Current status and outlook for silicon-based optical biosensors

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\textbf{A B S T R A C T}

The importance of silicon photonic devices extends beyond passive structures for light guiding and light emission. Nano- and microstructured silicon photonic devices have emerged as viable gas, chemical, and biological sensors. The advantages of these silicon-based optical biosensors for high sensitivity detection include a low analyte volume requirement, reduced size, and compatibility with existing CMOS technology. Several advances in ring resonators, waveguides, and various porous silicon photonic structures for biosensing applications will be reviewed.

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1. Introduction

The promise of silicon photonics for integration with standard microelectronics has been discussed for more than two decades with the expectation that such optoelectronic integrated circuits would outperform electrical or optical circuits alone. In 1987, electro-optic effects in silicon were predicted to lead to the development of active components, including modulators and switches \cite{1,2}. It is only within the last few years that high speed CMOS-compatible electro-optic modulators and other high quality silicon photonic devices have been demonstrated \cite{3–7}. As silicon photonics technology matured, it also became apparent that non-traditional applications such as chemical and biological detection could be achieved using the same silicon photonics platform. Moreover, some silicon photonics technology, such as porous silicon-based devices, that has struggled to achieve the necessary low losses, fast modulation speeds, and high quality resonances for monolithic or hybrid optoelectronic integration, has excelled as high sensitivity chemical and biological sensors. In Section 2, an overview of porous silicon sensor technology is presented, along with a detailed examination of emerging porous silicon waveguide biosensors. Sections 3 and 4 highlight more conventional silicon photonics technology that was originally developed for optoelectronic integrated circuits and is now being utilized for sensing applications.

2. Porous silicon sensors

Porous silicon is a crystalline material that consists of nanometer to micron-sized columnar pores in a silicon matrix \cite{8}, as shown in Fig. 1. Due to its light emission properties and relatively simple fabrication techniques, porous silicon was considered a promising material for optoelectronic applications. However, with electroluminescence efficiencies on the order of 1\% \cite{9,10}, typical waveguide losses well above 1 dB/cm \cite{11–14}, and sub-MHz modulator switching speeds \cite{15–18}, porous silicon photonic components have struggled to compete with the capabilities of traditional lithographically defined silicon photonic components. Over the past decade, the major growth area for porous silicon has been in biological applications where porous silicon’s intrinsic material losses and low luminescence efficiency are not insurmountable limitations.

The large internal surface area of porous silicon structures, which can range up to a few hundred square meters per cubic centimeter, provides a significant advantage to porous silicon sensors. Porous silicon can serve as host to a far greater number of molecules than can be accommodated on a planar, solid surface. In most cases, the porous silicon both locally concentrates molecules and enables detection of those molecules via a change in porous silicon refractive index. For pore sizes much smaller than the wavelength of light, effective medium approximations are employed to determine the refractive index of porous silicon. The refractive index is a weighted average of the refractive index of silicon and the refractive index of the pores (e.g., air, chemical linkers, biomolecules, etc.) \cite{19,20}. The specific weighing factor depends on the porous silicon porosity and morphology.
simplest porous silicon sensors employ a single thin film [21–25], while more complicated designs including waveguides [26–28], Bragg mirrors [29,30], rugate filters [31–33], and microcavities [34–39] are often used for higher sensitivity and more versatile applications. Resonant microcavities and waveguides have the potential to achieve the lowest detection limits as the sensitivity scales with the light–matter interaction strength between localized electric fields and molecules under test. For porous silicon with pore sizes greater than a few hundred nanometers, photonic crystal architectures have been utilized to enable the detection of chemical and biological species [40,41].

Due to the relatively small pore size of mesoporous silicon, typically 2–50 nm, which has been the most highly characterized type of porous silicon for a variety of applications, the majority of early porous silicon sensing work focused on vapor detection by either optical or electrical transduction schemes [23–25,32,42–46]. Detection limits in the ppm–ppb range were commonly reported [23,43]. Chemical sensing was also performed using a variety of porous silicon structures, including single layers, Bragg mirrors, microcavities, and waveguides [28,33,39,47]. In most cases, the minimum detectable refractive index change was on the order of $1 \times 10^{-4}$ [30,38]. Fig. 2 shows an example of a porous silicon waveguide sensor response to the infiltration of various liquids.

The large internal surface area of porous silicon is also advantageous for biological detection. For label-free biosensors that do not require the attachment of a fluorescent tag on the species to be detected, the sensing protocol is illustrated in Fig. 3. The sensor surface is functionalized with appropriate chemical linkers and probe molecules. The design of the probe is the key to selective detection of a particular molecule; no other species should rigorously bind to the probes. The molecules to be detected, noted as target molecules, selectively attach to the probes. In practical conditions outside of a controlled laboratory environment, one of the primary challenges facing sensors is bringing the target molecules in contact with the probe molecules. The more probes that are present on the sensor, the greater the chance that a target molecule will find its way and attach to a probe. Several traditional sensing platforms, including surface acoustic wave [48], surface plasmon resonance (SPR) [49], and fiber optics [50] have explored the use of porous materials to improve their fundamental detection limits. Biomolecule detection using a porous silicon platform was pioneered by Sailor and coworkers in the late 1990s [21]. DNA has been the most commonly detected target molecule, although there have been several demonstrations of enzyme, virus, and protein detection using various porous silicon structures and optical transduction methods [22,31,35,36,38,51,52]. While typical detection limits for porous silicon biosensors are on the order of micromolar concentrations of target molecules, lower concentrations have been reported in several instances. For example, significantly lower DNA detection limits (<nM) have been reported based on an oxidation–hydrolysis process that implies a decrease in the effective optical thickness of porous silicon upon interaction with negatively charged DNA complexes [21,53]; the precision and selectivity of this method and its dependence on particular functionalization protocols remain to be rigorously investigated.

A recent advance in porous silicon biosensing has been the introduction of the porous silicon waveguide biosensor [26,27]. Porous silicon waveguides have been well characterized for potential optoelectronic applications and this knowledge is now being leveraged for sensing applications. One significant advantage of the waveguide structure over other porous silicon sensor geometries is that light is guided in the plane, which
facilitates monolithic or hybrid integration with optical source and detector components as well as microfluidic channels. Moreover, the active sensing region of the waveguide where the electric field is locally confined is the top layer, which is easily accessible to probe and target molecules. Using either a prism or grating to couple light into the porous silicon waveguides, the detection of DNA and various chemical species has been demonstrated [27, 54].

Most recently, in order to maximize the probe molecule coverage within the enormous internal surface area of porous silicon waveguides, stepwise synthesis of DNA molecules inside the waveguides was demonstrated [55]. It was estimated that probe coverage in the porous silicon was more than four times greater using the stepwise synthesis method compared to directly infiltrating pre-synthesized DNA strands. In addition, the high sensitivity of the porous silicon waveguide was illustrated by its ability to detect the addition of single DNA bases, as shown in Fig. 4.

3. Silicon ring resonator sensors

In contrast to porous silicon structures with limitations in switching speeds and optical quality, silicon ring and disk resonators have found broad applications in optoelectronic devices, especially as modulators and switches [3, 4]. The high quality resonances and small mode volumes of these resonators create localized regions of electric field enhancement. Light is typically coupled into these regions using a bus waveguide or tapered fiber. When biomolecules are immobilized on the ring or disk, there exists a strong field–matter interaction, which is highly favorable for low detection limit biosensing. The use of microrings and microdisks for high sensitivity sensing applications was experimentally demonstrated [58–62]. Molecular binding at micromolar concentrations and changes in refractive index as low as $10^{-5}$ for various liquids were reported. Very recently, a ring resonator made of Hydex, a low loss glass-based material, was used to detect 500 nM concentration of DNA [62].

4. Silicon waveguide sensors

Waveguides have been used for sensing applications for more than two decades [64–67, 73]. While propagating waveguide modes are confined to the core of the waveguides, evanescent fields extend into the substrate and cover regions. When the local dielectric in the cover changes, for example due to the presence of the chemical or biological molecules, the mode profile also changes. The molecules can be detected by either attaching fluorophores to the molecules and measuring the fluorescence that is excited by the evanescent field, or by creating a waveguide interferometer and measuring the phase change between the arm of the interferometer exposed to the molecules and the control arm that is not exposed to the molecules.

Recent advances in silicon photonics have led to significant increases in the sensitivity of silicon waveguide sensors. Denmure et al. [68] shrunk the size of the silicon core down to 0.26 μm to increase the intensity of the electric field at the waveguide core/cover interface. By reducing the waveguide core thickness, the waveguide mode becomes delocalized and expands into the cover region to increase the field–matter interaction with chemical and biological molecules on the surface. By fabricating these silicon wire waveguides in the form of a Mach–Zehnder interferometer, improved detection sensitivity compared to traditional slab waveguide was achieved.

Fig. 5 compares the electric field distribution in a silicon wire waveguide [68] and porous silicon waveguide [27]. The shaded areas in the figure show where light–matter interaction and active sensing can take place. The silicon wire waveguide, fabricated using a silicon-on-insulator wafer, only allows interaction of the electric field with chemical and biological species in the cover region above the waveguide. The porous silicon waveguide allows interaction not only in the cover region outside the waveguide, but also throughout the waveguide, given the porous nature of the material. As an example of the biological sensing capabilities of these two structures, a 4 nm add-layer of biomolecules with refractive index of 1.5 is considered. These molecules bind to the surface of the silicon wire waveguide and bind throughout the porous silicon waveguide internal surface area. The presence of these molecules will cause a change in the effective index of the waveguide mode by 0.0037 for the silicon wire waveguide and 0.1041 for the porous silicon waveguide.

Another approach to locally increasing the electric field intensity in order to create stronger light–matter interaction is to form slot waveguides. Slot waveguides allow light to be guided in a nanometer-scale slot of low refractive index material sandwiched between two strips of high index material, due to a large discontinuity of the electric field at the high index contrast interfaces [69]. The use of slot waveguides as biosensors is an emerging field. Recent theoretical reports suggest that the excitation efficiency of fluorophores in slot waveguides is up to 40% greater than the efficiency in slab waveguides, and slot waveguides can achieve improved sensitivity compared to silicon-on-insulator wire waveguides [70]. Very recently, Barrios et al. experimentally demonstrated chemical and biological molecule interaction for silicon ring resonator switches, modulators, and lasers, the expanded use of these devices as sensors is promising for the future. One important design consideration for these advanced sensor devices is how to best manage power dissipation and the effect of ambient temperature changes on the resonance wavelength. For very high-Q resonators, even small temperature drifts could cause a measurable resonance shift [63]; for sensor devices, these temperature drifts would cause false positive results.
progress. As the next steps towards integration with microfluidics and optoelectronic components are taken, the utility of these silicon photonic structures as practical and convenient sensing devices will continue to progress.

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References

[6] Luxtera is one example of a company formed in the last decade to develop a silicon photonics technology platform that enables monolithic opto-electronic devices manufactured in a CMOS process.