4th Micro and Nano Flows Conference
UCL, London, UK, 7-10 September 2014

Continuous Flow vs. Stationary μPCR Devices on Ultra Thin Polymeric Substrates

Vasileios E. PAPADOPOULOS, Ioanna K. KEFALA, George KOKKORIS*, and Angeliki TSEREPI

* Corresponding author: Tel.: ++30 2106503238; Fax: ++30 210 6511723; Email: gkok@imel.demokritos.gr
Department of Microelectronics, Institute of Advanced Materials, Physicochemical Processes, Nanotechnology & Microsystems, NCSR "Demokritos", Greece

Keywords: microflow, heat transfer, PCR, microfluidics, DNA amplification, polyimide, μTAS, LoC, FCB technology

Polymerase chain reaction (PCR) can create copies of specific fragments of DNA by thermal cycling. A typical PCR includes denaturation of double-stranded DNA (at 95°C), annealing of primers (at 60 °C), and extension of the primer-bound sequences (at 72°C). Each thermal cycle can double the amount of DNA, and 20–35 cycles can produce millions of DNA copies.

μPCR devices can be categorized to stationary and continuous flow devices. The stationary devices resemble the conventional thermo-cyclers at their operation; the sample is static in a well and both the device and the sample undergo thermal cycling. One type of continuous flow devices comprises fixed loop devices where the sample moves through fixed temperature zones to achieve the required thermal cycling; the number of cycles is determined at the fabrication stage. A second type of continuous flow devices comprises closed loop devices where the sample circulates in the temperature zones. The number of thermal cycles can be adjusted at will during the operation.

Efficient and fast amplification as well as and low power consumption are of a great importance for a μPCR device. For efficient amplification, good temperature uniformity and precise temperature control in the three thermal zones are required.[1]

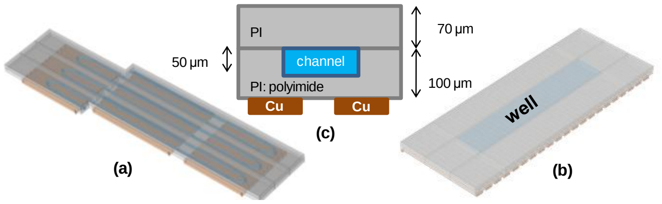

Figure 1. Schematic of a) 3 unit cells (3 thermal cycles) of a continuous flow fixed loop and b) a stationary μPCR device. c) Material stack of the devices integrated with thin metal heaters.

Since the early 1990s, several materials (Si, glass, and recently polymers), technologies, and designs have been utilized for fabrication of μPCR devices.[2] *In this work, continuous flow and stationary μPCR devices based on the same technology (material stack and fabrication process) are evaluated by simulation. In particular, a fixed loop μPCR device (Fig. 1a) is compared with a closed loop and a static (Fig. 1b) device in terms of temperature uniformity in the PCR zones, speed, and power consumption. All devices are based on flexible circuit board (FCB) technology*; the substrate is a biocompatible and thin (50 – 100 μm) polyimide (PI) layer coated with an even thinner metal layer on which resistive heaters are fabricated for sample thermal cycling. PI has been already used as a structural material for stationary μPCR devices.[3,4] Recently,[5] it has been used for fixed loop continuous flow devices but not for closed loop devices. *The aim of this work is the evaluation of FCBs as substrates for continuous flow and stationary μPCR devices.* The evaluation is performed by simulation of the μPCR performance with respect to temperature uniformity and power consumption. The mathematical model consists of the heat transfer equation which is coupled to momentum balance and continuity equations. The equations are numerically solved in 3d and at steady state by the finite element method implemented by a commercial code.

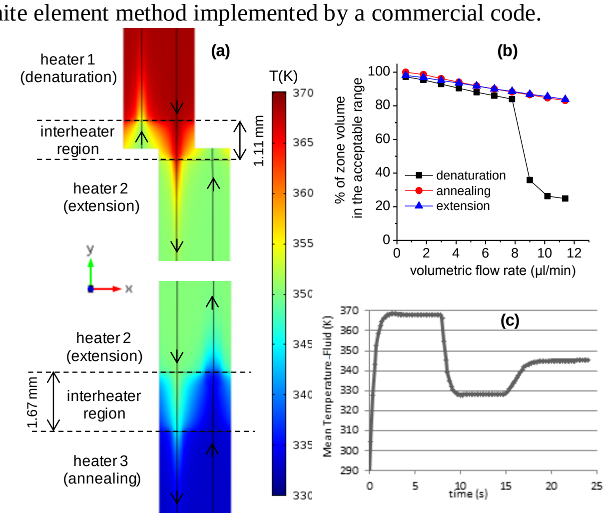

Figure 2. a) Temperature at a cross section (middle of the microfluidic channel height) of the unit cell of a fixed loop μPCR. The focus is on the interheaters region. Arrows show the direction of flow. b) The percentage of the volume of each zone in the acceptable temperature range (set point ±1.5 K) vs. flow rate. c) The mean temperature of fluid during one thermal cycle in a stationary μPCR.

In Fig. 2a the thermal "cross-talk" between different zones of a fixed loop μPCR is shown. The percentage of the volume of the zones in the acceptable temperature range (±1.5 K from the set point) is shown vs. the flow rate in Fig. 2b. The mean temperature of the fluid during one thermal cycle in the stationary μPCR is shown in Fig. 2c.

[1]Y. H. Zhang and P. Ozdemir, Anal Chim Acta **638,** 115 (2009).
[2]C. S. Zhang, J. L. Xu, W. L. Ma, and W. L. Zheng, Biotechnol. Adv. **24,** 243 (2006).
[3]B. Giordano, Analytical Biochemistry **291,** 124 (2001).
[4]K. Shen, X. Chen, M. Guo, and J. Cheng, Sensors and Actuators B: Chemical **105,** 251 (2005).
[5]D. Moschou, N. Vourdas, M. K. Filippidou, V. Tsouti, G. Kokkoris, G. Tsekenis, I. Zergioti, S. Chatzandroulis, and A. Tserepi, Proc. SPIE 8765, Bio-MEMS and Medical Microdevices **8765,** 87650L (2013).