0. Abstract

A miniaturized chemical analysis system for extracorporeal monitoring of blood pO$_2$, pCO$_2$ and pH is presented, combining a silicon-based sensor chip and an integrated flow-through channel. Classical electrochemical sensing principles are used, realized in a planar form. The sensor is fabricated entirely on wafer level using IC-compatible processes. By integrating a flow-through channel directly on chip, the sample size and the reagent consumption are drastically reduced. The device characterization has been performed in aqueous solutions, blood intended for transfusion and in whole blood. The sensor exhibits an excellent linearity, low drift and a functional lifetime of more than 2 months.

1. Introduction

The rapid development of silicon technology has strongly stimulated the fabrication of miniaturized electrochemical sensors based on solid-state devices. The largest effort has been made in the biomedical area where the drive is to monitor at the bedside important parameters (blood gases, K$^+$, Na$^+$ and glucose) thus avoiding time consuming centralized laboratory analysis. For all these species miniaturized electrochemical sensors based on Ion-Sensitive Field Effect Transistors (ISFETs) [1] or thin-film planar amperometric cells [2] have already existed for several years, however, their practical applicability remains rather limited. This is mainly due to the lack of longer term sensor stability which requires frequent sensor recalibrations. This important drawback can be overcome by incorporation of the sensor into a total chemical analysis system [3]. Such a complex analysis system, consisting of silicon μpumps, μvalves, sensors and electronics, performs sampling, calibration and signal processing. Due to its extremely small size, it offers improved efficiency with respect to sample volume, reagent consumption and response time. Thus, it is a promising tool for a handheld or bedside analyzer suitable for clinical applications.
2. Sensor Chip Design and Fabrication

The sensor chip provides a flow-through channel directly on chip, which is defined by a 600 μm thick polymeric ring (Fig. 1). In the channel, having an internal volume of 15 μl, nine individual sensing elements are aligned in a row, featuring a reference electrode, four amperometric pO2 sensors, two ISFET-based pCO2 sensors, one pH-ISFET sensor and one temperature sensor. The sensor cells, apart from the pH sensor, which is not covered, consist of a 1 mm x 1 mm hydrogel layer (HG), which is centered on top of the solid-state transducing element.

The Clark-type pO2 sensor provides a working electrode which is an array of 9 x 8 small Pt electrodes with 5 μm in diameter and with a spacing of 100 μm, connected in parallel. The working electrode, the Pt counter electrode and the Ag/AgCl reference electrode are covered with a HG layer, which is separated from the sample by a gas permeable membrane (GPM). The Severinghaus pCO2 sensor consists of a pH ISFET and a Ag/AgCl reference electrode, both covered with the HG and the GPM. The reference electrode for the pH sensor has a similar layout as the one for the pCO2 sensor, but has an opening in the GPM of 0.5 mm x 0.5 mm, which is used as the liquid junction. As pH transducing element, an uncovered pH-ISFET is used.