Intrinsic Limit of Detection for Coherent Biosensing Systems

Student Paper

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ABSTRACT

Optical biosensors have drawn great interest in the last years as they are able to detect trace amounts of biochemical substances without prior labeling. Interferometric structures with coherent phase read-out have recently shown to exhibit state-of-the-art limits of detections. Their fixed wavelength read-out system makes them a promising candidate for point-of-care devices for which cost is a critical factor. Over the last years the sensing community has mainly focused on the design of highly sensitive structures while little attention has been paid to the fundamental noise sources of the complete system and their influence on the optimization on the limit of detection. In this work, we analyze these noise and provide a series of guidelines to reach the fundamental limit of detection of coherent interferometric biosensors.

Keywords: photonic biosensor, Mach-Zehnder interferometer, coherent detection, fundamental limit of detection, evanescent field sensing

1 INTRODUCTION

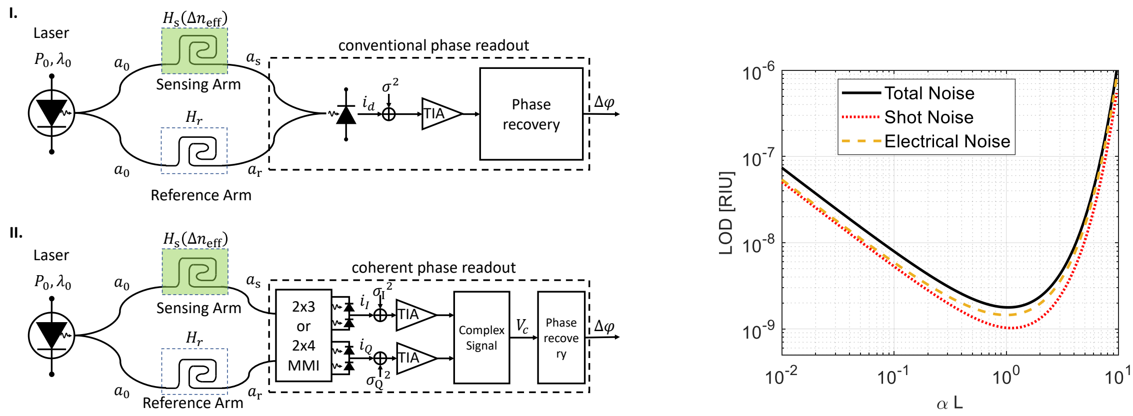
Photonic biosensors have shown to be capable of detecting trace amounts of biomolecules while keeping fabrication costs low and offering label-free detection [1]. Interferometric sensing architectures with coherent detection (using a 2x3 coupler at the interferometer output) have demonstrated *state-of-the-art* limit of detections (LOD) [2] [3], the smallest change in refractive index or concentration that can be measured with certainty. Due to the relaxed hardware requirements for the laser source compared to resonant structures which typically require wavelength sweeps, these interferometric systems are particularly suited for point-of-care devices for which cheap manufacturing is a critical factor. In the last decade there has been done a lot of research regarding the maximization of the biosensors overall sensitivity, for both resonant and interferometric architectures, using different waveguide geometries [4]–[6]. However, there is hardly any analysis about the fundamental limits of such biosensing systems. Here, we derive an analytical expression for the limit of detection of coherently detecting sensors, taking into account the noise and losses of such a system [7]. Based on this analysis, we provide clear guidelines on the optimization of sensing systems to improve the limit of detection.

2 COHERENT DETECTION

Direct and coherent detection schemes are compared in fig. 1(a). The sensing architecture consists in both cases of a Mach-Zehnder interferometer (MZI) with a sensing and a reference arm. Traditional phase read-outs typically recombine both signals in a Y-Junction or 1x2 Multi-Mode interferometer (MMI) resulting in an electrical signal

$$i_{\mathrm{d}} = \frac{RP_0}{2} \cdot \left[\frac{1 + e^{-2\alpha L}}{2} + e^{-\alpha L} \cos\left(k_0 L \cdot \Delta n_{\mathrm{eff}}\right) \right] \tag{1}$$

where R is the responsivity of the detecting photodiode (PD), P_0 the power of the laser source assuming perfect coupling, α the amplitude attenuation, L the length of the sensing arm, $k_0 = 2\pi/\lambda_0$ with λ_0 the wavelength of the propagating light, and Δn_{eff} the change in effective refractive index caused by any homogeneous refractive index change in the sensing arms surrounding buffer. Fading of the *architectural sensitivity* S_{a}, where S_{a} is defined as $|\partial i_{\mathrm{d}}/\partial \Delta n_{\mathrm{eff}}|$, and directional phase ambiguity arise directly from the sinusoidal dependency. Different approaches have been suggested to circumnavigate these effects such as slightly modulating the phase [8] of the laser or thermally modulating the phase of the reference arm [9]. Coherent detection, shown schematically in fig.1(b), a more advanced approach from the telecommunication field [10], was suggested in [3] for the first time for photonic biosensors.



(a) (b)

Figure 1. (a) Schematically comparison between the a directly (I.) and coherently (II.) detecting phase read-out. (b) Limit of detection as a function of the sensor length , including losses, with shot, electrical and superimposed noise limit.

The resulting complex current follows

$$i_c = i_I + j \cdot i_Q = \frac{RP_0}{2} e^{-\alpha L} \cdot e^{j \cdot k_0 L \cdot \Delta n_{eff}}, \tag{2}$$

with j the imaginary unit, obviously having a constant architecture sensitivity

$$S_a = \frac{RP_0}{2} k_0 \cdot L \cdot e^{-\alpha L}. \tag{3}$$

It is worth highlighting that this expression is equal to the sensitivity of a system with a conventional direct detection scheme at its point of maximum sensitivity. Therefore, to this special case the derived expressions can be extended. The complex signal readout can be accomplished by a 2x3 or 2x4 MMI with their consecutive three to four PDs for detection, both showing equal performance [10].

3 INTRINSIC LIMIT OF DETECTION

The LOD is generally defined by

$$LOD = \frac{3\sigma}{S} = \frac{3\sigma}{S_{wg} S_a} \tag{4}$$

where σ represents the standard deviation of the measured signal, and $S_{wg} = |\partial \Delta n_{eff} / \partial n_c|$ the *waveguide sensitivity* transforming any homogeneous change in refractive index to its according change in effective refractive index of the propagating sensing mode. Maximizing *waveguide sensitivity* and *architecture sensitivity* has so far been the main focus to optimize the LOD, while little attention has been paid to the linear dependency of the LOD to σ. The fundamental noise σ seen in the complex plane can be formulated as follows

$$\sigma = \sqrt{\sigma_I^2 + \sigma_Q^2} = \sqrt{\sigma_{shot}^2 + \sigma_{elec}^2} \tag{5}$$

$$= \sqrt{q \frac{RP_0}{2} \left(1 + e^{-2\alpha L}\right) B + \eta_{elec} B} \tag{6}$$

where σ_{shot}^2 and σ_{elec}^2 are the shot and electrical noise powers monitored in the in- (I) and/or quadrature-phase (Q) component of the complex signal, B the inverse of the integration time (i.e. the bandwidth of the electrical low-pass filter), and $q = 1.6 \cdot 10^{-19}\,\mathrm{C}$ being the electron charge [7]. The resulting LOD can be formulated as

$$LOD = \frac{3}{\sqrt{2\pi}} \frac{\lambda_0}{S_{wg} L} \frac{1}{\sqrt{SNR}} \overset{L_{opt}}{\approx} \begin{cases} 1.94 \cdot \frac{\alpha \lambda_0}{S_{wg}} \cdot \sqrt{\frac{qB}{RP_0}}, & \text{if } \sigma_{shot}^2 \gg \sigma_{elec}^2 \text{ and } L_{opt} \approx \frac{1.11}{\alpha} \\ 2.6 \cdot \frac{\alpha \lambda_0}{S_{wg}} \cdot \frac{\eta_{elec} \sqrt{B}}{RP_0}, & \text{if } \sigma_{elec}^2 \gg \sigma_{shot}^2 \text{ and } L_{opt} = \frac{1}{\alpha}. \end{cases} \tag{7}$$

The signal-to-noise ratio SNR is defined as the ratio between the complex signal strength $\left(RP_0/2 \cdot e^{-\alpha L}\right)^2$ and its noise power σ^2. In figure 1(b) the LOD as a function of length L is shown for the following parameter set of $R = 1.05\,\mathrm{A/W}$, $P_0 = 0.05\,\mathrm{mW}$, $\lambda_0 = 1.55\,\mu\mathrm{m}$, $S_{wg} = 0.8\,\mathrm{RIU/RIU}$, $\alpha = 4.8\,\mathrm{Np/cm}$, $\eta_{elec} = 3\,\mathrm{pA}/\sqrt{\mathrm{Hz}}$ and $B = 100\,\mathrm{Hz}$ for a shot, electrical and superposed limited system. The minimal reachable LOD of such a system is approximately $2 \cdot 10^{-9}$ RIU for an impressive short length of around $2\,\mathrm{mm}$. It is worth highlighting that in case that the losses α are mainly due to the mode overlap with the buffer, i.e. $\alpha = \alpha_\mathrm{b} S_\mathrm{wg}$, the minimal reachable LOD becomes independent of the *waveguide sensitivity*. However, increasing waveguide *waveguide sensitivity* allows to reduce the optimum length. Furthermore, by moving from the near infra-red to the visible, i.e. shorter wavelengths, the LOD is improved in two different ways. First, due to the its linear dependency to λ_0 and second by the reduced absorptions losses $\alpha(\lambda_0)$ caused in the buffer media. Regardless which noise source is dominating, by choosing the bandwidth of the low-pass filter as narrow as possible the LOD can be further minimized due to $\sim \sqrt{B}$. But depending on the limiting noise source the LOD responds differently to increasing laser power P_0, scaling with $1/\sqrt{P_0}$ or $1/P_0$ for shot or electircal noise limit, respectively.

4 CONCLUSION

It has been demonstrated that the MZI based biosensors with coherent phase read-out are capable of reaching extraordinary LODs while maintaining small or moderate footprints. We have shown that reaching for the smallest LOD, the fundamental noise sources of the detection system and the absorption losses in the sensing window play a critical role in the design process. Depending on the limiting source different optimal lengths exits but $L = 1/\alpha$ results essentially in the same LOD in both cases. Furthermore, if losses increase at the same rate as the *waveguide sensitivity*, the optimization process of ultra highly *waveguide sensitivities* becomes less relevant. Using a narrow-band low pass filter for signal extraction has an improving effect on the LOD. By choosing a shorter wavelength, for example the visible regime ($\lambda_0 \approx 380 - 780\,\mathrm{nm}$), in comparison to the near infra-read ($\lambda_0 \approx 1.53 - 1.56\,\mu\mathrm{m}$) (C-Band), it has a drastic effect on the detection limit as the losses are lower by a factor of approximately 10^3. As moving to the visible light has a high impact on the photonic design process and performance the aforementioned has to be considered with caution. Nevertheless, already moving from the C to the O-Band ($1.26 - 1.36\,\mu\mathrm{m}$) will have an improving effect.

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