Design of a microneedle biosensor array for minimally-invasive transdermal detection of drug addiction biomarkers

Conception d'un réseau de biocapteurs à micro-aiguille pour la détection transdermique peu invasive de biomarqueurs de toxicomanie

Responsable : SAULNIER Joëlle
Institut des Sciences Analytiques
UMR 5280, CNRS/Université Lyon 1
5, rue de la Doua, 69100 Villeurbanne Cedex
joelle.saulnier@isa-lyon.fr
http:// Tél : 33 (0)4 37 42 35 56
http://isa-lyon.fr/

The detection of illicit drug use is of great interest to the field of addiction medicine. At present, detecting drug use relies upon data obtained from testing biological specimens (e.g., qualitative screens of urine) or self-report. Both methods obtain discontinuous data that cannot provide real-time information about drug using behaviors. Wearable biosensors have the potential to provide continuous data indicating the timing and durations of drug use in individuals and enhance monitoring/intervention strategies. In this context microneedle-based sensor arrays appear as attractive solutions to collect and detect biomarkers in body fluids.

Microneedles are sub-millimeter needle-like structures predominantly used in minimally-invasive transdermal drug delivery. They have also shown potential in the extraction of blood and interstitial fluid (ISF) from the skin. ISF is advantageous for biosensing applications since it does not contain any particulates (red blood cells or platelets) and contains at least 5–10 times less protein than blood serum, minimizing interferences and fouling. However, only extremely low volumes can be found on the skin, making the process of ISF extraction rather difficult. Small amounts of up to 200 nL per microneedle can be collected by capillary action. [1]

Compared to single microneedle, microneedle arrays collect larger ISF volumes.

Lab-on-a-chip devices with integrated hollow microneedles have been reported for biosensing applications using ISF collected by capillary action. These devices require transfer of collected ISF out of the microneedle lumen to the analyte detector. This transfer of ISF presents major limitations due to extremely small volumes of accessible ISF in the skin and the slow extraction that can lead to slow sensor response. Therefore, ISF extraction using hollow microneedles combined with integrated biosensing capabilities for extremely low sample volumes would provide significant opportunities for minimally-invasive diagnostics. [1]

In this work, we propose to develop an enzyme-based microneedle electrochemical biosensor that can detect biomarkers under the skin rapidly, selectively and directly in a single-step.

Sensitive, accurate, fast response and low-cost electrochemical biosensors to detect addictive and dangerous drugs of abuse, such as alcohol have been already reported[2]. Advances in electronics have allowed electrochemical sensors to rival the most advanced optical protocols. The performance of the developed biosensors has been checked in terms of reproducibility, repeatability, capability of detection and application to complex matrices.

Electrochemical enzyme-based electrodes exploit the reaction of an enzyme with an analyte, which creates a charge/proton transfer, resulting in an electrical signal proportional to its concentration in blood. The procedure of enzyme immobilization on the electrodes strongly influences the biosensor performances (response time, sensitivity, stability and lifetime). Particular attention must be paid to avoid enzyme denaturation. The enzyme immobilizing technique should promote a rapid propagation of generated electrons/protons and avoid nonspecific binding and electrode failing. Electrode features can be optimized by using matrices in which enzymes can be dispersed (hydrated gels, polymers, …). Microneedles fabricated from poly(ethyelene glycol) diacrylate (PEGDA) have been recently proposed for the immobilization of glucose and lactate oxidases and quantification of glucose and lactic acid in solutions.[3]

The work will be divided in four steps:

1) Microneedles (MN) array fabrication will include shape design and choice of materials that facilitate the penetration/insertion into the stratum corneum, the access to the ISF without their break or bending and, ensure minimal damage upon piercing the skin and reproducible response.

2) Enzyme immobilization into microneedle will require the selection of a suitable immobilization method (entrapment versus covalent binding) in an adequate hydrophilic environment to guarantee the specificity, the selectivity and the stability of the enzyme but also the transduction of the biochemical signal to an electrical change.

3) Combination of the enzyme-based MN with the transducer (electrodes) and the detector in a patch format.

4) Evaluation of the performances of the biosensor will be conducted with artificial ISF and mice skin model especially for sensitivity, linear dynamic range, LOD, LOQ, limited interferences with ISF compounds and the ability to operate over prolonged periods with minimal deterioration in the response.

[1]Sci. Rep. 6 (2016) 29075

[2]Biosens. Bioelectron. 91 (2017) 574–579

[3]Sens. Actuators B 236 (2016) 343-349