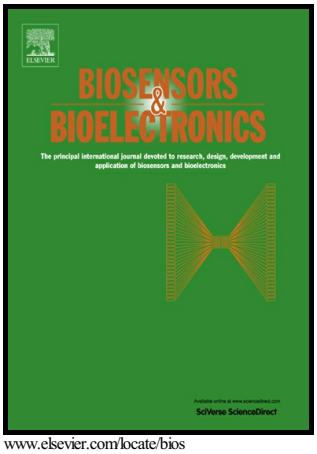

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Ultra-miniaturization of a planar amperometric sensor targeting continuous intradermal glucose monitoring

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Abstract

An ultra-miniaturized electrochemical biosensor for continuous glucose monitoring (CGM) is presented. The aim of this work is to demonstrate the possibility of an overall reduction in sensor size to allow minimally invasive glucose monitoring in the interstitial fluid in the dermal region, in contrast to larger state-of-the-art systems, which are necessarily placed in the subcutaneous layer. Moreover, the reduction in size might be a key factor to improve the stability and reliability of transdermal sensors, due to the reduction of the detrimental foreign body reaction and of consequent potential failures. These advantages are combined with lower invasiveness and discomfort for patients. The realized device consists of a microfabricated three-electrode enzymatic sensor with a total surface area of the sensing portion of less than 0.04 mm^2, making it the smallest fully integrated planar amperometric glucose sensor area reported to date. The working electrode and counter electrode consist of platinum and are functionalized by drop casting of three polymeric membranes. The on-chip iridium oxide (IrOx) pseudo-reference electrode provides the required stability for measurements under physiological conditions. The device is able to dynamically and linearly measure glucose concentrations in-vitro over the relevant physiological range, while showing sufficient selectivity to known interfering species present in the interstitial fluid, with resolution and sensitivity (1.51 nA/mM) comparable to that of state-of-art commercial CGM systems. This work can therefore enable less invasive and improved CGM in patients affected by diabetes.

Keywords: Glucose biosensor; MEMS; Diabetes; Continuous glucose monitoring; Amperometry; Iridium oxide reference electrode.

1. Introduction

Diabetes mellitus (DM) is a set of metabolic disorders caused by either a faulty bodily response (T2DM) or an underproduction in the pancreas (T1DM) of insulin, which regulates the metabolism of carbohydrates and controls hyperglycemia. These diseases lead to unstable and dangerously high oscillations of the glucose level in the body (Vaddiraju et al., 2010a). According to the International Diabetes Federation, diabetes is now affecting 387 million people, and was responsible for 4.9 million deaths worldwide in 2014. Although diabetes is not curable, proper diabetes management is essential to avoid numerous possible complications, both on a short and a long term, such as hypoglycemia, cardiovascular diseases, neuropathy, retinal damage, nephropathy and amputations (Bailes, 2002). Traditionally, patients perform self-monitoring of their glycaemia through capillary blood sampling by finger pricking. Even though the measurement results are very reliable, there are several drawbacks for the patient, such as pain, risk of infections, lesions, and sensory loss, combined with an incomplete temporal picture resulting from 4-5 daily data points (Le Floch et al., 2008). To limit risks and improve the treatment, research in the field of real-time glucose monitoring of interstitial fluid (IF) has gained much attention in the last two decades. In fact, continuous glucose monitoring (CGM) can significantly enhance the quality of the treatment, offering a