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Capacitive sensing of amphetamine-type stimulants based on immobilized molecular imprinted polymers

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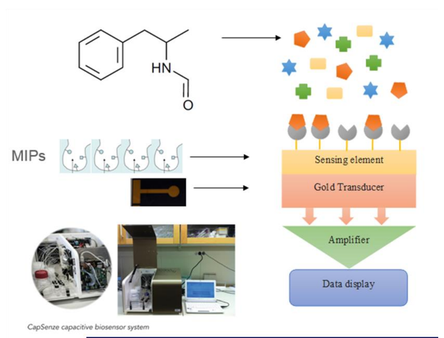
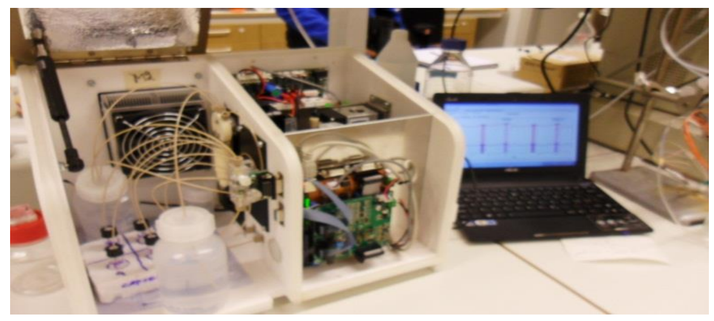


Schematic illustration of a biosensor.



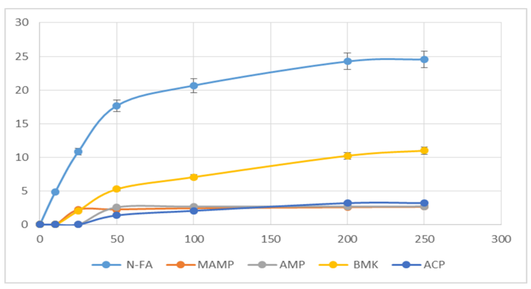
Why Amphetamine-type stimulants?

The threat of synthetic drugs is one of the most significant current drug problems worldwide. Amphetamine-Type Stimulants (ATS) are globally the second most widely used drugs after cannabis. ATS production contributes to environment pollution, so there is a demand to develop robust and sensitive sensors that can detect ATS and in environmental water samples.

Why capacitive biosensor?

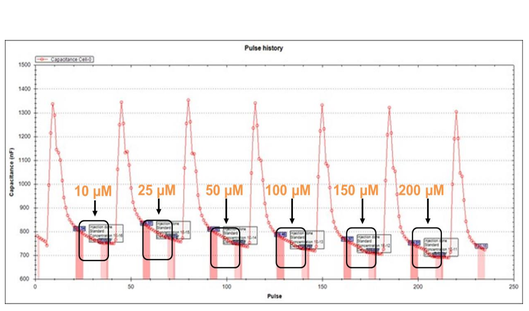
- High sensitivity, high selectivity, and capability to quantify trace amounts of target in a short time frame.
- Capacitance-based label-free biosensors offer a unique platform which does not require complicated sample pretreatment or concerns about by products, nor solvent waste.
- A typical capacitive sensor generates a signal upon binding of the target analyte due to changes in charge displacement and dielectric properties.
- Capacitance values depend on the nature of the targeted molecules and their interaction with the capacitor.
- The observed change in the capacitive signal can thus be used to quantify interactions between ligands immobilized on the metal surface and the target compound.

Cross-reactivity test



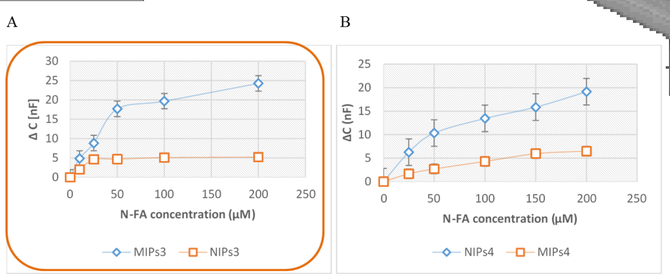
The graph presenting capacitance changes (nF) of the MIP functionalized electrode in function of concentration (µM) for separate injections of N-formylamphetamine (N-FA), methamphetamine (MAMP), amphetamine (AMP), benzylmethylketone (BMK), acetophenone (ACP).

Choice of the optimal MIP



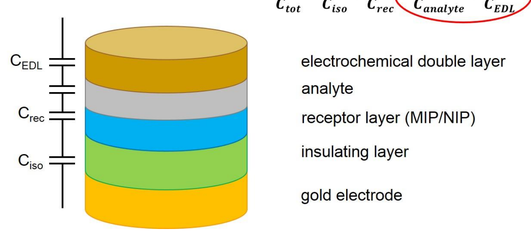
Response of the MIP – functionalized electrode showed a steep inclination after injection of N-FA

Limit of detection (LOD) of the developed system for N-FA detection was 10 µM and the working range was 5- 200 µM.



Difference between capacitance changes (nF) of the MIP and NIP functionalized electrodes in function of N-FA concentration (µM), differences in sensitivity according to implemented initiator (A) AIBN MIPs3, (B) Irgacure 651 MIPs4. The measurements with use of regeneration buffer between each injection was performed in triplicate.

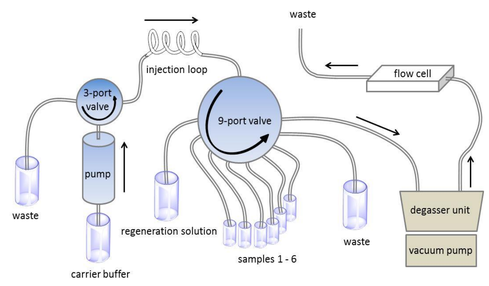
Construction of working electrode



$$\frac{1}{C_{tot}} = \frac{1}{C_{iso}} + \frac{1}{C_{rec}} + \frac{1}{C_{analyte}} + \frac{1}{C_{EDL}}$$

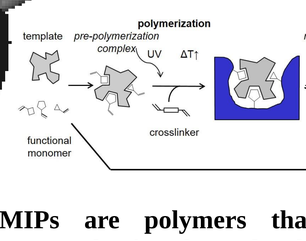
The working electrode consists of several layers that contribute to the system's total capacitance. The electrode's gold surface is first insulated to impede surface-buffer faradaic currents, then recognition elements are bound to this layer. If analyte binds, the electrochemical double layer will be displaced further away from the gold surface. Assuming a good insulation, the insulating and receptor layers will contribute the least to the total capacitance. Hence, the partial capacitances of the analyte and the electrochemical double layer will be the most pronounced. Binding of analyte typically leads to a measurable decrease of the total capacitance.

Automated flow-injection system



An automated flow-injection system was used to simulate continuously flowing systems, using a peristaltic pump to maintain a buffer or carrier solution flow. It is connected to an injection loop via a 3-port valve, and the loop is connected to a 9-port valve. This latter allows injection of up to six different samples, and a regeneration solution, into the continuous flow system. An inline degasser unit removes air bubbles from the solution before it is introduced into the flow cell.

Why molecularly imprinted polymers?



MIPs are polymers that has been processed using the molecular imprinting technique which leaves cavities in polymer matrix with affinity to a chosen "template" molecule.

Synthesis of MIPs

- **Bulk polymerization (MIPs 1) –** bulky shape
- **Precipitation polymerization (MIPs 2)** - insufficient reaction yield
- **Electropolymerization:**

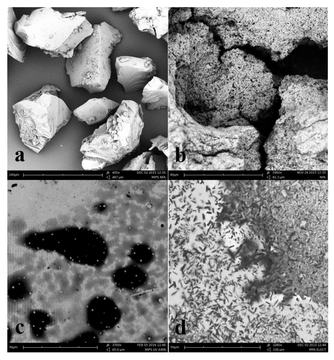
Thermo-initiated (MIPs 3) 2,2-azobis-2-isobutyronitrile (AIBN), 24 h, 60 °C

UV initiated (MIPs 4) Ciba® IRGACURE® 651 (2,2-Dimethoxy-1,2- diphenylethan -1-one), 1 h, UV wave length range between 300-400 nm

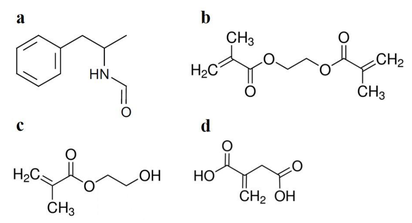
	MIPs 1	NIPs 1	MIPs 2,3,4	NIPs 2,3,4
N-FA	50 µM	n.a.	50 µM	n.a.
DMF	10 mL	10 mL	2,5 mL	2,5 mL
MAA	15 mM	15 mM	n.a.	n.a.
EGDMA	60 mM	60 mM	9 mM	9 mM
HEMA	n.a.	n.a.	3 mM	3 mM
IA	n.a.	n.a.	3 mM	3 mM
initiator	50 mg	50 mg	50 mg	50 mg

Acronyms: IA – itaconic acid; HEM – hydroxyethyl methacrylate; MAA – methacrylic acid; EGDMA – ethylene glycol dimethacrylate; DMF – dimethylformamide.

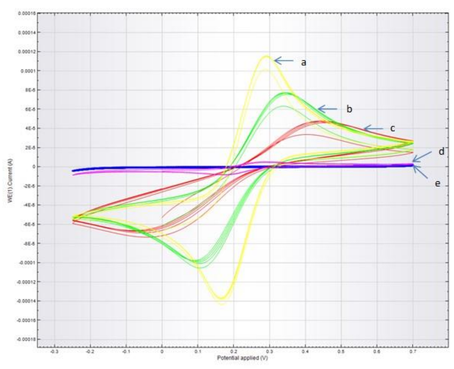
Synthesis of MIPs



Scanning Electron Microscopy (SEM) pictures of synthesized molecularly imprinted polymers (MIPs), (a) MIPs for N-formylamphetamine (N-FA) prepared using bulk polymerization; (b) MIPs for N-FA prepared by precipitation polymerization, (c) MIPs for N-FA prepared using in situ polymerization, (d) commercial MIPs for amphetamine.



Molecular structure of: (a) template, N-formylamphetamine (N-FA); (b) cross-linker,ethylene glycol dimethacrylate (EGDMA); (c) monomer: 2-hydroxyethyl methacrylate (HEM), (d) functional monomer, itaconic acid (IA).



Comparison of electrodes insulation with the use of cyclic voltammetry recorded in 10 mM K3[Fe(CN)6] in 0.1 M KCl. The potential was swept in the range between -300 and 800mV (vs Ag/AgCl) with a sweep rate of 100 mVs-1; electrodes (a) bare; (b) modified with MPA and MIPs; (c) modified with LA and MIPs; (d) MIPs electropolymerization with tyramine; (e) after treatment with 1-dodecanethiol.

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