. Drawing from the tenets of CMOS technology, it is anticipated that ensuing research endeavors will crystallize the vision of a wholly integrated, portable biosensing milieu. Stemming from this integration quandary is the secondary challenge of augmenting the sensitivity of in silico sensing for the label-free discernment of petite molecular analytes. Notwithstanding the heightened sensitivity of biophotonic chips, ensuring specificity, particularly in the labyrinthine milieu of biological samples, remains elusive. Non-specific interactions and aberrant binding events could precipitate data inaccuracies.

In addition, the dearth of standardized fabrication and evaluation protocols for biophotonic chips complicates comparative analyses across diverse device genres and experimental outcomes. While the prowess of CMOS technology may palliate these concerns, inherent performance constraints of silicon-based entities remain formidable adversaries. The fourth challenge orbits around material constraints. Striking a harmonious balance between biocompatibility, optical lucidity, and manufacturability renders the material selection for crafting biophotonic chips a conundrum. Although silicon derivatives exhibit potential in these domains, their efficacy mandates further scrutiny. Last but not least the operational robustness of biophotonic chips, especially under varied environmental conditions, is of paramount importance. Ensuring resilience against environmental vicissitudes is imperative. Nevertheless, the tantalizing prospects offered by biophotonic chips (encapsulating sensitivity, rapidity, and portability) have galvanized prodigious research endeavors. It is by surmounting these challenges that we can pave the way for biophotonic chips replete with nuanced functionalities, thereby actualizing the profound vision of facilitating accurate analyses of intricate biological samples using a solitary chip. This capability would undoubtedly revolutionize future diagnostic paradigms. As the global scientific community fervently champions the potential of biophotonic chips, we remain sanguine that genuine lab-on-a-chip and portable biosensing platforms will materialize, heralding a transformative epoch in global healthcare

7. Conclusion

Hierarchical structural organization and diverse chemical reactions enable biophotonic structures to finely control the propagation, scattering and emission of light, thus showing that biophotons have

great potential for applications in transparency, camouflage, protection, imitation, signal transmission and exchange. In this review, we have summarized the research progress of biophotonic chips, including their conceptual composition, working principle, preparation, and measurement characterization. Its main applications are also described. These results will provide useful insights into the design and application of biophotonic chips. As a result, biophotonic chips have become an efficient platform for biosensing, medical diagnostics, drug screening, and bio-microfluidics.

8. Author Contribution

All the authors contributed equally and their names were listed in alphabetical order.

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