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Submicroliter-Volume Bulk-Micromachined Si-PMMA Thermal Cycler with a Multi-Stacked Dielectric Membrane

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A micromachined submicroliter-volume thermal cycler with a multistacked dielectric membrane for the polymerase chain reaction (PCR) has been designed and fabricated; it has a fast thermal response and very low power consumption. The chip consists of a bulk-micromachined Si component and hot-embossed polymethyl methacrylate (PMMA) component. The Si component contains an integral microheater and temperature sensor on a thermally well-isolated membrane, while the PMMA component contains a 200 nL PCR chamber, valves and channels. The micro-hot membrane under the chamber is a silicon oxide/silicon nitride/silicon oxide (O/N/O) diaphragm with a thickness of 1.9 μm, which results in a very low thermal mass. In experiments, only 45 mW is required in the chip to heat the chamber to 92°C, the denaturing temperature of DNA. In addition, the heating and cooling rates are about 80°C/s and 60°C/s, respectively. From the fluorescence results from DNA stained with SYBR Green 1, we validated that the chip amplified the DNA from a vector clone that contained tumor suppressor gene BRCA 1 (127 base pairs at the 11th exon), after 30 thermal cycles each of 3 s, 5 s and 5 s at 92°C, 55°C and 72°C, respectively, in the chamber. As for the specificity of DNA products, because of the difficulty in analyzing results in the very small volume chips, we instead utilized the larger volume PCR products after cycling with the chip over the same sustaining temperatures but with much slower ramping rates (2.5–3.3°C/s) within about 20 min on a commercial PCR machine and confirmed the specificity with agarose gel electrophoresis. The proposed microchip can be used in the fully integrated, battery-powered instrument for DNA lab-on-a-chip applications.

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