LAB-IN-A-SUITCASE
FOR DRUG SCREENING AND PROTEOMICS APPLICATIONS

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ABSTRACT
This paper reports the development of a Lab-in-a-Suitcase setup aimed for drug screening and proteomics applications. This setup is capable of automatically performing on-line electrochemical experiments using low volume (μL) samples with stable flow rates down to 30nL/min. The total volume of valves, fluidic capillary and chip-interconnects is below ~5μL, excluding syringes. Moreover, we have decreased experiment start-up times down to 5 minutes.

KEYWORDS: Lab-in-a-Suitcase, Drug Screening, Proteomics, Electrochemistry

INTRODUCTION

In general, the Lab-on-Chip community is focused towards miniaturization of specific functions or devices on-chip. However, miniaturization poses strong demands on auxiliary equipment, such as pumps and measurement devices. We have encountered this problem during the development of a chip for electrochemical oxidation of drugs to mimic the metabolism of the enzymes of the cytochrome P-450 family [1,2]. A photo of this chip is shown in figure 1. This chip is currently in use for electrochemical cleavage of peptides in proteomics applications [3]. Typically, a fixed potential is applied to the work electrode of the chip while the current is measured as an indication of the conversion rate of the introduced species.

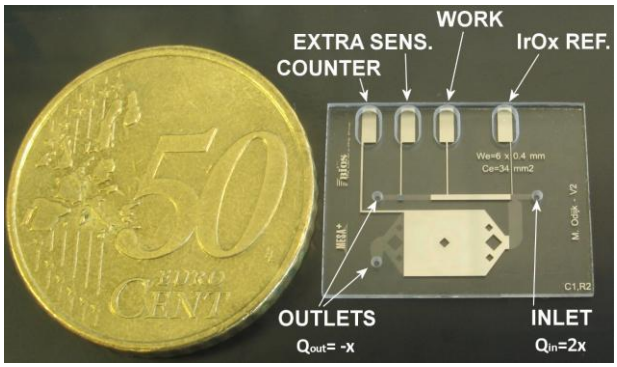

Figure 1: Photo of the electrochemical cell on-chip. In the picture, fluidic inlet and outlets are indicated. The chip also contains a three electrode electrochemical cell with a platinum working and counter electrode and an iridium oxide pseudo-reference electrode.

THEORY

The design of electrodes and channel dimensions on the chip are optimized for total conversion of analyte. Design details are published elsewhere [1]. In summary, the height of the channel is only 4μm to ensure that all ions present above the working electrode have sufficient time to diffuse towards this electrode at limited flow rates. For simple, fast reacting ions it is already shown that a conversion efficiency of 97% can be reached at sufficient overpotential [1]. If total conversion of ions is assumed, the measured current (i [A]) can be linked directly to the bulk concentration (C^* [mol/L]) and the flow rate (Q [L/s]) over the working electrode using the following equation:

$$i = C^* \cdot F \cdot Q \qquad (1)$$

This equation clearly indicates the dependence of the current to the flow rate. Changes in flow rate have direct influence in measured current, putting high demands on the stability of the flow.

EXPERIMENTAL

We have realized a stable flow by reducing dead volumes and by using special syringe pumps (Cetoni GmbH, Germany). A picture of the setup is shown in figure 2, while a schematical overview is shown in figure 3. In the suitcase, two syringes are connected to two switching valves (type C75X-6694EMH, VICI Valco Instruments Co. Inc.). The switching valves are connected to several sample vials for automated sample uptake and cleaning of the setup. One of the ports of each switching valve is also connected to one of the inlets of the chip, using an in-house developed chip-holder and commercially available fluidic connectors (nanoports, Upchurch scientific). Products generated on-chip can be collected in a sample loop, connected to an injection valve (type C72MX-4698ED, VICI Valco Instruments Co. Inc.). Potentials are applied to the chip using a portable potentiostat (Palmsens, Palm Instruments BV). The total setup is connected to a laptop via a single USB cable. A Labview program controls all parts of the setup and makes automation of common tasks or protocols possible.

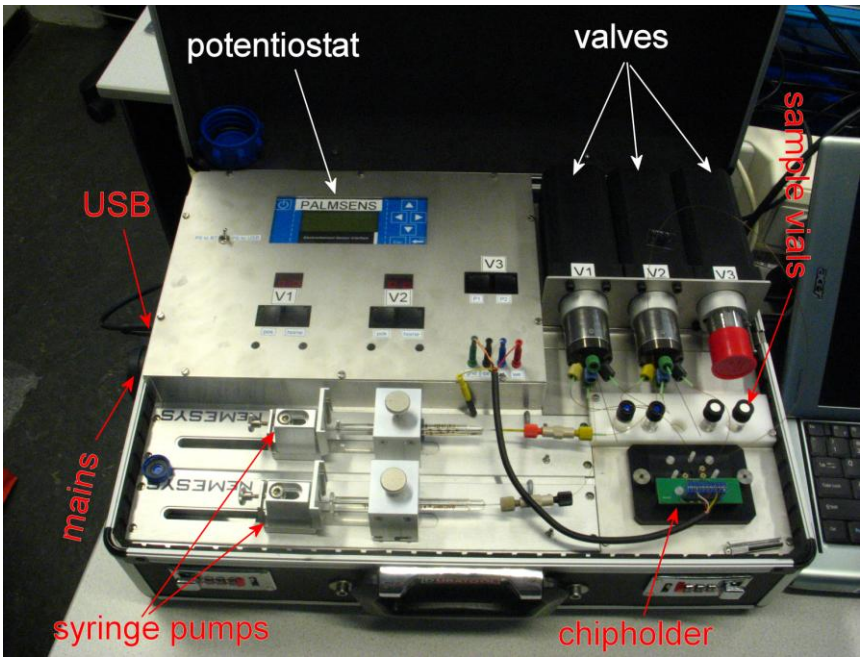

Figure 2: Photo of the Lab-in-a-Suitcase. In the picture, chipholder, syringe pumps, fluidic switching and injection valves, sample vials and the portable potentiostat are indicated.

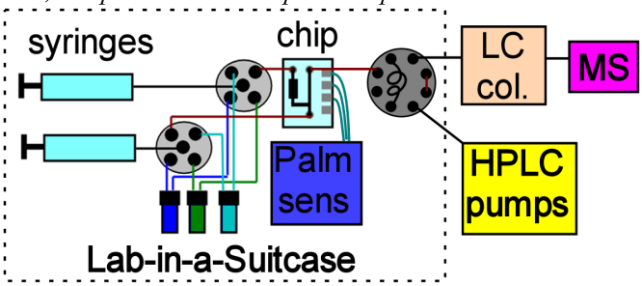

Figure 3: Schematic overview of the total setup including the Lab-in-a-Suitcase and possible use in combination with LC pumps and mass spectrometer.

RESULTS AND DISCUSSION

In figure 4, the current is measured at various volumetric flow velocities using the Lab-in-a-Suitcase setup. The analyte contained 1mM $[Ru(NH_3)_6]Cl_3$ and 100mM KNO_3 supporting electrolyte. A fixed potential of -0.6V was applied vs. the iridiumoxide pseudo-reference electrode. As indicated in figure 1, the inlet flow is split into two equal volumetric parts over the side and main channel, to prevent gas formation or unwanted products to reach the pseudo-reference electrode. The flow rates indicated in figure 4 are of the main channel, containing the working electrode, only.

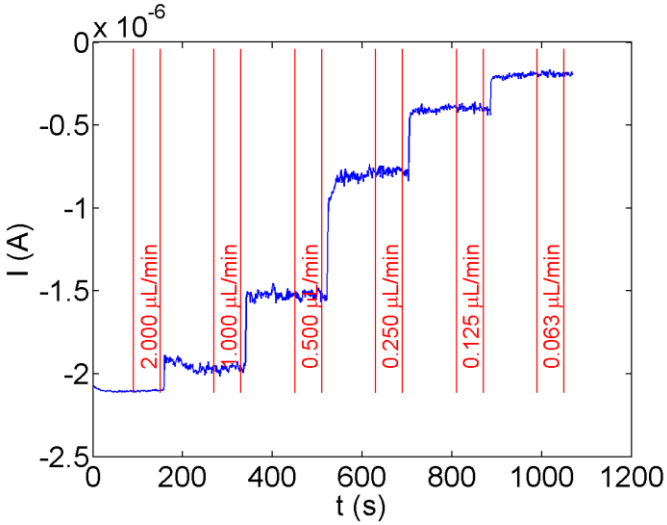

Figure 4: Current measured at various flow rates (indicated in red) with a fixed potential of -0.6V (vs. pseudo-reference) applied to the work electrode. The analyte contained 1mM $[Ru(NH_3)_6]Cl_3$ and 100mM KNO_3 supporting electrolyte.

As shown in figure 4, the measured current is strongly dependent on the flow rate. Changes in flow rates have almost immediate effect. An average response time within 3 seconds between enforced changes in flow rate and measured current is observed. At 63nL/min, the coefficient of variation of the measured current is 5%. This noise level is depending on several factors like electrical noise, pseudo-reference electrode stability and flow rate. Therefore, we expect the flow rate to be even more stable.

CONCLUSION

Our experiments take place in various laboratories. Upon arrival, it takes 5 minutes typically to connect all electrical and fluidic connections. Therefore, the Lab-in-a-Suitcase decreases experiment preparation time significantly. Using our Lab-in-a-Suitcase, measurements are far more reproducible at the various locations, because the same auxiliary equipment is always used. The automation features of the developed software decrease the required time for measurements and cleaning even further. The system has a response time of less than 3 seconds. Moreover, the flow rate is stable within less than 5% deviation. Finally, our Lab-in-a-Suitcase also has high demonstrative value.

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