# Rapid antigen detection with antibody-doped hydrogels on impedimetric biosensors

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The current pandemic situation has evidenced the needs and demands for simple, sensitive and rapid biosensors. Among the available sensing formats, impedance spectroscopy [1] is a popular one due to its high sensitivity, label-free nature, and miniaturization possibilities. Usual impedance biosensors rely on 2D models, with bioreceptors immobilized on electrode surface through covalent or electrostatic means. This could lead to a loss of receptor activity due to conformational changes or wrong orientation, and increased nonspecific interactions. Hosting antibodies in hydrogels can help overcoming these issues [2]. Hydrogels provide a friendly 3D environment, where antibodies can be immobilized in a larger amount and maintaining their conformation. The solution-like system enables a free range of motion with higher interaction probability between target and bioreceptor compared to the limited kinetics of a solid-liquid interface. We have compared the biosensing performance of three gels (polyethylene glycol or PEG-based hydrogel, silicate-based sol-gel and alginate) containing antibodies against IgG as model, and accommodated on a glass chip with photolithography fabricated gold electrodes for measuring the impedance after IgG incubation. The three gels can be formed in short time (2 min for the alginate, 30 min for the sol-gel, and 1 h for the PEG), without the need of ultraviolet crosslinking that can change protein conformation or toxic catalysts. The presence of antibodies was confirmed in all cases through a colorimetric reaction using horseradish peroxidase (HRP) labelled antibodies which react with 3,3′,5,5′-tetramethylbenzidine developing a blue colour. The measurements were done with the chip mounted on a portable reader, compatible with smartphone operation of the potentiostat via Bluetooth. PEG gel showed the best results (Figure 1), with detection capabilities down to pg/mL levels (equivalent to femtomolar concentration considering the estimated 150 kDa size of the IgG). No significant increase of the signal was observed with albumin as nonspecific target, a protein with high presence in serum. On the other hand, alginate could be easily removed by incubation in calcium chelating buffer in order to regenerate the electrodes, as shown in a previous work [3]. Despite the high sensitivity of the approach, we expect that transferring the gels to nanomaterial containing transducers will further boost it significantly.

## REFERENCES

[1] M. Medina-Sánchez et al., Nano Letters, 16(7) (2016) 4288
[2] B. Randriantsilefisoa et al., J Mater Chem B, 7 (2019) 3220
[3] B. Ibarlucea et al., Microchim. Acta, 187 (9) (2020) 1

## FIGURE

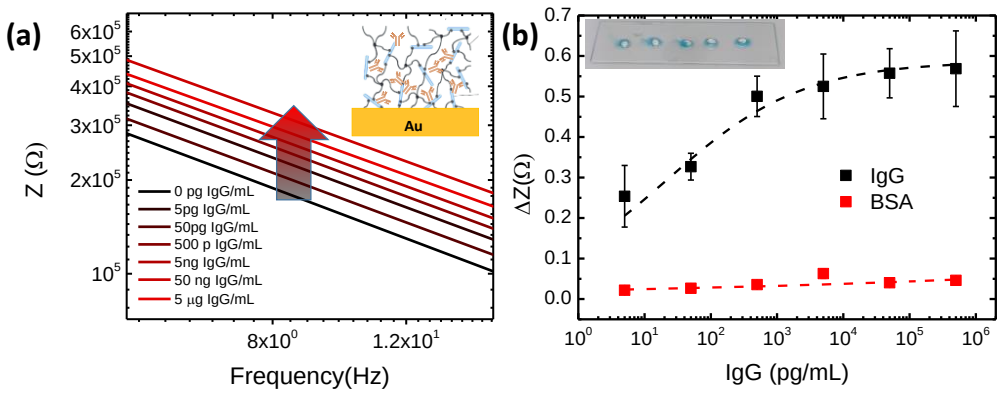


**Figure 1:** (a)Bode plot and (b) calibration (n=3) obtained with PEG-based hydrogel containing biosensors. Inset to (a) depicts the hydrogel network with the antibodies. Inset to (b) shows hydrogels on glass, with a blue colour development originated from an enzymatic reaction using HRP-labelled antibodies.