# Plasmonic biosensor for SARS-CoV-2 detection.

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## ABSTRACT

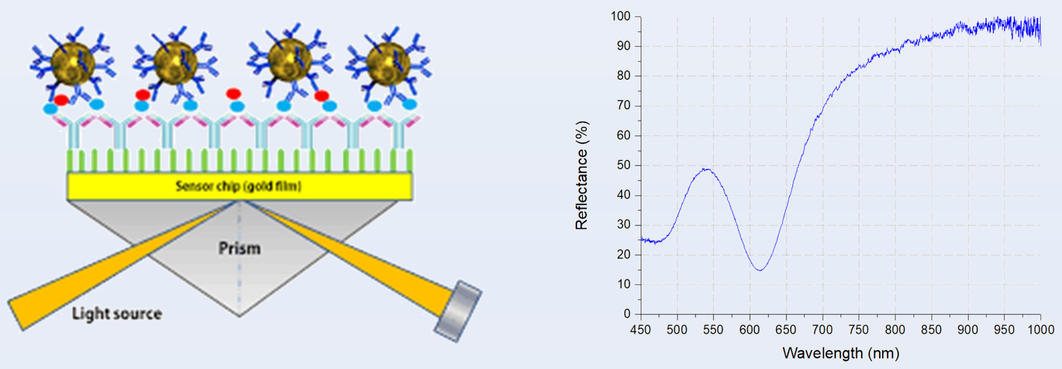
Optical biosensors have shown their outstanding performance by detecting proteins, antibodies, RNA chains, etc. We present a prototype of optical biosensor based on surface plasmon resonance principle; this device can detect the SARS-CoV-2 virus with an interferometric method measuring the differential phase around the plasmonic resonance. The general characteristics of this biosensor are high specificity, low limit of detection and short detection time, thus offering a promising alternative and complementary diagnosis of COVID-19.

**Keywords**: Biosensor, Surface plasmon resonance, SARS-CoV-2.

## INTRODUCTION

A biosensor is a device able to transform a biological into an electrical signal; it is composed of four parts: the bioreceptor, the analyte, the transducer and an electronic system. Its applications are very large because by correctly choosing the analyte and the bioreceptor, viruses, proteins, antibodies, etc. ,can be detected[1]. The main parameters like sensitivity or limit of detection are related with the transducer and its characteristics.

Surface plasmon resonance (SPR) is a phenom based on collective and coherent oscillations of the electrons at the metallic interface, under TIR conditions. The plasmonic response is observed in the intensity drop of the reflected beam, their quality depends critically on the geometry of the nanoparticles, their separation and size, among other parameters.




a) b)

Figure 1. a) General scheme of biosensor based on SPR effect[2]. b) Typical plasmonic response for gold nanofilm.

## OBJECTIVES

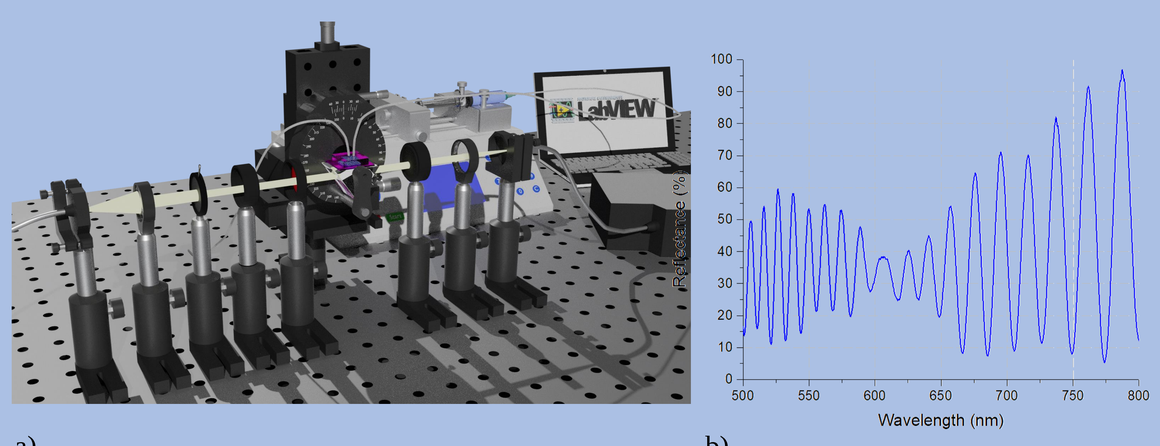
Implementation of a prototype of a SPR biosensor for the detection of the SARS CoV-2 virus.
Specific objectives:

- Fabrication, characterization and optimization of the sensor transducer consisting of gold nanofilm.
- Assembly of common path spectral interferometer for optical biosensing, as well as a LabView-based signal acquisition and processing system.
- Functionalization of gold nanofilm surface with complementary oligonucleotides to the specific RNA sequences of SARS-CoV-2.

## METHODS

Gold nanofilms were fabricated via sputttering method; to improve mechanical stability, a very thin film of titanium was deposited on the substrate. Then, the gold is deposited on the titanium and we found that under laboratory conditions, the optimal thickness of gold nanofilm is $d = 56nm$.

In order to functionalized the gold surface, we used oligonucleotides thiol-terminated, they were injected into a microfluidic device placed on the gold nanofilm. Afterwards, a buffer is injected on the chip and it is placed in an incubator at 37°C for many hours. Lastly, to complete the functionalization process, the surface must be washed several times with phosphate buffered saline (PBS) and resuspend it a few minutes in phosphate buffered.

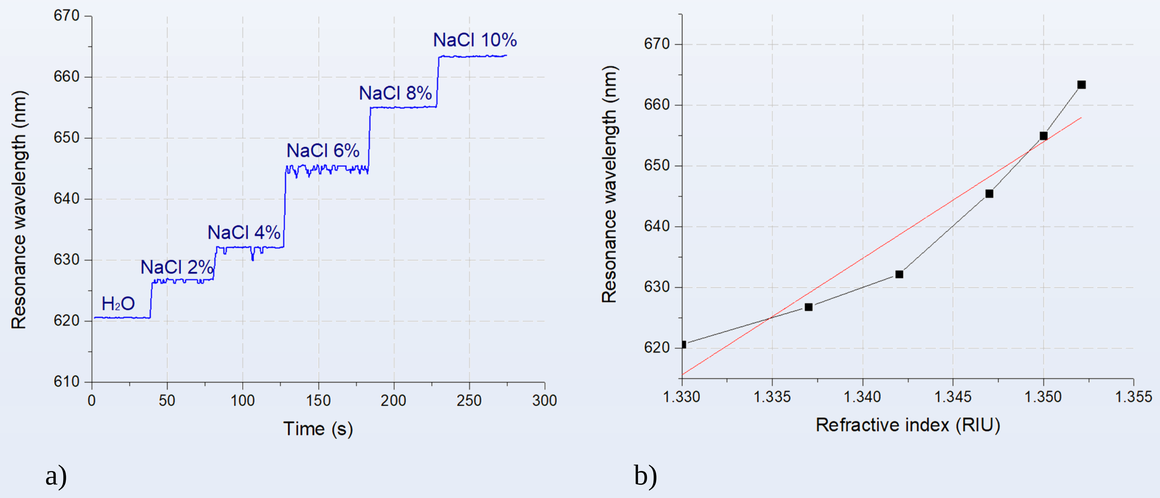



a) b)

Figure 2. a) Common path spectral inferometer[3] for SPR biosensing. A broad-spectrum source (400-100nm) is collimated, passes trough a linear polarizer, a birefringent crystal and interacts with the dielectric-gold interface. A microfluidic device is placed on the gold nanofilm surface to confine the different solutions at controlled speed. The reflected beam is collected by an optical fiber adapted to a spectrometer; then, the signal is processed in real time by a LabView script. b) SPR spectral interferometric response for gold nanofilm of thickness $d = 56nm$.

## RESULTS

In order to obtain the sensitivity of the sensor, a gold nanofilm ($d = 56nm$) was used to perform the calibration. The reference used is water and subsequently different saline solutions (2%, 4%, 6%, 8% and 10%), whose refractive indices are known, were gradually injected.




a) b)

Figure 3. a) Calibration sensogram. b) Linear fit of resonance position in function of the refraction index. Therefore, the sensitivity is: $S = 1917.33$nm/RIU and the $LOD = 2.77x10^{-4}RIU$.

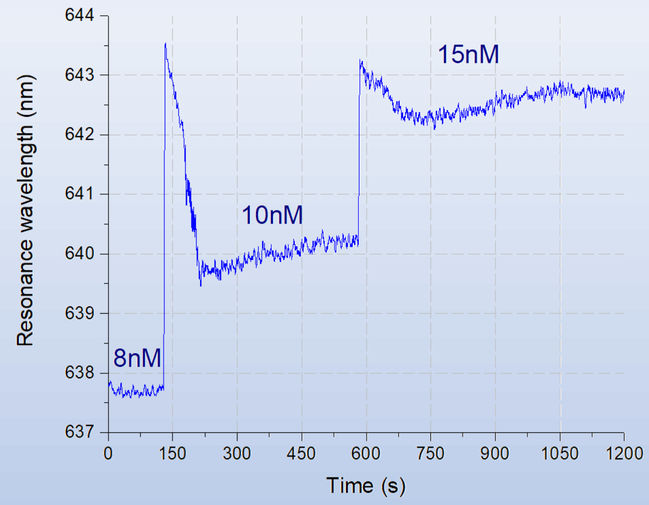



Figure 4. Detection in real time of functionalization process of gold nanofilm ($d$=56$nm$). Three different solutions of oligonucleotides tiol-terminated diluted in nuclease-free water containing 8nmol, 10nmol and 15nmol were injected, as consequence, the SPR response jumps gradually.

## CONCLUSIONS

We showed the development of an optical biosensor based on SPR , the experimental set up is simple, short length ($\approx 30cm$) and short biosensig area ($1cm^2$). We also developed a LabView script where we acquire and process the interferometric signal, then we retrieved the phase, we detect the resonance wavelength and then, we display this point in function of time, the result is a sensogram showed on Figures 2 and 3. The experimental results demonstrates the high sensitivity of the biosenor ($S = 1917.33$nm/RIU) and low limit of detection ($LOD = 2.77x10^{-4}RIU$). Finally, we showed the functionalization of goldnanofilm, in real time, at diffetent concentrations of oligonucleotides (8nM, 10nM and 14nM ) .

## REFERENCES

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