

APPLICATION OF 3D PRINTING FOR CREATING AND PROBING BIOPHOTONIC ARRAY SENSOR BASED ON OPTICAL RESONANCE METHODS

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We have used several schemes for experimental realization of WGM optical resonance in dielectric microspheres method [1–7]. For further sensitivity and accuracy improvement we introduced a new scheme for microcavity array construction. Developed arrays are designed as a series of columns with microspheres. These columns are separated from each other by polymer boxes or trapezes.

In current setup we did not start our sensitive layer preparation with thin adhesive layer placing on the substrate [1–7]. For polymer structures construction 3D printer (RepRap X400) has been used (Fig. 1). This 3D printer has been chosen, since the RepRap project is an initiative to develop a 3D printer that can print most of its own components and now RepRaps are constructed to be printed in any type of materials. RepRap (replicating rapid prototype) uses an additive manufacturing technique called Fused Filament Fabrication to lay down material in layers; a plastic filament (e.g. ABS, PLA) is unwound from a coil and supplies material to produce a structure. To produce structures for microcavities' row creation, one or several polymer layers have been extruded on the surface of substrate. In order to produce a sensitive cell we prepared a structure-model (StereoLithography file format) in the stereo lithography open-source CAD software were all boxes or trapezes are connected on the edges with each other. The distance between two neighbour boxes was adjusted in a range of 80÷120 microns. Then two other open source, free to use, relatively quick, and extremely customizable software packages (Slic3r and German RepRap Repetier-Host) were used in order to slice prepared model into layers and create a g-code file that has to be sent to the 3D printer.

Two different techniques have been used for microspheres fixation. First technique has been former developed and it has been discussed in previous publications [1–7], where microspheres were superimposed on the surface of adhesive layer and were fixed just by this layer (Fig. 2, b). Compact spin-coater system with digital dosage was used to put and dry previously a thin film of adhesive directly in the wells. After that, microspheres were superimposed on the surface of adhesive layer and final drying procedure by free solvent evaporation

during 12 hours followed (Fig. 2, d). All microspheres, that did not fall into wells, were being washed away. Under optimized experimentally parameters of the process microspheres were reliably fixed as it was tested. The most part of microsphere surface turned out to be in contact with tested solution and thus could react to variation of the solute concentration. Another possibility is to fix microspheres without any adhesive layer (Fig. 2, c). This technique is more complicated for obtaining the microsphere-substrate contact and less stable for long-term experiments (microspheres can be washed out due to worse contact). In addition, there is possibility to induce additional strain on a microparticle in current approach, which might influence on resonance spectra; therefore, first technique has been preferably used.

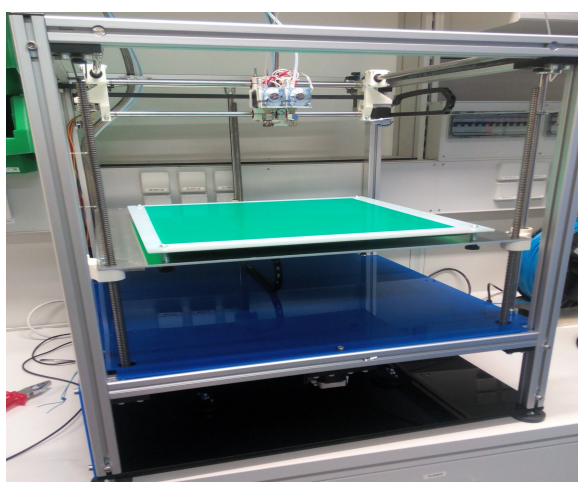


Fig. 1. 3D printer setup (RepRap X400)

In our experiments we used microspheres made of quartz glass, which are stable in case of WGM optical resonance spectra in water environment. This choice was determined by the fact, that in former experiment we have found long-term spectral shift of WGM optical resonance maxima while using PMMA microspheres [4].

Different rows of one array can be functionalized by different biological agents or by gold nanoparticles (plasmonic improvement) [5, 7]. In plasmonic-improved with gold nanoparticles experiments sensitive layers were kept inside water suspension of gold nanoparticles during several hours. More details are represented in [5].

The developed method to determine parameters of solutions of the biological agents, based on whispering-gallery modes optical resonance was presented in [1–3]. However, some important features that are different from the published method need to be noticed. The microspheres are submerged into a fluidic cell (in between two polymer structures) and brought into contact with the prism. The cell contains initially de-ionized (DI) water and in order to vary the

optical path distance, a solution of biological agent or particles is incrementally added to the fluidic cell with a digital syringe. As published before, light scattered by the microspheres after passing through a microscopes was captured by a CMOS camera. Region of interest (area with microcavities' line) has been selected, which permits the increase of capturing speed for selected microspheres and, as a result, improving the sensitivity. Then each microsphere has been selected and independently processed as it was published in [4–7]. Scattered light power measured as integrated on the frame area intensity after filtering to minimize noise was used as relative scattered intensity (Fig. 3). To observe several WGMs, the laser repeatedly scans across a spectral range of approximately 3 nm at a frequency of about 0.01 nm/s. Intensity variation following laser tuning WGM spectral position was being recorded by data acquisition card and computer.

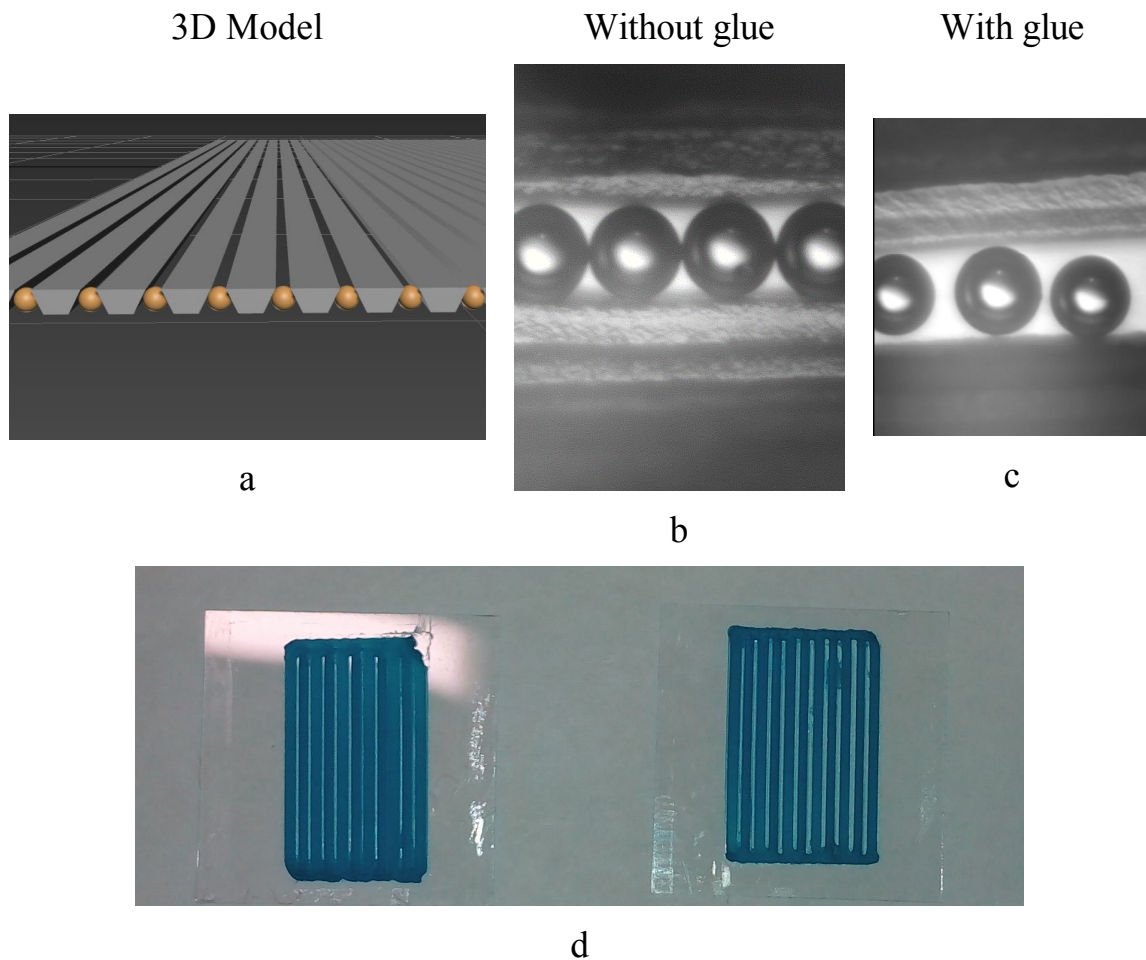


Fig. 2. Microsensors array overview: (a) 3D model of array, (b) photo of an array constructed without using thin adhesive layer, (c) photo of an array constructed with using thin adhesive layer, (d) photo of an arrays

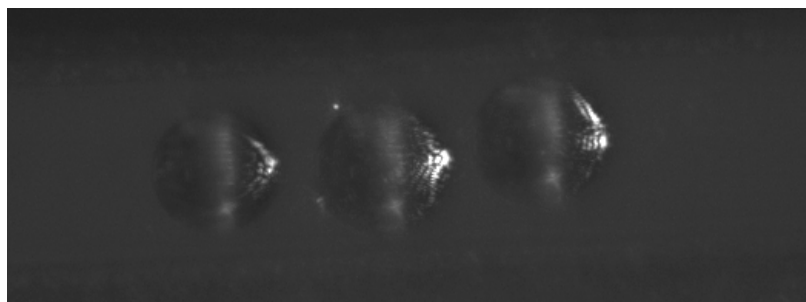


Fig. 3. Resonance in microcavity array

Laser beam was sharply focussed on the investigated microspheres to increase the contrast and intensity of the resonance scattering signal. If the wavelength of the tuneable laser corresponds to the resonance of the sphere, the power of the light scattered by the microsphere increases, and a spectral maximum indicating the WGM spectral position is recorded.

A new technique for microcavity array sensor construction used for detection and identification of drugs on the basis of spectroscopy of optical resonance of WGM has been developed. In our approach glass microspheres with diameter of around 100 μ in bounded with polymer sensitive cells has been used to read-out biological response in high-throughput experiments. Sensitivity of different sensitive cells (rows) of array sensor can be improved or functionalized with biological agents and proteins treating or also combining resonance of WGM with plasmonic resonance nanoparticles. Developed array sensor provides simultaneous analysis of interaction of biological sample under investigation with other biological agents that have been used for sensitive cells functionalization.

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