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Integration of a surface acoustic wave biosensor in a microfluidic polymer chip

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Abstract

SAW devices based on horizontally polarized surface shear waves (HPSSW) enable label-free, sensitive and cost-effective detection of biomolecules in real time. It is known that small sampling volumes with low inner surface areas and minimal mechanical stress arising from sealing elements of miniaturized sampling chambers are important in this field. Here, we present a new approach to integrate SAW devices with sampling chamber. The sensor device is encapsulated within a polymer chip containing fluid channel and contact points for fluidic and electric connections. The chip volume is only 0.9 μl. The polymeric encapsulation was performed tailor-made by Rapid Micro Product Development 3Dimensional Chip-Size-Packaging (RMPD® 3D-CSP), a 3D photopolymerisation process. The polymer housing serves as tight and durable package for HPSSW biosensors and allows the use of the complete chips as disposables. Preliminary experiments with these microfluidic chips are shown to characterise the performance for their future applications as generic bioanalytical micro devices.

Keywords: SAW biosensor; Microfluidic polymer chip; RMPD®; 3D photopolymerisation; 3D-CSP; Disposable

1. Introduction

Surface acoustic wave (SAW) devices based on horizontally polarized surface shear waves (HPSSW) enable label-free, sensitive and cost-effective detection of biomolecules in real time. Due to their high operating frequencies, SAW sensors have the highest sensitivity of all gravimetric methods. A SAW device typically consists of a piezoelectric substrate with interdigital transducers (IDTs) as a planar electrode structure. The wave is generated on the substrate by applying a high frequency alternating voltage via the IDTs. Integration of the SAW device in an oscillator circuit leads to an oscillation with a specific resonance frequency which is mainly defined by the surface wave velocity of the device substrate. This frequency is highly sensitive to the presence of any mass or viscosity changes caused by interactions with the sensor surface and can be used as output signal. To enable specific biological interactions with analyte molecules, the devices are coated with an appropriate sensitive layer (Länge et al., 2003).

The substrate material used for SAW biosensors has to fulfil several conditions. It has to support HPSSW and feature both a high electromechanical coupling coefficient and a low temperature coefficient. Besides, the high dielectric constant of the medium water ($\varepsilon_r \approx 80$) has to be considered. Substrates with low dielectric constants (e.g., quartz, $\varepsilon_r \approx 4.7$) can only be operated as Lamb wave devices (Vellekoop, 1998) or as Love wave devices, i.e., after coating with an acoustically thick wave-guiding layer (Gizeli et al., 1997). The transducers of the latter are typically further shielded by an additional layer preventing a close contact of the medium water with the transducer area. Substrates with a sufficiently high dielectric constant can be used for SAW biosensors without additional wave-guiding or transducer shielding layers (Shiokawa and Moriizumi, 1987; Rapp et al., 1995). All the required conditions are best met by lithium tantalate, $LiTaO_3$ ($\varepsilon_r \approx 43$).

IDTs for SAW sensors are usually made of aluminium. When resistance to corrosion is a major issue, as it is for biosensors, gold (on a chromium or titanium adhesion layer) is preferred. In analytical sensing applications where the device is exposed

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to the environment the weakest link in the chain often is the electrical contact to the IDTs.

There are different ways to contact the IDTs. The usual way is wire bonding. In common high frequency applications, a thin bond wire usually connects the electrode structures with the driving electronics. The wire bonding process requires flexible wires. This implies for our application that the connection is susceptible to failure, especially when exposed to liquid streams. In liquid media, air bubbles are an additional problem as they tend to develop around the bond wires and may interfere with the measurements. Besides, the bonding connection between electrode structures and electronics is permanent, impeding replacement of the SAW device. This problem can be circumvented by attaching (and bonding) the sensor device to a replaceable holder. However, in this case, the device has to be rigidly attached to the holder by clamping or gluing which will deteriorate the response behaviour of the sensor due to mechanical stress. Finally, earlier results have shown the importance of small sampling volumes with low inner surface areas (Länge et al., 2003; Bender et al., 2004), but the presence of the delicate arched wire is an obstacle in the design of small sampling cells or sensor housings.

Alternatively, it is possible to apply some kind of mechanical pressure to make electrical contact, e.g., by using spring contact pins. However, the applied pressure may influence the signal of the sensitive SAW device, leading to drifts or sudden jumps in the output signal. In addition, the contact may degrade due to corrosion or contamination of the contacting surfaces.

On the other hand, since SAW devices are operated at ultrahigh frequencies (UHF), the UHF signal may be coupled into the SAW device by capacitive or inductive coupling instead of a direct ohmic contact. In the case of inductive coupling, the IDT is designed as part of a coil or antenna, which communicates with a second external coil. The feasibility of this approach has been demonstrated (Freudenberg et al., 1999; Beck et al., 1999), however, a more compact and less sophisticated technique remains desirable.

Sensor systems based on capacitive coupling have been developed for sensing applications in gas and liquid phases (Bender et al., 2003; Länge et al., 2003). These systems have been optimised with regard to simple handling and quick replacement of individual SAW devices, small flow cell volumes, short response times and robustness. The approach takes advantage of large electrodes, aluminium or gold, on the SAW sensors enabling capacitive coupling. The SAW devices are simply faced down onto an electronic board on isolated contact pads and fixed on a small milled channel within the board allowing the fluid passing only along the SAW path. This configuration enables cell volumes of only a few microlitres. However, especially when exposed to liquid media, this setup has shown a rather inaccurate sensor calibration. This is because sealing elements made it necessary to apply a minimum of pressure to fix the sensor, and the signal was strongly affected by this pressure on the sensor fixation. Probably the main reason for this unwanted behaviour are different capacities due to different water layer thicknesses between the coupling pads at different contact pressures. This is reinforced by the high dielectric constant of water which is about 80 (at 20 °C). These capacities result in constant but different phase positions of the sensor within its oscillator. From earlier work we know that exactly this effect is critical (Reibel et al., 1998). In contrast to that, this setup is not as critical when used for gas sensor arrays due to the lower dielectric constants of air or most of all other gases (e.g., air has a dielectric constant of 1 at 20 °C). Besides, gas sensors usually are designed to be regenerated, i.e., the sensor signals are reversible. So, sensor calibration and various measurements can be performed repeatedly on the same sensor. Using biosensors, regeneration often is not possible, so a sufficient sensor to sensor signal reproducibility is indispensable, because sensor calibration and measurements have to be performed on different sensors.

Considering all these issues, we decided to develop a new approach which additionally enables a remarkably higher level of miniaturization. The sensor device is completely packed within a tailor-made polymeric housing produced by Rapid Micro Product Development 3Dimensional Chip-Size-Packaging (RMPD® 3D-CSP), a 3D photopolymerisation process (Bohlmann et al., 2001; Götzen, 2003). RMPD® technologies are tool-less production procedures and belong to the generative technologies, i.e., all of the production steps are based on an accumulative procedure. Components can be built up in layers up to 1 μm and with a resolution in any direction of up to 10 μm. 3D-CSP is based on RMPD® technology and enables the integration of components from any microtechnology sector during the production process. Since all three dimensions are accessible in 3D-CSP, the single active and passive elements cannot only be arranged side by side but also on top of each other.

In our case, the result is a polymer chip as a tight and durable package for SAW biosensors which are completely encapsulated within the polymer chip, together with a flow channel leading across the SAW path. The volume of the whole chip is only 0.9 μl. The contact to the IDTs is done by conducting paths made of copper. They are also buried within the chip and lead from the pads of the sensor to the margin of the chip. From outside, they can be contacted with standard spring contact pins. These SAW biosensor chips are widely insensitive towards mechanical stress or phase position changes due to a durable encapsulation and pure ohmic contacts. Preliminary measurements applying these sensor chips are shown. Their performance is compared to that of a previous sensor system based on a capacitive coupling technique.

2. Experimental

2.1. SAW device and instrumentation

The SH-SAW resonator type E062 was designed in cooperation with Siemens, München, Germany, and delivered by EPCOS, München, Germany. The resonator is based on a 36°YX-$LiTaO_3$ substrate with gold transducers (see Fig. 1) and has a frequency of operation of 428.5 MHz (medium: air). The area of the SAW device is 4 mm × 4 mm, the thickness is 0.5 mm. The aperture of the IDTs is 0.2 mm.