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A disposable microfluidic biochip with on-chip molecularly imprinted biosensors for optical detection of anesthetic propofol

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ABSTRACT

This paper presents a disposable microfluidic biochip with on-chip molecularly imprinted biosensors for optical detection of anesthetic propofol. So far, the methods to detect anesthetic propofol in hospitals are liquid chromatography (LC), high-performance liquid chromatography (HPLC), and gas chromatography–mass spectroscopy (GC–MS). These conventional instruments are bulky, expensive, and not ease of access. In this work, a novel plastic microfluidic biochip with on-chip anesthetic biosensor has been developed and characterized for rapid detection of anesthetic propofol. The template-molecule imprinted polymers were integrated into microfluidic biochips to be used for detecting anesthetic propofol optically at 655 nm wavelength after the reaction of propofol with color reagent. Experimental results show that the sensitivity of the microfluidic biochip with on-chip molecularly imprinted polymers (MIPs) biosensor is 6.47 mV/(ppm mm^2). The specific binding of MIP to non-imprinted polymer (NIP) is up to 456%. And the detection limit of the microsystem is 0.25 ppm with a linear detection range from 0.25 to 10 ppm. The disposable microfluidic biochip with on-chip anesthetic biosensor using molecularly imprinted polymers presented in this work showed excellent performance in separation and sensing of anesthetic propofol molecules. While compared to large-scale conventional instruments, the developed microfluidic biochips with on-chip MIP biosensors have the advantages of compact size, high sensitivity, high selectivity, low cost, and fast response.

1. Introduction

Propofol (2,6-di-isopropylphenol) is an intravenous anesthetic widely used in induction of anesthesia, total intravenous anesthesia, and sedation of intensive care unit patients. For total intravenous anesthesia, propofol is unique and not replaceable. The effect of anesthesia depends on concentration of propofol in brain correlated to concentration of propofol in blood that could be affected by several factors, such as blood loss, volume replacement, and metabolism. Nowadays, target control infusion (TCI) applies pharmacokinetic programs for clinical anesthetic injection (Leslie et al., 2008; Schnider and Minto, 2007). Although concentration of propofol in blood can be detected by high-performance liquid chromatography and/or gas chromatography (Teshima et al., 2001; Cussonneau et al., 2007; Miekisch et al., 2008), these methods are time-consuming and not easy for access. Clinically, the distinction of anesthesia depth must be obtained immediately for diagnostics and treatment during operations, and the distinction of anesthesia depth will not only be used to know the anesthesia condition of patients, but also for further control of anesthesia dose. Besides, it will enable surgery to be completed under the safest condition. To achieve effective blood concentration and avoid adverse effect produced by excessive or insufficient propofol, clinically, we need a more convenient access to monitor blood concentration within desired clinical concentration range from 1 to 10 μg/mL.

Molecular imprinting is a newly developed technique that provides molecular assemblies of desired chemical structures and properties. In the presence of a template molecule, functional monomers are polymerized and immobilized complementarily to this molecule. After polymerization, the template is removed by solvents. As a matter of fact, molecular imprinting method is quite simple and easy to perform in a tailor-made fashion, and all we need are functional monomers, templates, solvents, and cross-linking agents. Then, polymerization is followed by the removal of template. During these processes, a number of functional monomers are assembled in an orderly fashion with their functional groups placed at the desired sites within the cavities of the desired size. Therefore, molecular imprinted polymers with binding sites, with specific shape and functional group recognition, will enjoy high selectivity and high sensitivity sensing the

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target molecular compound (Sellergren, 2001). In addition, MIP technology has the advantages of high selectivity, high sensitivity, low cost, and robustness, whereas several researches have used these MIP materials to realize molecular imprint to conduct separation or sensing materials (Thoelen et al., 2008; Bossi et al., 2007). Times before, MIPs had been realized with optical sensing techniques in biosensing for several analytes, such as Ca^{2+} ion detection in serum, atrazine detection, and glucose detection (Caglar et al., 2006; Piletsky et al., 1995; Malitesta et al., 1999).

The performance of propofol imprinted polymer material has been extensively investigated using HPLC and spectrophotometer systems (Petcu et al., 2004, 2009). However, the propofol imprinted polymer was fabricated in bulk forms, and propofol MIPs have not yet been used as on-chip propofol biosensors with microfluidic systems. Also, the detected signals of MIP from spectrophotometer systems are incapable to reach high accuracy and high sensitivity at low concentrations.

The objective of this work is to develop a disposable microfluidic biochip with on-chip molecularly imprinted biosensor, with the advantages of compact size, high sensitivity, high selectivity, low cost, and fast response, and it is for accurate measurement of propofol concentrations. In this work, molecularly imprinted anesthetic biosensors are integrated with disposable microfluidic biochips.

2. Design and materials

The optical microfluidic system includes a microfluidic biochip, MIP biosensors, laser diodes, photodetectors, and a control circuit. As shown in Fig. 1(a) and (b), it is found with a schematic illustration of microfluidic biochips with on-chip molecularly imprinted

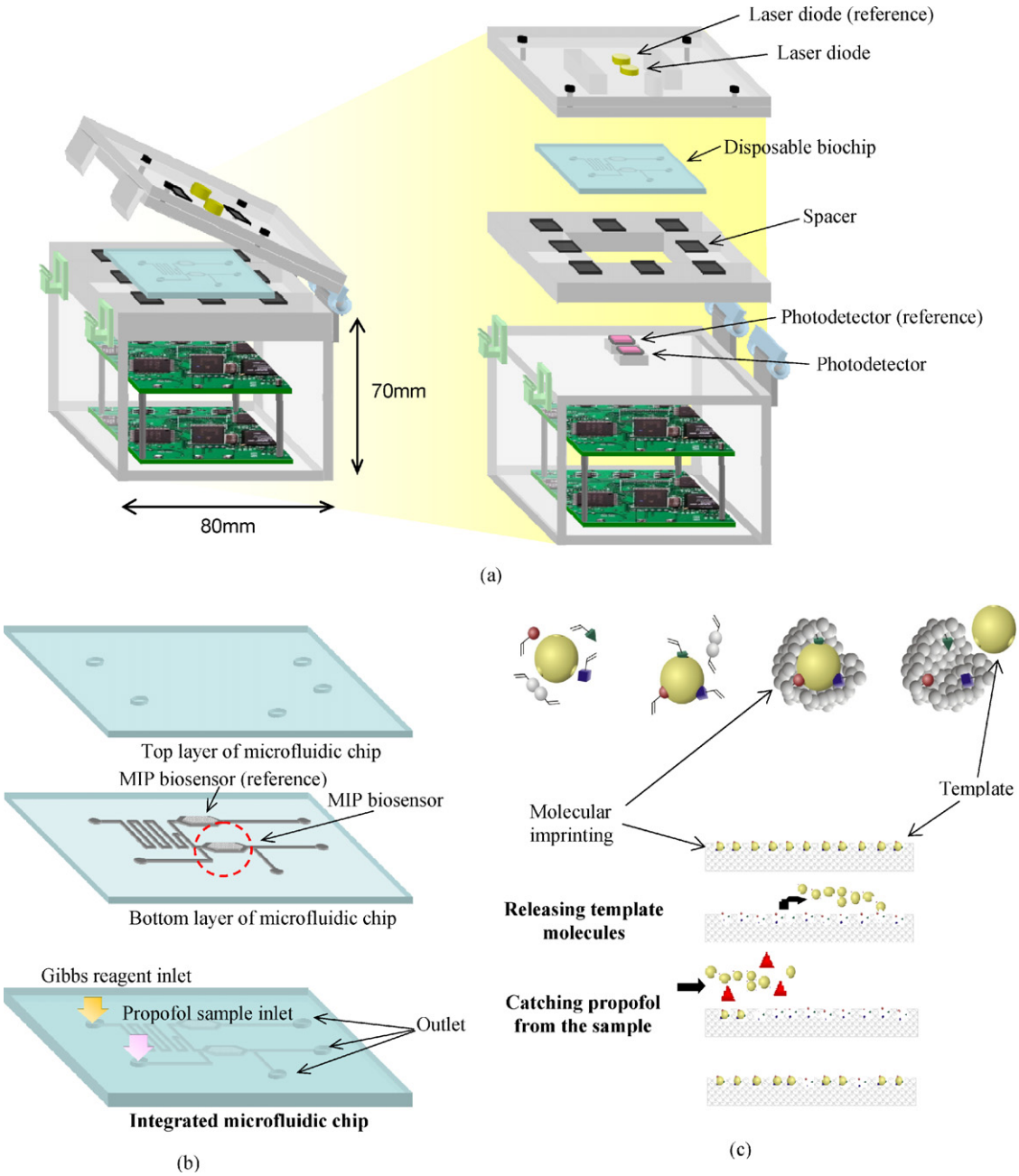

Fig. 1. Schematic illustration of the microfluidic biochips with on-chip molecularly imprinted biosensors for anesthetic sensing and the working principle: (a) the whole microfluidic system, (b) the microfluidic biochip, and (c) the working principle of molecular imprinting.