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FONDAZIONE BRUNO KESSLER

DESIGN AND FABRICATION OF A MICRO PCR MODULE FOR POC APPLICATIONS

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Overview

This work deals with the development of a disposable miniaturized Polymerase Chain Reaction (PCR) module that will be integrated in an innovative Lab on a Chip (LOC) as Point of Care Testing (POCT) platform to detect the susceptibility of complex diseases with genetic profiling. The amplification system consists of a micro-chamber reactor with a hybrid silicon-polymer structure. The temperature control system has been implemented by means of Platinum microheaters and thermometers integrated on a Silicon substrate and the reaction chamber has been completely made of Polydimethylsiloxane (PDMS) since it is biocompatible, transparent and easily moldable. To assure a perfect sealing, an oxygen plasma bonding process step has been implemented. The device design has been supported by analytical and finite elements simulations in such a way to evaluate the thermal requirements. A first PCR chamber prototype has been fabricated and packaged.

1. The selected approach: a micro chamber PCR

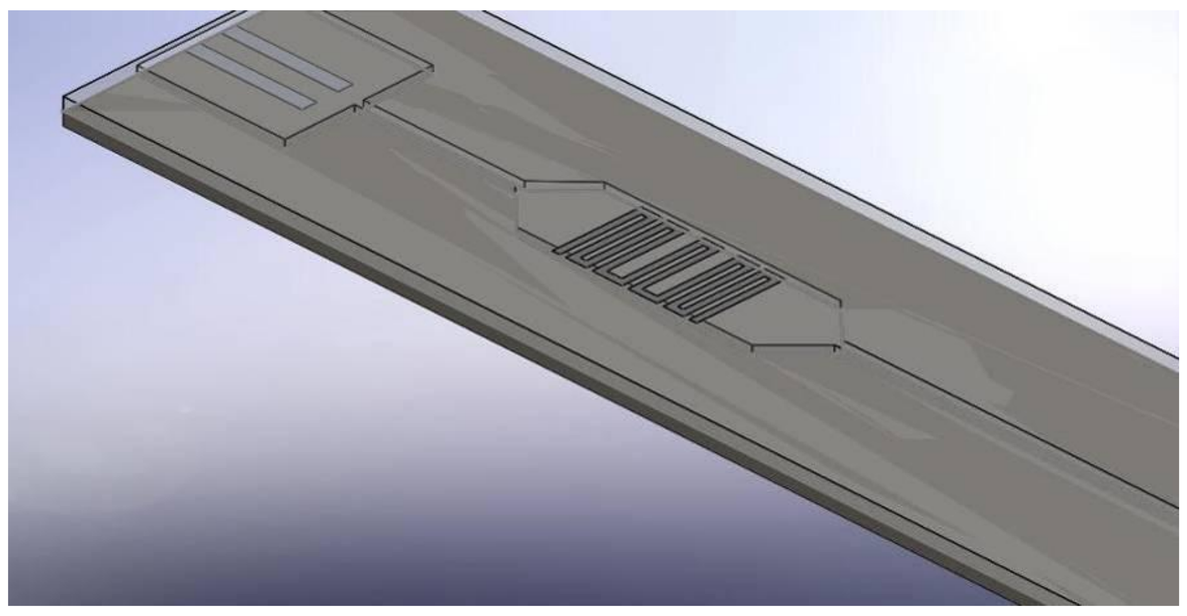


Figure 1. Schematic sketch of the micro PCR module

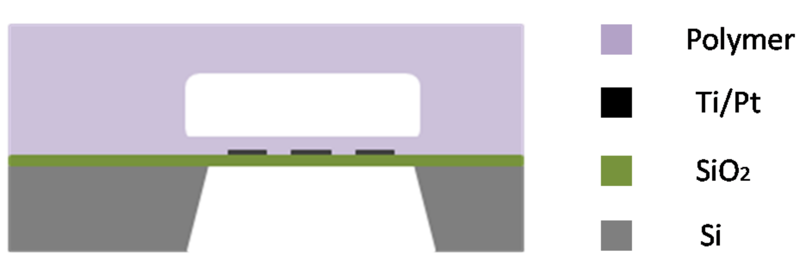


Figure 2. Cross section of the first µPCR prototype

Main advantages of the chamber type:

- ✓ No need for complex fluidic
- ✓ Reduced sample absorption on the channel walls
- ✓ Easier fabrication
- ✓ Possibility of parallelization (multi chamber)
- ✓ Increased flexibility over the cycles number

2. Design and materials selection

The layout reported in Figure 3 includes the reaction chamber, two channels and two inlet/outlet ports, thermal valves and the electrolytic pump for the fluidic management and heaters and thermometers for the temperature control.

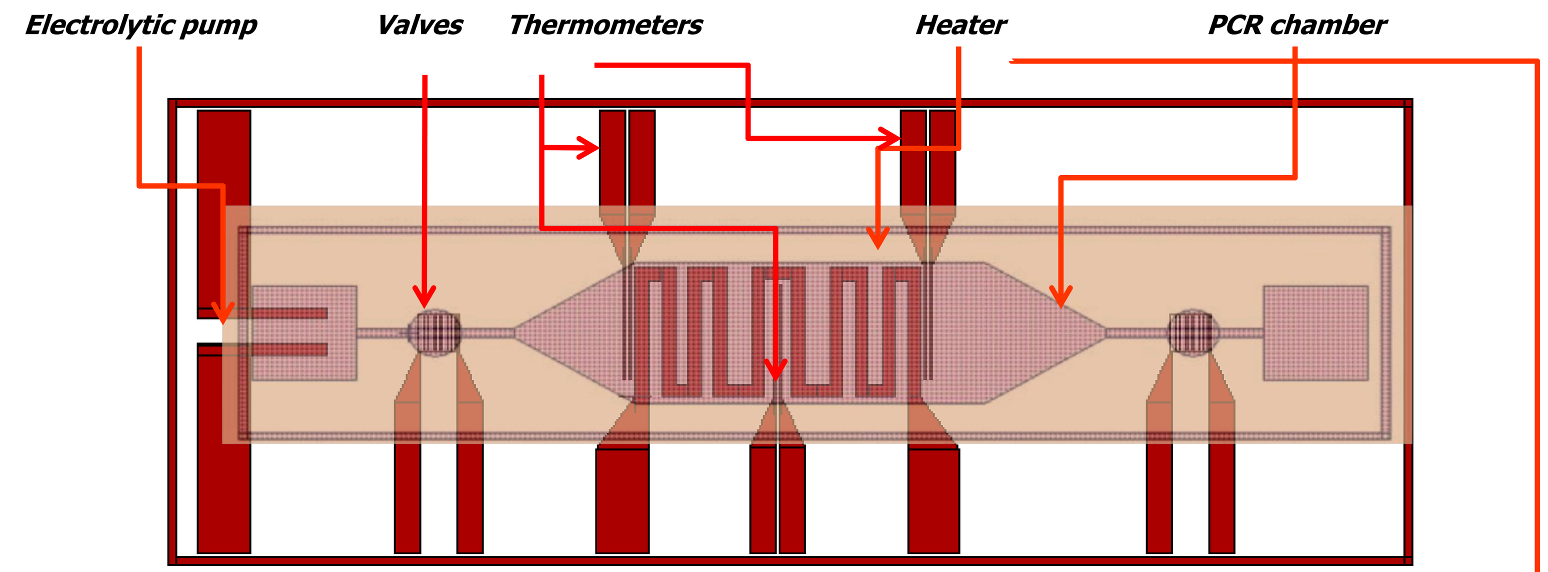


Figure 3. Design of the preliminary PCR module for stand-alone testing purpose

Material	Advantages	Resistivity Ω/square	Thermal conductivity (W/mK)	Heat capacitance (J/KgK)
Platinum	Thermal stability, Ideal TCR	0.96	71.6	130
PDMS	Biocompatible, easily moldable	-	0.15	1460
Silicon	Well-established fabrication process, thermal conductivity (faster cooling)	-	148	1000

Material	Platinum
Wire width	250 µm
Wire length	33.5 mm
Resistance	125 Ω
Power	0.4 W
ΔT (and time)	40º in 3 s
Voltage	6 V

Table 2. Heater's design parameters

3. 2D and 3D FEM simulations

Finite Element Simulations have been used to estimate the heating and cooling time (Fig. 5-6) and the required power (Fig. 7) and to assess the heat uniformity in the chamber (Fig. 4).

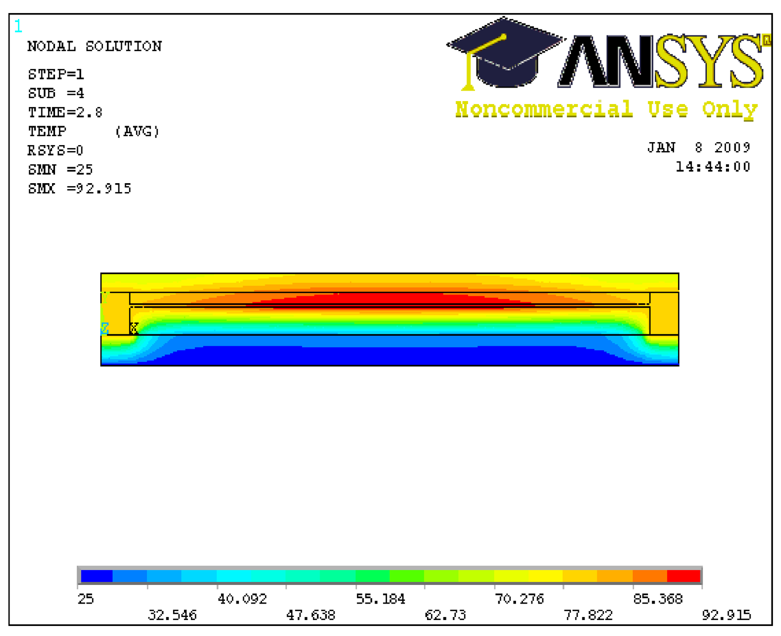


Figure 4. Temperature contour plot (C) (2D)

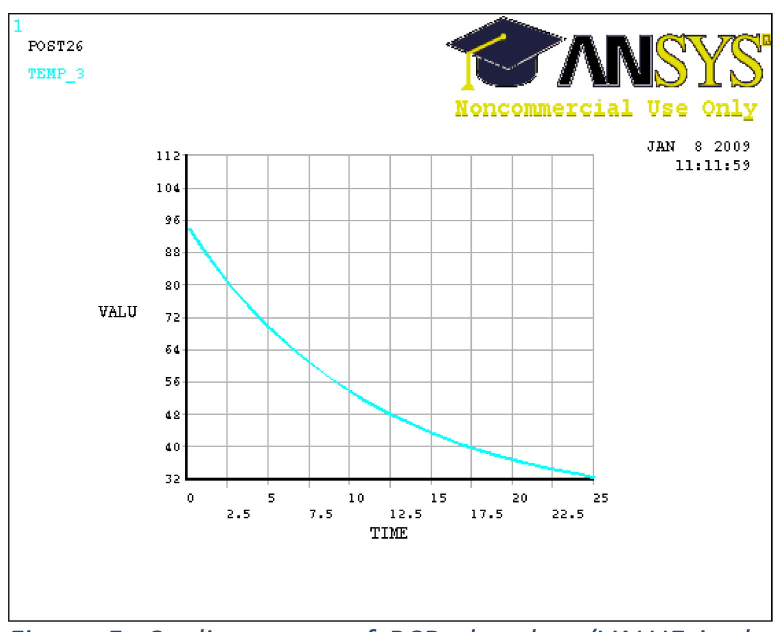


Figure 5. Cooling curve of PCR chamber (VALUE is the temperature (°C) and TIME is in seconds) (2D)

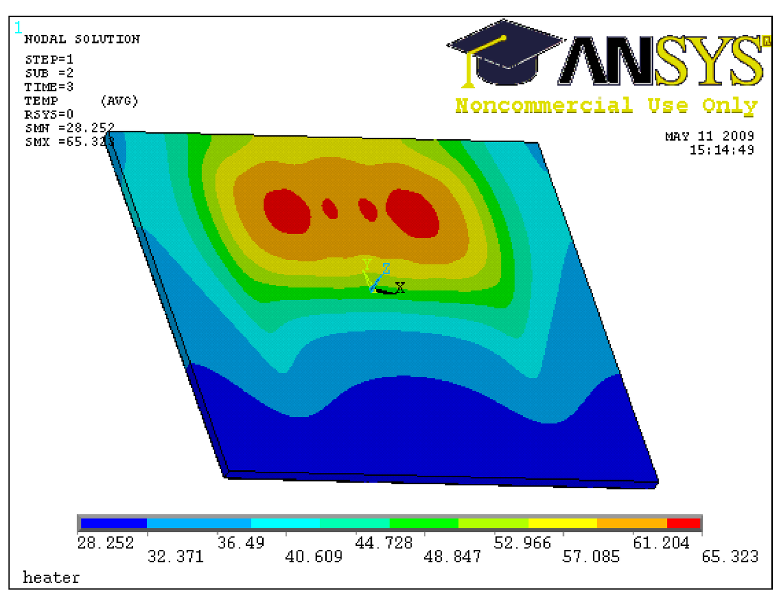


Figure 6. Temperature contour plot after 3s (°C) (3D)

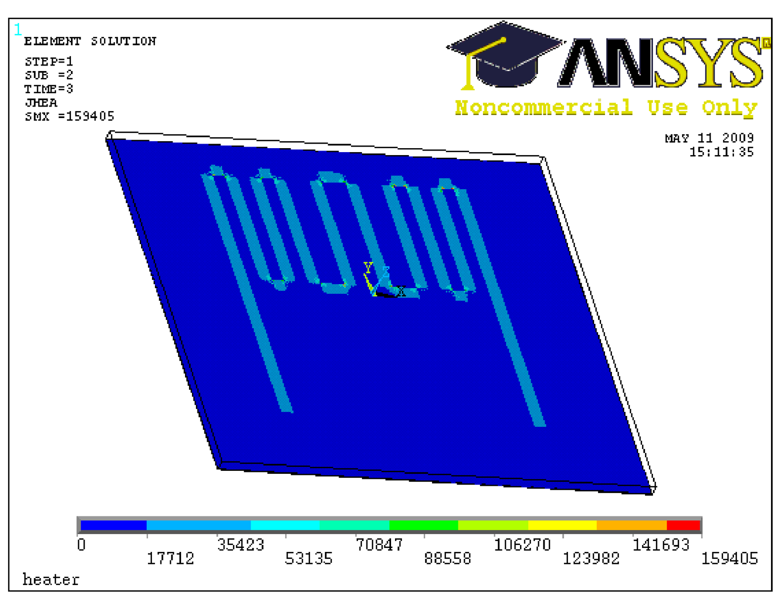


Figure 7. Heater Joule heating (10^{6} W/m^{3}) (3D)

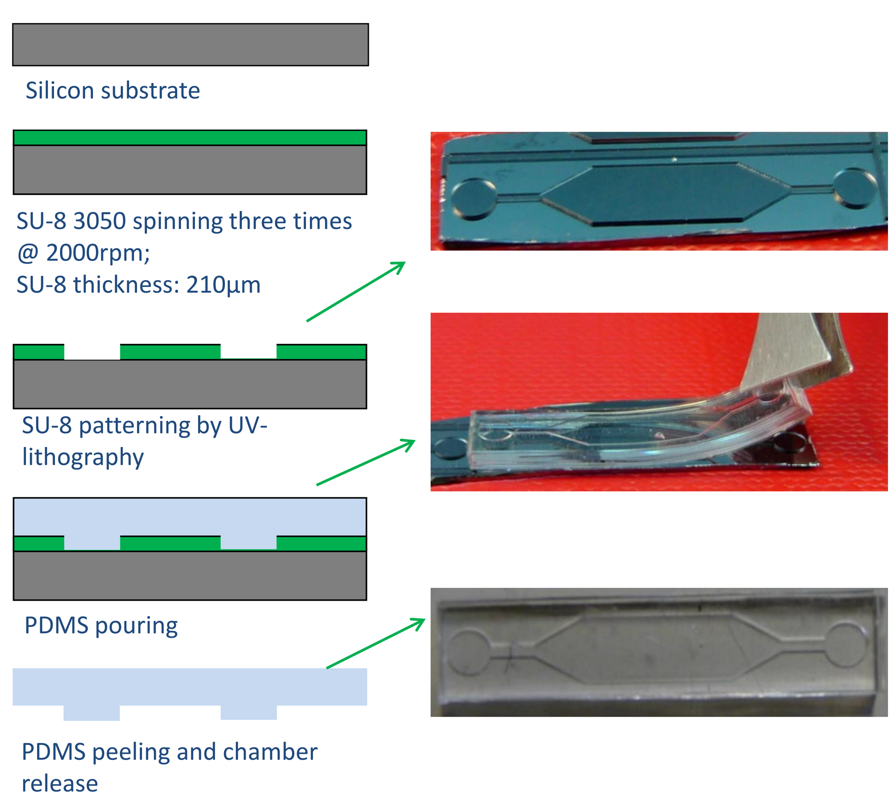
2D Simulation conditions		3D Simulation conditions	
Material	PDMS 500µm Air 500µm Silicon 50µm Water 210µm PDMS 300µm	Material	Silicon 50µm Water 210µm
Boundary condition	Convection on the external surface h=25, T=25ºC Heat flux = 0.4W/AREA	Boundary condition	Convection on the external surface h=25, T=25ºC Applied voltage=6V

Table 3. 2D and 3D simulation parameters (Material and boundary conditions)

4. The microfabrication process

The fabrication process is divided in two parts:

Realization of the PDMS cover



Realization of heaters and thermometers on a silicon wafer

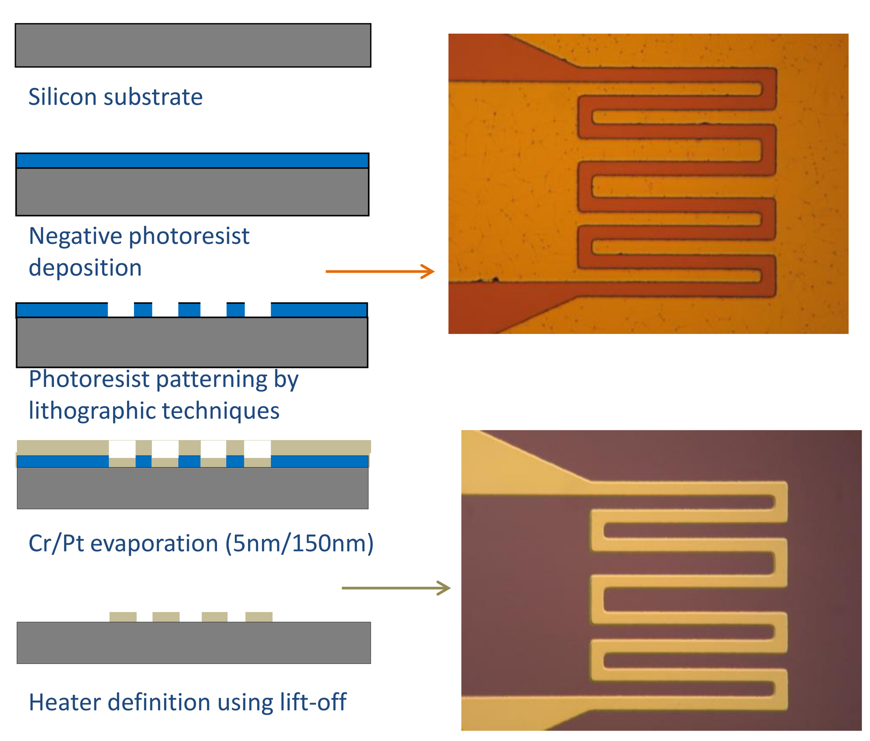


Figure 8. Picture of the assembled PCR device

7. Conclusions and future works

This work reports the design, modeling and realization of a microdevice for PCR, realized with silicon and soft lithography fabrication techniques. The final micro reactor will be coupled with a label-free Single Nucleotide Polymorphisms (SNP) microarray based on microcantilevers. To match the requirements of the detection module, a multiplex asymmetric PCR (MAPCR) will be required. The coupling of the proposed PCR module with a cantilever-based detector would provide a really portable and automated multifunctional system able to fulfill a wide number of critical clinical practices.