proceedings

Proceedings

Aptamer-Based Plasmonic Plastic Optical Fiber Biosensors: a focus on relevant applications †

Laura Pasquardini [1,*], Nunzio Cennamo [2] and Luigi Zeni [2]

1 Indivenire srl, Via Alla Cascata 56/C, 38123, Trento, Italy; l.pasquardini@indiveni.re
2 Department of Engineering, University of Campania "L. Vanvitelli", Via Roma 29, 81031, Aversa, Italy; nunzio.cennamo@unicampania.it; luigi.zeni@unicampania.it
* Correspondence: l.pasquardini@indiveni.re;
† Presented at the 2nd International Electronic Conference on Applied Sciences (ASEC 2021), online event, 15/10/2021 - 31/10/2021.

Abstract: Optical detection is one of the most used techniques as transduction method in biosensors and apart the conventional platform based on surface plasmon resonance (SPR), an emerging class of devices based on optical fibers, both silica and specially plastic optical fibers (POFs), is finding its route. On the other hand, aptamers represent the next frontier as biorecognition elements in biosensors, thanks to several advantages with respect to antibodies. The coupling of plasmonic plastic optical fiber probes with aptamers is here reported focusing on different relevant biological applications (e.g., Thrombin, Vascular Endothelial Growth Factor (VEGF), and SARS-CoV-2 Spike protein).

Keywords: surface plasmon resonance (SPR); aptamers; plastic optical fiber; biosensors

Citation: Pasquardini,.L; Cennamo, N.; Zeni, L. Aptamer-Based Plasmonic Optical Fiber Biosensors: a Focus on relevant applications. *Proceedings* **2021**, 68, x. https://doi.org/10.3390/xxxxx

Published: date

1. Introduction

Surface plasmon resonance (SPR) or localized SPR (LSPR) represent a gold standard in the optical characterization of biomolecular interaction due to the high sensitivity of this optical platform, and it is a widely used transduction method in biosensors. In particular, SPR/LSPR systems based on fibers are an emerging field also due to the employment of plastic optical fibers (POF). Recent advances in POF-based devices opens the way to develop a new class of sensors [1–3], not only for their excellent flexibility, large diameter and great numerical aperture but also for the possibility to use different geometries, such as U-bent, D-shaped, side-polished, and tapered shapes of POF fibers. Furthermore, these kinds of optical fiber sensors can be used to realize small-size and low-cost optical biosensors, like those based on aptamers (aptasensors).

Aptamers are short single-stranded DNA or RNA fragments selected for a wide range of analytes, ranging from very small molecules (pesticides, toxins) up to entire microorganism; they exhibit an affinity constant in the nanomolar range minimizing the probability of false-positive results [4]. Moreover, they can be easily modified and are characterized by a high batch to batch reproducibility, resistance in acidic environment and high temperature. Aptamers find applications in different fields [5], from the detection of small molecules [6–8], in point-of-care diagnostic system [9,10], for the detection of bacteria [11] or circulating tumor cells [12].

Here we focus on the particular employment of POF-SPR biosensors that use aptamers as molecular recognition elements (MRE) in some biomedical applications.

2. Aptamer-based POF biosensors

In this last decade, different MRE have been immobilized on POF-based sensors, such as antibodies, molecularly imprinted polymers (MIP), and aptamers, proving the high versatility of this kind of platform [2]. With respect to more standard MRE, aptamers represent a new emerging class increasingly employed to realize biosensors. Up to now very few examples have been reported in the literature of the coupling between aptamers and POF-based biosensors [13–18], and most of them came from our group.

In 2015, we developed an aptamer-based POF-SPR sensor for the detection of Vascular endothelial growth factor (VEGF), selected as a circulating protein potentially associated with cancer [13]. A thiolated aptamer was directly immobilized on the gold film deposited on the sensing region of the POF. A scheme of the optical platform with the aptamer-layer is reported in Figure 1a. Results obtained suggested that passivation was an important element of the interface building, allowing a limit of detection of 0.8 nM (see Figure 1b) [13]. Even in agreement with other detection systems, the dissociation constant measured was two orders of magnitude lower with respect to that measured in solutions, probably caused by a loss in the immobilization procedure.

For this reason, in the subsequent works, we changed the approach and developed an interface based on short Poly Ethylene Glycol (PEG). So, the detection of thrombin (THR), a clinical marker of the blood coagulation cascade, was performed modifying the gold-coated POF with a mixed interface (a short-PEG and a biotinylated-PEG) and immobilizing though avidin-biotin chemistry a THR binding aptamer [15] (see Figure 1c). The performances of the obtained interface were confirmed by POF-SPR measurement resulting in a detection limit of 1.6 nM and increasing the dissociation constant of one order of magnitude.

We recently tested the PEG-based aptasensor to detect the receptor-binding domain (RBD) of the SARS-CoV-2 spike glycoprotein [18]. The interface has been tested not only on specific target but also on aspecific targets (BSA, AH1H1 hemagglutinin protein, MERS spike protein) and in diluted human serum (50%). A limit of detection in the nanomolar range was achieved, confirming the good performances of this aptamer-based optical sensor (see Figure 1d).

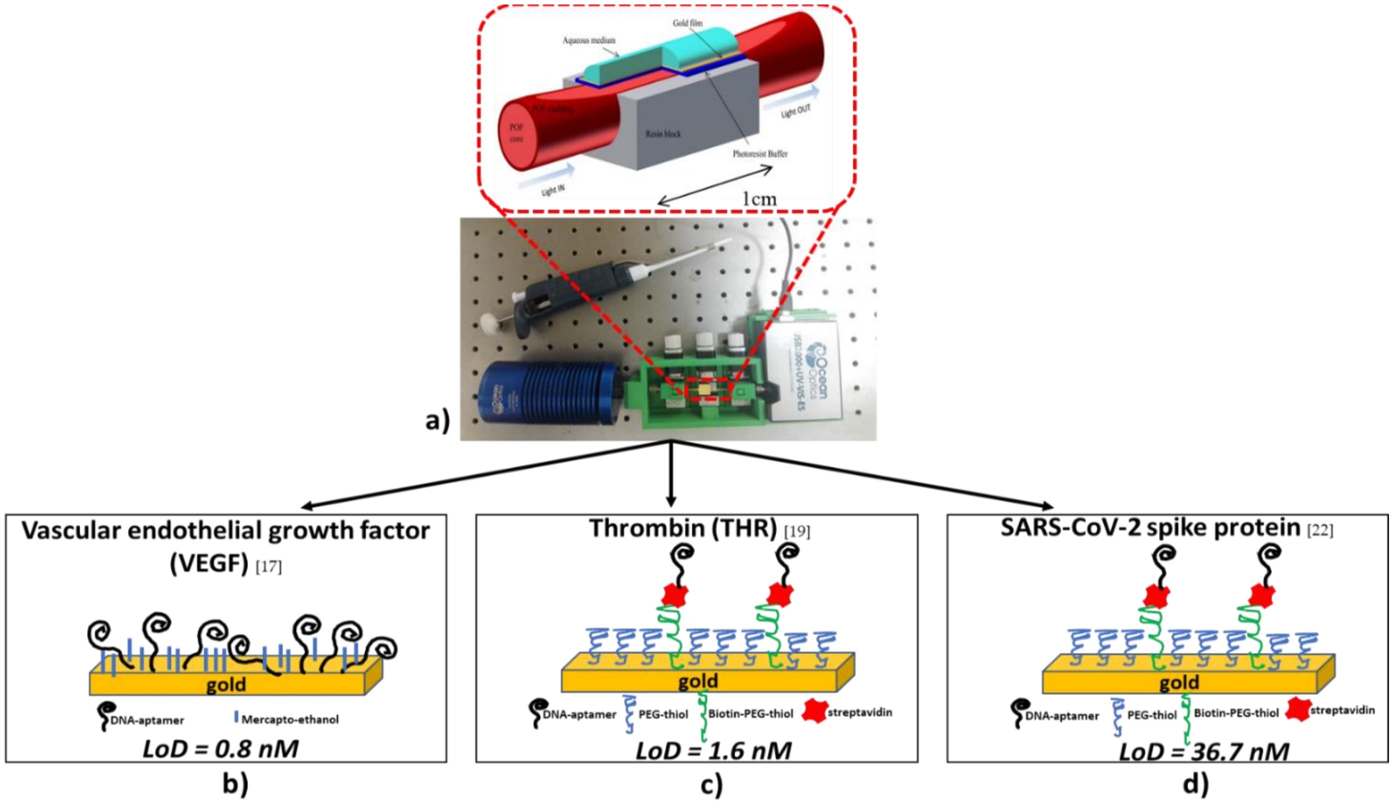

Figure 1: a) Image of the sensor system with a zoom of the plasmonic optical sensor [15] and different biological applications: b) Vascular Endothelial Growth Factor (VEGF)[13], c) Thrombin [15], and d) SARS-CoV-2 spike protein [18].

4. Conclusions

Aptamers represent an emerging class of biorecognition elements increasingly used in the development of optical biosensors. Their performances make them ideal elements to be immobilized on plasmonic optical fibre-based devices. On the other hand, the POF-based platform exhibits excellent flexibility, making it extremely interesting to coupling with aptamers in order to develop sensitive biosensors easily integrable in a portable, small-size, and simple devices for clinical applications.

Author Contributions: Conceptualization, Writing - original draft, Writing - review & editing, L.P. and N.C. Writing - review & editing L.Z. All authors have read and agreed to the published version of the manuscript.

Acknowledgments: This work was supported by the VALERE program of the University of Campania "Luigi Vanvitelli" (Italy).

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Jin, Y.; Granville, A. Polymer Fiber Optic Sensors – A Mini Review of their Synthesis and Applications. *J. Biosens. Bioelectron.* **2016**, *07*, 194, doi:10.4172/2155-6210.1000194.
2. Cennamo, N.; Pesavento, M.; Zeni, L. A review on simple and highly sensitive plastic optical fiber probes for bio-chemical sensing. *Sensors Actuators, B Chem.* **2021**, *331*, 129393, doi:10.1016/j.snb.2020.129393.

3. Kadhim, R.A.; Abdul, A.K.K.; Yuan, L. Advances in Surface Plasmon Resonance-Based Plastic Optical Fiber Sensors. *IETE Tech. Rev. (Institution Electron. Telecommun. Eng. India)* **2020**, *0*, 1–18, doi:10.1080/02564602.2020.1854060.
4. Tombelli, S.; Minunni, M.; Mascini, M. Analytical applications of aptamers. *Biosens. Bioelectron.* **2005**, *20*, 2424–2434, doi:10.1016/j.bios.2004.11.006.
5. Yan, S.R.; Foroughi, M.M.; Safaei, M.; Jahani, S.; Ebrahimpour, N.; Borhani, F.; Rezaei Zade Baravati, N.; Aramesh-Boroujeni, Z.; Foong, L.K. A review: Recent advances in ultrasensitive and highly specific recognition aptasensors with various detection strategies. *Int. J. Biol. Macromol.* **2020**, *155*, 184–207, doi:10.1016/j.ijbiomac.2020.03.173.
6. Feng, C.; Dai, S.; Wang, L. Optical aptasensors for quantitative detection of small biomolecules: A review. *Biosens. Bioelectron.* **2014**, *59*, 64–74, doi:10.1016/j.bios.2014.03.014.
7. Chen, W.; Lei, W.; Xue, M.; Xue, F.; Meng, Z.H.; Zhang, W.B.; Qu, F.; Shea, K.J. Protein recognition by a surface imprinted colloidal array. *J. Mater. Chem. A* **2014**, *2*, 7165–7169, doi:10.1039/c4ta00048j.
8. Cunha, I.; Biltes, R.; Sales, M.G.F.; Vasconcelos, V. Aptamer-based biosensors to detect aquatic phycotoxins and cyanotoxins. *Sensors (Switzerland)* **2018**, *18*, 1–34, doi:10.3390/s18072367.
9. Hassan, E.M.; DeRosa, M.C. Recent advances in cancer early detection and diagnosis: Role of nucleic acid based aptasensors. *TrAC - Trends Anal. Chem.* **2020**, *124*, 115806, doi:10.1016/j.trac.2020.115806.
10. Citartan, M.; Tang, T.H. Recent developments of aptasensors expedient for point-of-care (POC) diagnostics. *Talanta* **2019**, *199*, 556–566, doi:10.1016/j.talanta.2019.02.066.
11. Majdinasab, M.; Hayat, A.; Marty, J.L. Aptamer-based assays and aptasensors for detection of pathogenic bacteria in food samples. *TrAC - Trends Anal. Chem.* **2018**, *107*, 60–77, doi:10.1016/j.trac.2018.07.016.
12. Safarpour, H.; Dehghani, S.; Nosrati, R.; Zebardast, N.; Alibolandi, M.; Mokhtarzadeh, A.; Ramezani, M. Optical and electrochemical-based nano-aptasensing approaches for the detection of circulating tumor cells (CTCs). *Biosens. Bioelectron.* **2020**, *148*, 111833, doi:10.1016/j.bios.2019.111833.
13. Cennamo, N.; Pesavento, M.; Lunelli, L.; Vanzetti, L.; Pederzolli, C.; Zeni, L.; Pasquardini, L. An easy way to realize SPR aptasensor: A multimode plastic optical fiber platform for cancer biomarkers detection. *Talanta* **2015**, *140*, doi:10.1016/j.talanta.2015.03.025.
14. Galatus, R.M.; Cristea, C.; Feier, B.; Cennamo, N.; Zeni, L. SPR based hybrid electro-optic biosensor for β-lactam antibiotics determination in water. **2017**, 10, doi:10.1117/12.2273318.
15. Cennamo, N.; Pasquardini, L.; Arcadio, F.; Vanzetti, L.E.; Bossi, A.M.; Zeni, L. D-shaped plastic optical fibre aptasensor for fast thrombin detection in nanomolar range. *Sci. Rep.* **2019**, *9*, doi:10.1038/s41598-019-55248-x.
16. Sun, J.; Jiang, S.; Xu, J.; Li, Z.; Li, C.; Jing, Y.; Zhao, X.; Pan, J.; Zhang, C.; Man, B. Sensitive and selective surface plasmon resonance sensor employing a gold-supported graphene composite film/D-shaped fiber for dopamine detection. *J. Phys. D. Appl. Phys.* **2019**, *51*, doi:10.1088/1361-6463/ab08c1.
17. Sanjay, M.; Singh, N.K.; Ngashangva, L.; Goswami, P. A smartphone-based fiber-optic aptasensor for label-free detection of: Plasmodium falciparum glutamate dehydrogenase. *Anal. Methods* **2020**, *12*, 1333–1341, doi:10.1039/c9ay02406a.
18. Cennamo, N.; Pasquardini, L.; Arcadio, F.; Lunelli, L.; Vanzetti, L.; Carafa, V.; Altucci, L.; Zeni, L. SARS-CoV-2 spike protein detection through a plasmonic D-shaped plastic optical fiber aptasensor. *Talanta* **2021**, *233*, 122532, doi:10.1016/j.talanta.2021.122532.