

Lab-on-a-Chip

DNA amplification in a flow-through microreactor

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Chip-based flow-through PCR implements the PCR as a continuous process for nucleic acid analytics. The sample is transported in a winding channel through temperature zones required for denaturation, annealing and extension. Main fields of application are the monitoring of continuous processes for rapid identification of contaminants and quality control as well as high throughput analysis of cells or microorganisms. A modular arrangement with five heating zones for flow-through PCR is discussed and evaluated. The special heater arrangement allows the implementation of up to 40 cycles on the footprint of a microscope slide, which is placed on top of a 5 zones heating plate. Liquid/liquid two phase flow of PCR reaction mixture and mineral oil has been applied to create a segmented flow process scheme. All-glass microfluidic chips and disposable chip devices, made from polycarbonate by replication of the all-glass device with identical geometry have been fabricated and tested.

Thermal concept

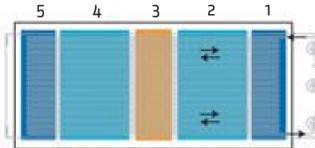


Fig.1: Scheme of the flow-through PCR module

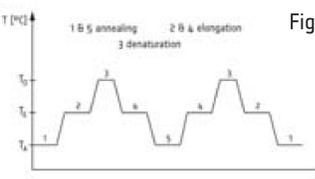


Fig.2: Temperature profile of a sample running 2 cycles over the 5 temperature zones in one of the 20 channel loops of the fluidic module

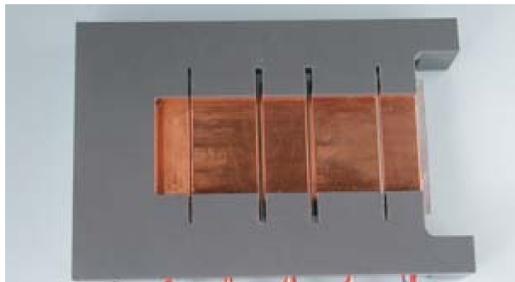


Fig.3: Picture of the heating module. Clearly recognisable the 5 temperature zones, thermal isolated by air gaps

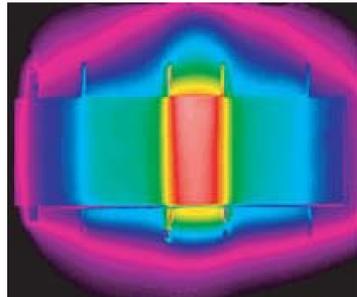


Fig.4: Thermal image of the heating module with dropped fluidic module

Fluidic concept

The PCR sample buffer is divided into droplets. These droplets are embedded into mineral oil and transported through the winding microchannel of the Lab-on-a-Chip device. The microchannel surface has been treated with Octadecyl-trichlorosilane for optimized compatibility with the transport regime of a reliable segmented flow.



Fig.5: Picture of the all-glass prototype of the fluidic module with fluidic interface

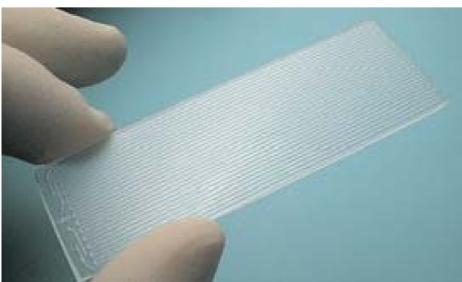


Fig.6: Picture of the final fluidic module made from polycarbonate (disposable)

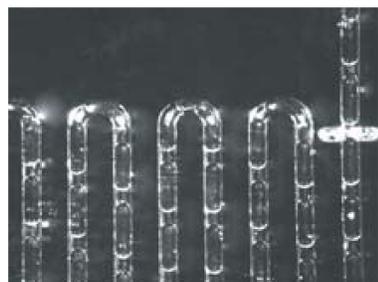


Fig.7: Picture of the segmented flow, sample droplets embedded in mineral oil

Results

Determination of the optimal flow rate

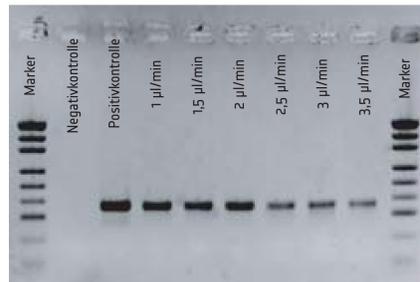


Fig.8: Gel electrophoresis of the PCR reactions with different flow rates

Application of alternative materials

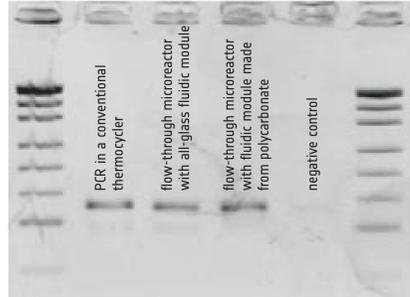


Fig.9: Gel electrophoresis of the amplification of the tumor suppressor gene p53

The developed 5 zones arrangement allows the implementation of one PCR cycle in a half channel loop. With this condition the microreactor possesses a 40 cycles flow-through thermocycler on the footprint of a microscope slide. The segmented-flow conditions of the fluidic module were designed for high-throughput analysis of PCR samples in a small volume of 10 – 100 nL. Each droplet of PCR solution in a flow of mineral oil may contain a single sample that is independently processed during movement through the microchannel. The PCR conditions can be adapted to different applications by variation of the flow rate, the arrangement of the temperature zones and the geometry of the microchannel.