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Manufacturing and replication of sub-10 µm micro-bowls for biomedical sensor systems

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Abstract
The technical implementation of a novel biosensor for the highly parallelized screening of biochemical binding reactions depends on the manufacturing of an array of micro-bowls with a diameter $d_B \leq 10$ µm with an aspect ratio $a_r \geq 1$. Since the operating principle of the biosensor is based on the stimulation of stationary optical waves in micro-spheres, micro-bowls for the immobilisation of these spheres in a microfluidic environment are necessary. Due to this operating principle, the micro-bowls need to separate the spheres from the fluid flow and ensure the careful adherence of single spheres, coincidently. Moreover, the pathway for the optical accessibility of the micro spheres should be unrestricted.
This work presents a process chain for the manufacturing of microfluidic chips with an array of $n \geq 1{,}000$ micro-spheres by ultra-precision milling of mold inserts, the replication by precision injection molding as well as experimental trial results. With regard to manufacturing of the mold inserts, the uniform and burr free ultraprecision milling of large aspect ratio micro posts was investigated within a parametric study. Furthermore, the replication of the micro-bowls was examined by taking the consistent replication of the entire bowl array, the adverse formation of fillets, and the replication of surfaces with optical functions into special account. By the analysis of the microfluidic and optical properties of the replicated structures, the correlation between mold manufacturing, replication, and operating conditions can be performed.

Keywords: ultraprecision milling, injection molding, biosensor, micro-bowl

1. Introduction

Scaling of high-precision analysis systems for highly parallelized applications in medical or pharmaceutical applications is one of the key fields of development in current measurement technology. Furthermore, the substitution of immobile and large equipment is an ambitious goal with regard to the development of point of care diagnostic systems. By the use of surface plasmon resonance as measurement principle, measurement accuracy meets the requirements of demanding real time analysis purposes.

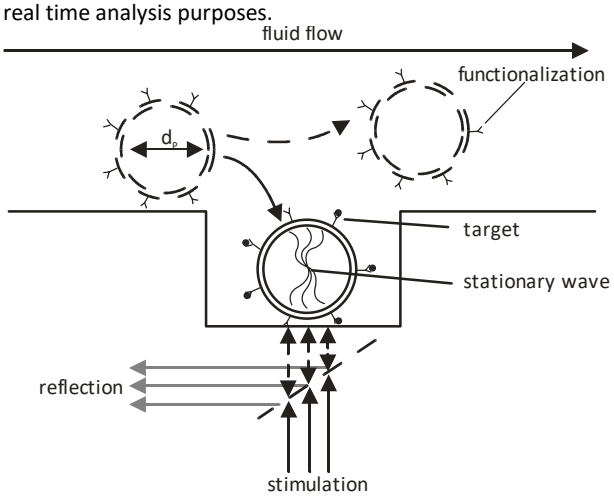

Figure 1. Schematic representation of the investigated measurement priciple

Nevertheless, demanding optical setups and the necessity of high-precision spotter systems rules out mobile or point-of-care applications. By the use of polymeric micro-spheres and the induction of stationary optical waves, the surface plasmon resonance effect can be transported into an easy to monitor analysis environment. Using a customary fluorescence microscope and a spectrometer, a wavelength shift of the reflected light due to a mass change of a single micro-sphere can be measured. By a functionalisation of the shell of the micro-particle, the adsorption of target molecules can be controlled. The measurement pricinciple is schematically illustrated in figure 1 [1, 2].

2. Upscaling approach

For the transport of the measurement principle into real applications, two general requirements must be met. On the one hand, the positioning of functionalised micro-spheres with a diameter $d_P \leq 10$ µm in the investigation area of the analysis system is necessary. On the other hand, the application-specific scaling from single sphere investigation to a multi-channel analysis system must be ensured.
Hence, a microfluidic chip with an array of micro-bowls with a diameter $d_B \leq 10$ µm and a hight $h_B \leq 10$ µm was designed for immobilisation, stimulation and read out of the optical answer of the micro-spheres. As a result of this approach, the transport of the micro-spheres can be progressed by the flow of a transport fluid. The immobilisation of the spheres is affected by their deposit into the micro-bowls.
To ensure the economic acceptance, the replication of the microfluidic chip by injection moulding is intended.

3. Machining of mould inserts

The manufacturing of mould inserts, needed for the replication by injection moulding, was performed by ultraprecision milling with a single crystal diamond end-mill. On a surface of aluminium (Al) with the main dimensions width w = 75 mm and hight h = 25 mm, an array consisting of n = 1,323 posts was machined. Due to a path length of l_c = 35 m, compensation of tool wear in longitudinal direction was done to ensure consistent post height h_P. The general layout of the mould insert, the milling setup and the machining results are presented in figure 2.

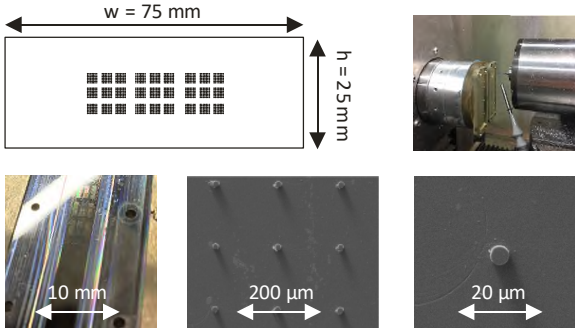

Figure 2. Schematic layout of the mould insert, milling setup and processing results

As a result of a parametric study and taking burr formation and dimensionally accuracy as key quality indicators, the manufacturing of a mould insert according to the specification was realised [4].

4. Replication of microfluidic chip by injection moulding

Using an Allrounder 270, ARBURG GMBH, Loßburg, Germany injection moulding machine tool with a reciprocating screw diameter of d_S = 18 mm and the ultraprecision machined mould inserts, the micro-structured chips of ZEONEX K330R, ZEON CORP., Tokio, Japan, polymer were replicated.

Figure 3. Machining area of the used injection Moulding machine tool, replicated microfluidic chip and inverted representation of the replicated micro-bowls, measured by laser scanning microscopy

As presented in figure 3, the replication of the micro-bowls could be performed with extremely small edge fillet and excellent quality of the surfaces with an optical functionality. To meet these quality requirements and again as a result of a parametric study, variothermal mold tempering was the key technology adaptation. Varying the wall temperature between ϑ_1 = 135 °C and ϑ_2 = 110 °C and the accompanying undercut of the glass transition temperature ϑ_G = 123 °C, the replication of the full micro-bowl array could be verified [5, 6].

6. Summary and Outlook

By the experimental study, the feasibility of the presented process chain for mould manufacturing and replication of micro-bowls could be proven. As a cost effective alternative towards process chains based on lithographic micro-structuring and etching, the presented process allows an equivalent quality level with a far wider design scope.
Nevertheless, durability of the micro-structured mould inserts with regard to a desired number of cycles between $100 \leq n_C \leq 1{,}000$ as well as influence and effects of surface topography, main dimensions and the form of the micro-bowls on the primary function of the analysis method have to be investigated.

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