Detection of Antibiotics with Molecularly Imprinted Polymers: Theoretical Understanding of Detection Mechanisms using EIS and Molecular Dynamics

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***Abstract* — In this work, a material sensitive to antibiotics in aqueous phase based on a conducting and Molecularly Imprinted Polymer (MIP) is developed. This polymer is synthesized by oxidative polymerization of a mixture of pyrrole and pyrrole 3-carboxylic acid in presence of the target molecule and deposited on a substrate fitted with Interdigitated Electrodes. The detection signal is the change of impedance between the electrodes. Sensors showed significant responses and a good selectivity to the target molecule in the ppb range. The sensing mechanisms were studied by molecular dynamics simulations and by Electrochemical Impedance Spectroscopy (EIS).**

Keywords: Theoretical Modelling; Chemical Sensors; Molecularly Imprinted Polymers; Conducting Polymers.

I. INTRODUCTION

Antibiotic detection has become a major issue in many fields such as water analysis, food control, health, etc. requiring the development of new detection methods.

This work aims to understand and characterize the sensing mechanisms of a sensor for antibiotics based on molecularly imprinted polymers (also called MIP) using conducting (i.e., chemically doped conjugated) polymers. The working principle is based on the fact that once the target molecule is captured in the cavities of the MIP, its conductivity is modified in a way linked to the concentration of the target molecule in the liquid. This kind of sensors appears to be promising for the detection of one (or more) antibiotic(s) in liquid phase, [1],[2].

II. MATERIALS AND METHODS

Polypyrrole (PPy) is chosen as conducting polymer to be molecularly imprinted. Pyrrole (Py) is used as the cross-linker and pyrrole-3-carboxylic acid as the functional monomer, to promote chemical interactions between the polymer and the target molecule (also called "template"). The synthesis is performed in-situ (also referred to as bulk polymerization) in aqueous media by mixing the target molecule, the functional monomer and the cross-linker with the oxidizer, ammonium persulfate (APS), while the pH value is set to around 2.2 with sulfuric acid, below the template pKa to allow better interactions between monomers and the template. While oxidative polymerization takes place, temperature is kept at 30 °C, for 2 hours. The next step, so-called extraction, consists in removing the template from the polymer. It is performed by using a solution of methanol and HCl (9:1) wherein substrates are immersed for 2 hours [3]. Then, substrates are stored in PBS (phosphate buffered saline) solution before being tested. Non-Imprinted Polymers (NIP) are also synthetized following the same steps, except that the template is not present during the synthesis.

EIS data have been obtained using Power Suite. and EIS fitting has been carried out using ZView 2 software. Theoretical Modeling has been performed within the Material Studio package using the Dreiding force field for geometry optimizations and molecular dynamics simulations.

III. DISCUSSION

After the extraction step is carried out on the various substrates, detection is performed by adding the target antibiotic into the PBS solution. Only the results with impedance spectroscopy and mass measurements will be shown here.

A. Finding the optimal amount of reactants in order to obtain the best molecular imprinting

Modelling has been used to find the best polymerization conditions by optimizing the molar ratio of functional monomer/template (1) and cross-linker/template (2). The estimation of these ratios aims the best imprinting efficiency and the lowest waste resulting from the polymerization step. These computations are essentially based on finding the most energetically stable structures. Most of the time, the lowest energy structure is the one presenting the largest number of hydrogen bonds between the functional monomers and the template, which implies a good interaction between the sensitive material and the analyte and hence a good selectivity.

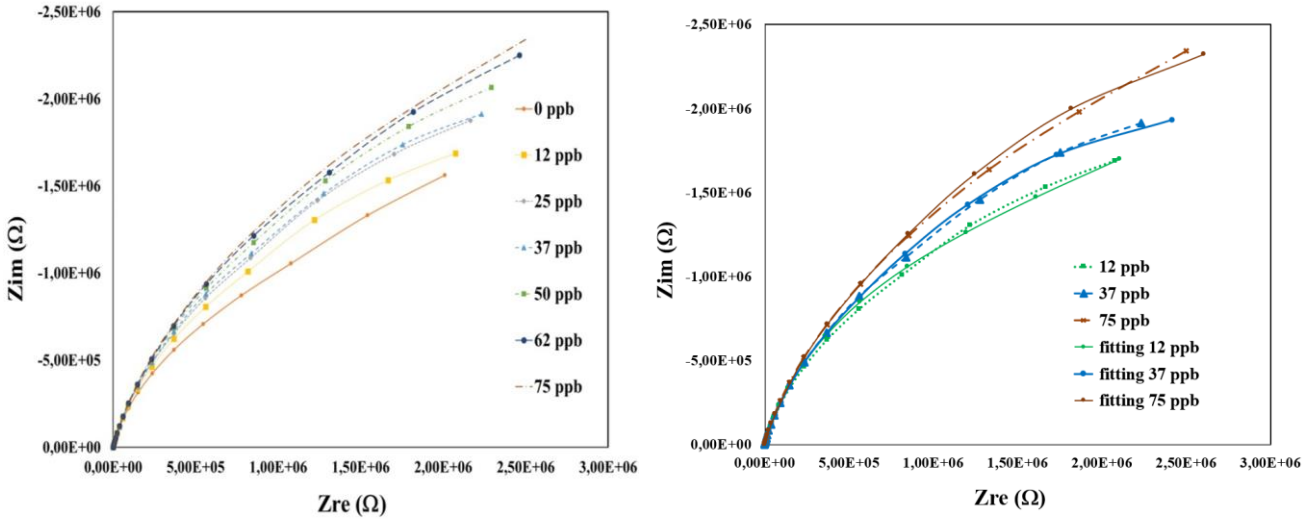

Figure 1. (a) MIP sample brought into contact with target molecule; (b) MIP experimental response fitted with EIS fitting model

In our case, it appears that ratio (1) is between 4:1 and 10:1 and ratio (2) between 11:1 and 20:1.

B. *Impedance Measurements*

Impedance Measurements can be used to fulfill 2 objectives: it is a good detection method and it allows to understand detection mechanisms.

Fig. 1(a) shows impedance measurements pointing to nearly linearly growth of the impedance as soon as we add a dozen ppb of the antibiotic. Using the same measurement method, the NIP barely reacts when we add the template (not presented here), which demonstrates that the imprinting is functional and significantly increases the sensor performances.

It is also possible to understand physicochemical mechanisms using an equivalent circuit to model the response observed and to fit the curve as much as possible. Fig. 1(b) shows 3 of the curves presented on Fig. 1(a), fitted with a specially designed EIS equivalent circuit presented on Fig. 2. On this scheme, resistors and capacities in parallel represent the charge transmission from one medium to another. Warburg moduli (W_s) are used to consider the diffusion phenomenon present in the polymer while serial resistors represent the conventional resistance of a conducting medium.

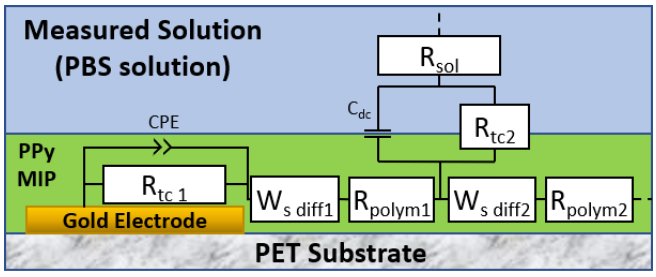

Figure 2. Equivalent Circuit build to fit experimental data

IV. CONCLUSION

In conclusion, the sensors were found to be able to detect concentrations of approximately 15 ppb and are close to the detection limits of conventional methods (10 ppb). They can obviously be optimized by adjusting the functional monomer/template ratio, as guided by modeling. In addition, it has been shown that it is possible to understand the physicochemical mechanisms involved when there are interactions between the target molecules and the sensitive layer.

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