

DISPOSABLE AFFINITY MICROCHIPS WITH ELECTROCHEMICAL AND NANOSPRAY DETECTION

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INTRODUCTION: In modern (bio)chemical analysis, the need for contamination free platforms offers great commercial potential to plastic μ -systems. This is reinforced by simplified manufacturing procedures (compared to glass μ -chips) that enable mass production of low cost disposable devices. In addition to the variety of polymers that can be chosen to adsorb biological materials, polymer μ -chips are particularly well suited for high performance analysis and medical diagnosis, since they allow reduced analysis time, low reagent consumption, as well as parallelism and multi-analyte testing.

We present here Enzyme Linked Immunosorbent Assays (ELISA) with electrochemical detection in industrial μ -chips manufactured by plasma etching of polyimide foils. This method is further used here to produce disposable nano-electrospray interfaces for applications in proteomics.

FABRICATION: Mass production of μ -chips is performed by plasma etching, a method developed for printed circuit boards [1]. A polyimide foil coated with a copper mask is exposed at low temperature to a plasma of oxygen. The plastic is thus etched to produce (e.g. 40 μ m deep x 100 μ m wide) μ -channels and/or openings, and the copper is then removed in such a manner that only contact pads remain at the bottom of the μ -channels.

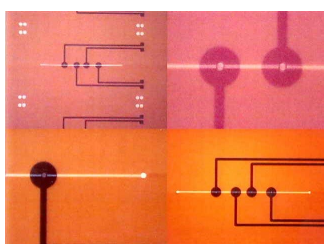


Figure 1: Top views of μ -channels with integrated gold electrodes

Gold is then electroplated on these copper tracks, thereby leading to electrodes that are thus integrated during the fabrication process (see Fig. 1). The μ -chips are finally sealed by lamination of a second polymer layer.

EXAMPLES OF APPLICATIONS: ELISA with electrochemical detection

Micro-chips are well suited for the development of fast immunoassays. It is demonstrated here that very short incubation time (<5 min) can be used

due to the small diffusion distance between the bulk solution and the surface (<20 μ m) [2]. The use of electrochemical detection is advantageous because it is proportional to the concentration of redox molecules even in these small volumes (<60 nL) [3]. The performances of the chips are illustrated here by presenting a highly sensitive immunoassay for the measurement of alkaline phosphatase with a detection limit of 5×10^{-21} mol.

Plastic μ -chips as disposable mass spectrometry (MS) interfaces for protein analyses

Plasma etching has also been used to fabricate hydrophilic μ -channels with an open end surrounded by an hydrophobic surface in order to produce nano-electrospray tips. As presented in Fig. 2, the soft generation of the nano-spray of proteins is demonstrated here by the MS detection of myoglobin (applied voltage: 1.4 kV; spray solution: 4 μ M myoglobin in 50 % methanol, 49 % water, 1 % acetic acid). In this system, no additional flow is needed to generate the spray, the alignment to the MS entrance is simplified, low flow rate can be used and multiplexing is easy.

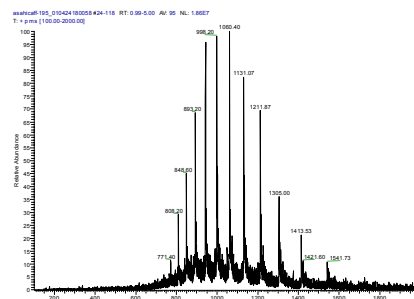


Fig. 2: Mass spectrum of a 4 μ M myoglobin sample sprayed with plasma etched micro-chips (acquisition time: 3 min; flow rate: 50nL/min)

CONCLUSIONS: Plasma etched μ -chips are industrial platforms suitable for sensitive medical tests and high-throughput MS analysis. This robust method is also very attractive to produce lab-on-a-chip, affinity platforms and disposable biosensors.

REFERENCES: ¹ see: www.dyconex.com. ² Rossier et al (2000) *Langmuir* **16**: 8489. ³ Rossier et al (1999) *Anal. Chem.* **71**: 4294. (Abstract also presented at the 3rd HPLPuS meeting in Amsterdam in October 2001)