Microfluidic-Integrated Capillary Electrophoresis for Metabolite Detection in Miniaturized Bioreactor

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Lactose is a key biochemical metabolic marker in cell cultures[1,2] and we used this parameter to demonstrate that metabolites from a miniaturized bioreactor can be retrieved by microfluidic-integrated capillary electrophoresis. Previously, we developed a hydrogel/ poly-dimethylsiloxane (PDMS) hybrid microbioreactor, which enables a low shear stress 3D culture. The PDMS facilities the reversible adhesion of the microbioreactor to a smooth and flat surface, for example, a multi-electrode array.[3] Here, we extend this miniaturized bioreactor cell culture concept with microchip capillary electrophoresis (CE).[4] We used the MiniLab© (CE-Mate B.V., Enschede, The Netherlands), which is a commercial point-of-care microchip CE system applying contactless conductivity detection for ion analysis.[5] To demonstrate that lactate ions can be measured from a culture chamber as small as 15 µl in volume, our microbioreactor was assembled with the Minilab© chip-cartridge using a partially cured PDMS layer (Fig Ia. and 1b.). Background electrolyte and CE high-voltage settings for the separation were defined by the protocol of the Minilab©. The culture chamber was filled with a 1% agarose hydrogel as an analytically well-defined substitute for the cell culture. A volume of 10 µl of 1 mM sodium lactate dissolved in deionized water was added into the hydrogel and incubated for 5 min. A fraction of the spiked hydrogel was dispensed from the culture chamber into the CE chip by slightly pressing the top of the microbioreactor. The cartridge was inserted into the Minilab© (Fig. I.c) and the separation showed a lactate and a sodium peak in the electropherogram (Fig. II.). The result confirms the feasibility of microfluidic-integrated capillary electrophoresis for metabolite detection in miniaturized bioreactors. For future measurements of lactate from cell cultures, ions from the culture medium, such as chloride, can be used as internal standard for a quantitative analysis.

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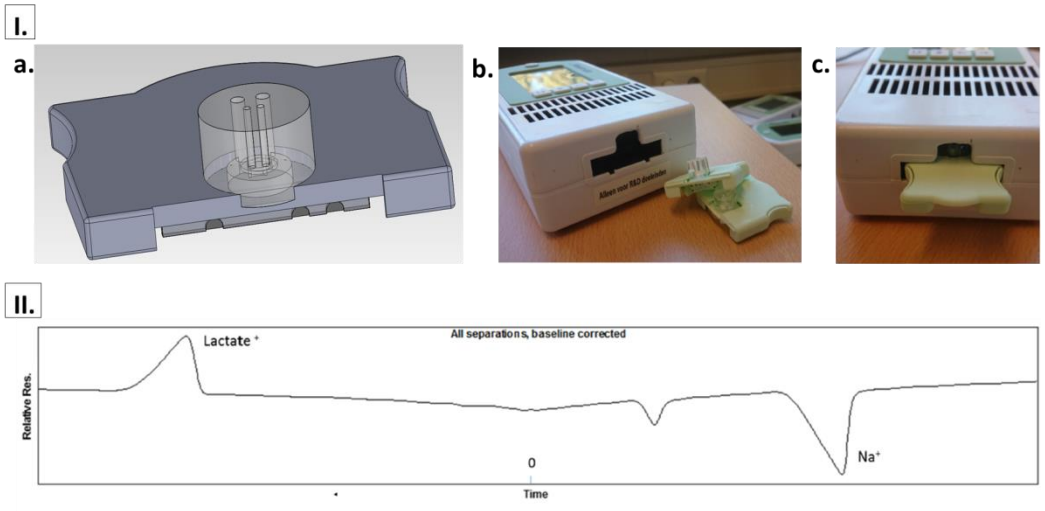

Figure I. Schematic illustration of the microbioreactor assembled with the microchip CE-cartridge (a). Commercial point-of-care capillary electrophoresis Minilab© consisting of an integrated high-voltage system and a contact-less conductivity reader as well as the realized microbioreator assembled with the chip cartridge depicted in the front (b). The cartridge assembly shown inserted into the Minilab© (c).
Figure II. The obtained electropherogram of the measurement of sodium lactate in deionized water spiked to the culture chamber of the microbioreactor.