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XXXVII Cycle

3D printed Molecularly Imprinted Polymers as synthetic receptors

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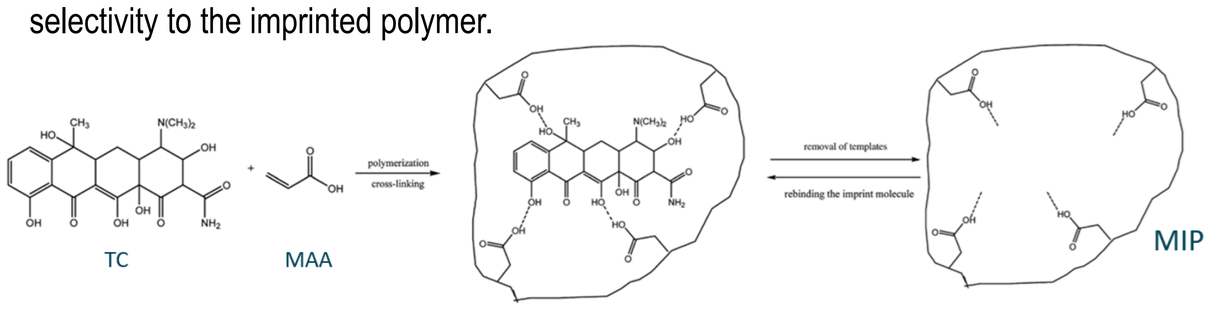
Research context and motivation

- Molecularly Imprinted Polymers (MIPs) as artificial receptors have received considerable scientific attention in the past years in the field of biosensors. MIPs aim to retain the selectivity of biological material, but overcoming some of the typical disadvantages, like limited shelf-life and high cost, meanwhile gaining in robustness, facile preparation, stability under extreme operating conditions and versatility.
- The approach to preparing an imprinted polymer involves the complexation of functional monomers and the "template" molecules in the pre-polymerization stage, followed by polymerization in the presence of an excess of crosslinking agents. Subsequent removal of the template from the resulting rigid polymer matrix leaves behind imprinted cavities, complementary to the template molecules thanks to the binding sites exhibited by the functional monomer.
- As target molecule, the antibiotic Oxytetracycline (OTC) has been chosen, one of the worldwide most used antibiotics, belonging to the wide family of tetracyclines. Antibiotics need to be monitored in the environment and foodstuff, to prevent the development of antibiotic resistance that may make them ineffective. Furthermore, the separation/recovery of drugs is an issue of large interest in the pharmaceutical industry.
- The carboxylic group of methacrylic acid (MAA) can form strong hydrogen bonds with hydroxyl and amide groups of OTC, and these non-covalent interactions should provide selectivity to the imprinted polymer.



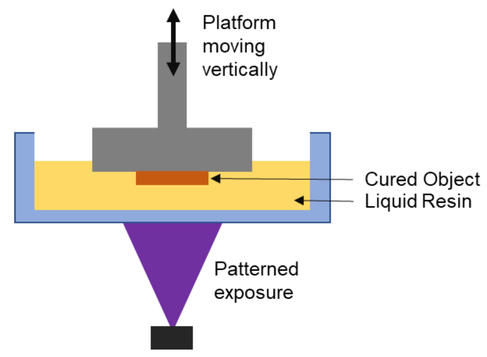
- The importance of 3D printing techniques has bloomed in the sensing world due to their essential advantages of quick fabrication, easy accessibility, processing of varied materials, and sustainability.

Addressed research questions/problems

- MIPs may represent a valid and versatile alternative to their biological counterparts, especially aiming to easy-to-use and scalable biosensors. The aim of this work is to make another step toward the customization of devices, developing a printable product, which operation ideally depends just on the choice of the ingredients of a photocurable blend.
- The MIP could be employed by printing it directly on the surface of the transduction unit of a biosensor, as recognition unit, or in a self-standing way, as smart polymer for filtering or as extraction adsorbent.

Adopted methodologies

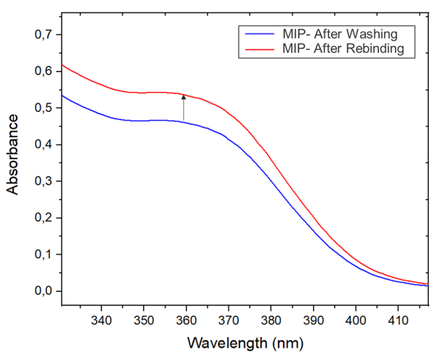
- MIPs are synthesized by photopolymerization of methacrylic acid and DPGDA (Dipropylene Glycol Diacrylate) in presence of Oxytetracycline, using Irgacure 819 as photoinitiator and DMSO as solvent. The ingredients are mixed together in the chosen ratio (OTC:MAA:DPGDA=1:4:20) through stirring, and US bath is employed to enhance the antibiotic powder dispersion.
- Multi-material samples (5 mm diameter dots) are printed with the Asiga MAX UV, a 385nm LED stereolithographic printer. The MIP active layer is 50µm thick (printed in two layers, 25µm each), on a support base 500µm thick. The thickness of the MIP layer has been minimized, in order to mimic the functionalization of a surface and to avoid template molecules to be trapped in the bulk.

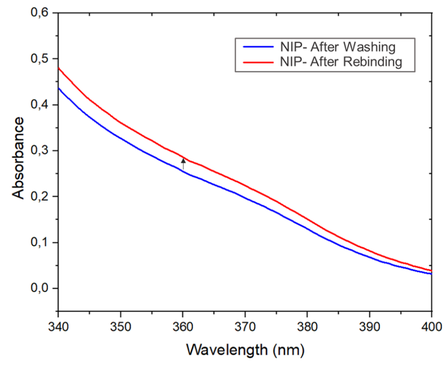


- As a comparison sample, also Non-Imprinted Polymers (NIPs) have been produced, with the same procedure as MIPs, but without the template.
- The main characterization of the adsorption of OTC into MIPs consisted in the spectroscopic analysis both of the samples themselves and of the washing/rebinding solutions. The spectra are collected in all the phases of the sample (after polymerization, after washing, after incubation in the rebinding solution, after the final washing) and compared.

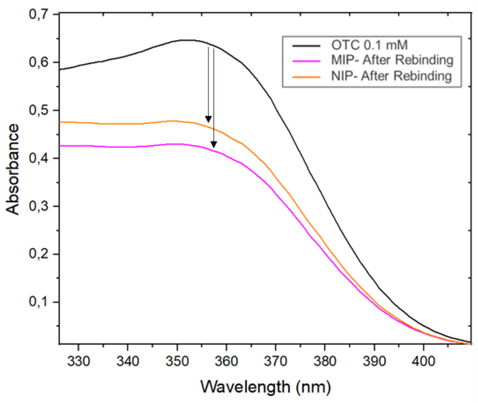
- The OTC presents a characteristic peak around 355nm, so a UV-vis spectrophotometer and a plate reader have been used to investigate the absorbance in the range between 250 and 450 nm.

The spectra collected directly through the printed disks show that the Molecularly Imprinted sample absorbed the antibiotic from the rebinding solution, while the Non-Imprinted one presents a less incisive variation at the same wavelength.





On the other hand, from the spectra performed on the rebinding solution (OTC 0.1mM in deionized water) before and after the incubation, it is possible to see that the concentration of the OTC decreased substantially in contact with the MIPs sample. Still, a variation is present also with the NIPs.



Future work

- The correct functioning of the MIP depends in first instance on the choice of its components. Therefore, it is necessary to determine the best crosslinker and the right ratio between ingredients in order to improve selectivity.
- Other types of template molecules are going to be tested (e.g. proteins), considering that of course the size and type of molecules play a crucial role in the fabrication and characterization of MIPs.
- The flatness of the surface of continuous MIP layer limits the diffusion of analyte towards less accessible imprinted cavities buried inside the films. One method to increasing the exchange of the molecules with the incubation solution is to have a porous polymer. Secondly to print samples with different and more complex geometries, in order to increase the surface area, by benefiting from the versatility of additive manufacturing
- Other characterization techniques with high resolution should be tested, as HPLC or QCM.

Novel contributions

- The most classic method shown in the literature to produce MIPs consists in the fabrication of nanoparticles, mostly obtained by the grounding of a bulk rigid polymer into a fine powder. During the years a large number of MIP fabrication methods have been developed by varying and improving the techniques depending on the type of application.
- Still, fabrication through additive manufacturing appears mostly as an unexplored field, and the effort of this work is focused right the development of 3D printed MIPs.

Submitted and published works

Bertana, V., Scordo G., Camilli E., Ge L., Lamberti A., Marasso S. L., Perrucci F., Scaltrito L., Zaccagnini p., "3D printed micro-Supercapacitor exploiting PEDOT-based resin and polymer gel electrolyte", Additive Manufacturing

List of attended classes

- 02UKHKI – Applied spectroscopic methods (13/06/22, 6CFU)
- 01VJXPE – Physics of technological process (27/06/22, 6CFU)
- 01QORRV – Writing Scientific Papers in English (16/06/22, 3 CFU)
- 01RISRV – Public speaking (7/03/22, 1 CFU)
- 02RHORV – The new Internet society: entering the black-box of digital innovations (25/02/22, 1 CFU)
- 01UNXRV – Thinking out of the box (4/05/22, 1 CFU)
- 01SWPRV– Time management (5/04/22, 1 CFU)

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