Amorphous Silicon Temperature Sensors Integrated with Thin Film Heaters for Thermal Treatments of Biomolecules

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Abstract. This work combines a lab-on-chip device with an electronic system for the achievement of a small-scale and low-cost thermal treatment of biomolecules. The lab-on-chip is a 1.2 mm-thick glass substrate hosting thin film resistor acting as heater and, on the other glass side, amorphous silicon diodes acting as temperature sensors. The electronic system controls the lab-on-chip temperature through a Proportional-Integral-Derivative algorithm. In particular, an electronic board infers the temperature measuring the voltage across the amorphous silicon diodes, which are biased with a constant forward current of 50 nA, and drives the heater to achieve the set-point temperature. The characterization of the whole system has been carried out implementing the thermal cycles necessary in the polymerase chain reaction technique for amplification of DNA. To this purpose, the lab-on-chip has been thermally coupled with another glass hosting a microfluidic network made in polydimethilsiloxane, and the time evolution of temperature has been carefully monitored. The measured performances in terms of heating rate, cooling rate and settling time demonstrate that the proposed system completely fulfills the requirements of the investigated biological application.

Keywords: Lab-on-chip · Thin film heaters · Temperature sensors · Amorphous silicon diodes · Polymerase chain reaction

1 Introduction

Lab-on-chip (LoC) technology is receiving a lot of attention thanks to their potential applications in biology and in genomics. The strength of these devices relies in the integration of multiple functionalities in a single chip [1, 2].

The development of LoC devices for biochemical analysis has several advantages including reduced volume of reagents and samples, portability, and low power

consumption [3–6]. Several clinical diagnostics techniques, such as Polymerase Chain Reaction (PCR) or cell lysis, require thermal treatments of the analyte [7–9], and therefore the temperature control is a critical parameter in managing many physical, chemical and biological applications. The thermal power can be provided by a bulky metal block thermally coupled with the LoC or by an integrated thin film heater. The standard on-chip heating approach uses a thin metal film (i.e. platinum) as both heater and temperature sensor, taking advantage of the resistance temperature dependence [10]. This way presents many advantages but is limited by the resistance temperature coefficient (TCR) of the heater: for some conductor the TCR is very low and in these cases is hard to obtain a good sensitivity. Furthermore, it is impossible to infer local information as the temperature in different points of the heated area since the resistor variation depends on the average temperature of the whole heater surface. Another approach relies on the integration of thin film temperature sensors and thin film heater in the same LoC to achieve high sensitivity regardless of the heater material [11].

In this context, we present the integration of amorphous silicon (a-Si:H) p-i-n structure and thin film heaters on the same glass substrate combined with a compact electronic board able to drive the heaters and monitor the temperature measuring the drop voltage across the diodes. Indeed, a-Si:H diodes are appealing as thin film temperature sensor since the voltage across them varies linearly with the temperature, when they are biased with a constant current, with a sensitivity greater than those found in crystalline silicon [12].

2   System Description

The proposed system, whose block diagram is depicted in Fig. 1, is constituted by the following components:
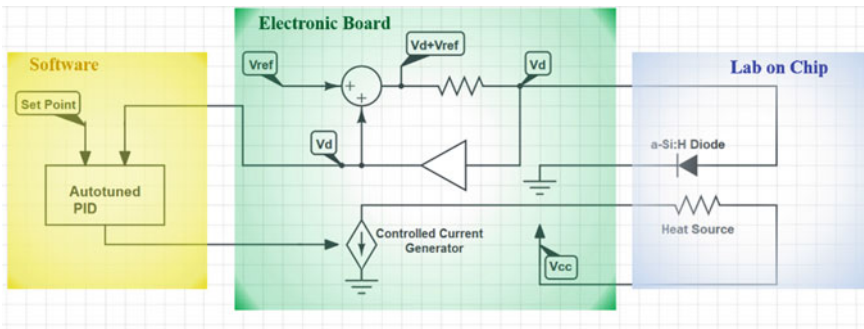

Fig. 1. Block diagram of the system

1. a lab-on-chip device;
2. an electronic board that controls the lab-on-chip temperature;
3. a software that controls the electronic circuit board.

A Graphical User Interface was developed in order to control all the functionalities of the electronic board. In particular, the set-point temperature (specified by the user) is achieved using a software Proportional-Integral-Derivative algorithm, which takes, as input, the temperature inferred by the diode. This is possible since the voltage across the diode varies linearly with the temperature when it is biased with a constant current. The output of the software is then used to provide a controlled current to the heater. The following parts of this section report the detailed descriptions of the lab-on-chip device and the electronic circuit board.

2.1 Lab-on-Chip System

The LoC integrates on a 1.2 mm-thick glass substrate different thin film technologies in order to develop a multifunctional platform suitable for thermal treatments. In particular, a 5×5 cm^2 glass substrate hosts:

- a thin metal film acting as heating sources on one side of the glass;
- a set of a-Si:H diodes, acting as temperature sensors, to monitor the temperature distribution on the active area of the heater.

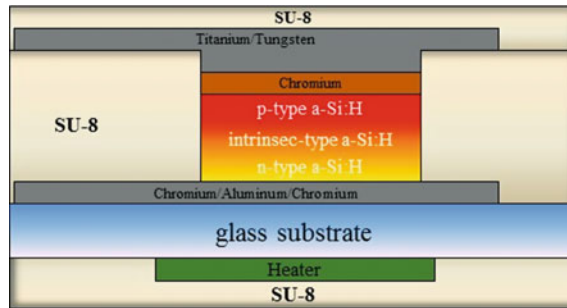A cross section of the fabricated device is shown in Fig. 2.

Fig. 2. Detailed cross section of the lab-on-chip

2.1.1 Heater Design, Fabrication and Characterization

The thin film metal resistor, deposited on a glass substrate, features an area comparable to the active area of the thermal treatment and low power consumption. The selected materials and thicknesses, determining the value of the electrical resistance, are mainly defined by the power requirement, while the resistor geometry is determined by the specification of uniform spatial temperature distribution over the thermal process area. Starting from the results published in previous works [13], we have developed a double concentric spiral with a heated area of about 120 mm^2.

The heater geometry was designed using finite element simulations with COMSOL Multiphysics software, coupling the electrical and the thermal problems with the Joule effect and obtaining the temperature profiles due to a potential difference applied across

the resistor. Basing on the simulations results, the thin film heater has been fabricated through vacuum evaporation of a 100/600/100 nm-thick Chromium/Aluminum/Chromium stacked layer and defined by conventional photolithography using the mask depicted in Fig. 3. The 5×5 cm^2 glass substrate hosts two mirrored heaters with elliptical shape. Each heater has four electrical contacts: the two external pads provide the current, while the voltage is measured between the internal ones. The obtained resistance was around 11 Ω.
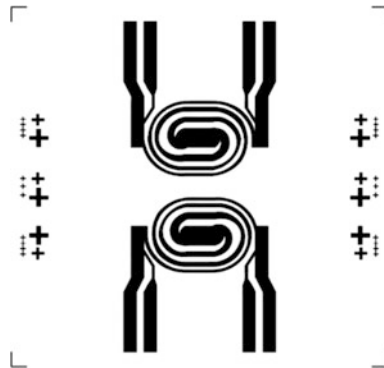

Fig. 3. Heater mask

An infrared thermo-camera (FLIR A325) has been used to measure the thermal distribution over the heated area in steady state condition. Results obtained applying a
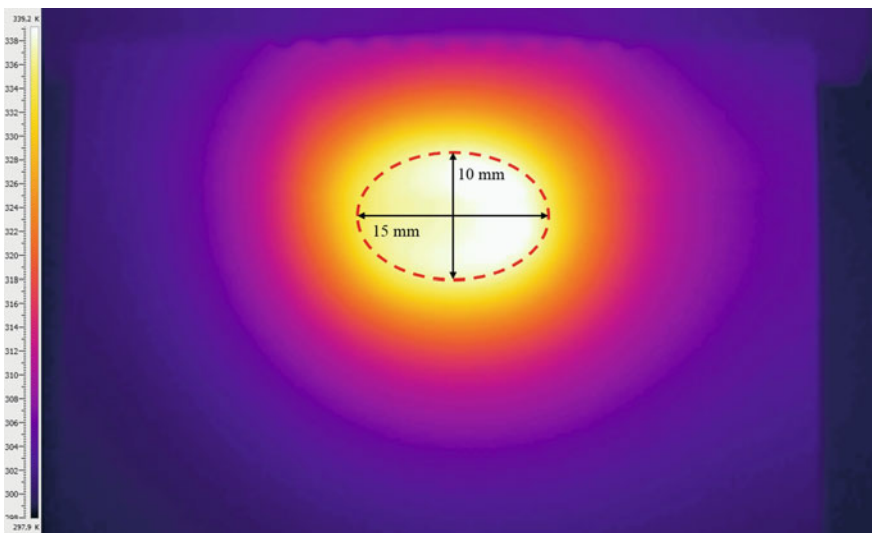

Fig. 4. Measured temperature distribution over the heater area

voltage equal to 2.9 V to the heater are reported in Fig. 4 in color scale. The elliptical shape, where the temperature is uniform, reproduces the heater geometry. In particular, inside the area ($\approx$120 mm^2) defined by the dashed red line, an average temperature of 338 K with a standard deviation of $\pm$1 K is achieved.

2.1.2 Sensors Fabrication

On the other side of the glass, the a-Si:H devices have been fabricated through Plasma Enhanced Chemical Vapor Deposition (PECVD) and standard microelectronic techniques (evaporation, sputtering, photolithography and etching). In particular, the fabrication steps are the following:

1. vacuum evaporation of 30/150/30 nm-thick Cr/Al/Cr stacked layer, which acts as bottom contact of the diodes;
2. patterning of the metal stack by conventional photolithography and wet etching process;
3. deposition by PECVD of the a-Si:H stacked structure n-type/intrinsic/p-type;
4. deposition by vacuum evaporation of a 50 nm-thick chromium layer, which acts as top contact of the sensors;
5. wet etching of the chromium and dry etching of the a-Si:H layers for the mesa patterning. The area of the diodes is 0.8×0.8 mm^2;
6. deposition by spin coating of a 5 µm-thick SU-8 3005 (from MicroChem, MA, USA) passivation layer and its pattering for opening via holes over the diodes;
7. deposition by sputtering of a 150 nm-thick titanium/tungsten alloy layer and its patterning for the definition of the top contacts and of the connection to the pad contacts;
8. deposition by spin coating of a 5 µm-thick SU-8 3005 passivation layer.

2.2 Electronic Circuit Board

The electronic board includes:

- a power circuit that drives the heater with the current required to achieve the specified temperature;
- a power circuit that drives a fan used to enhance the cooling of the LoC during thermal cycles;
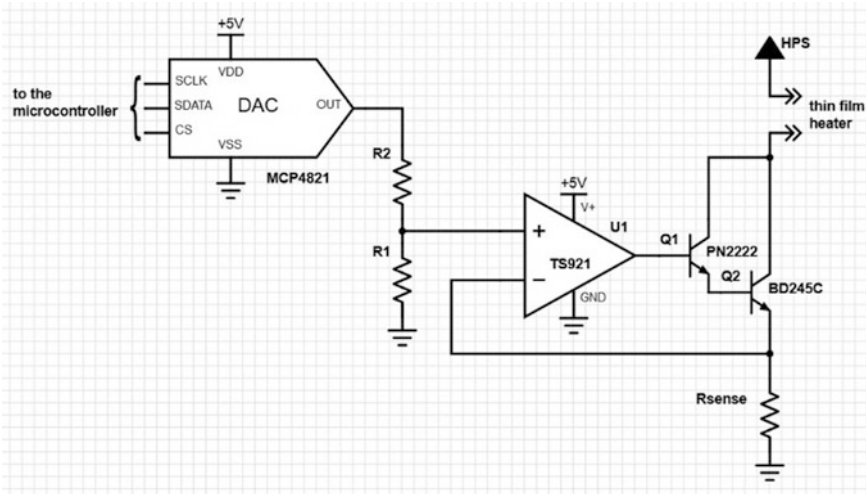- an electronic circuit that biases the diode at a constant current and reads the diode voltage.

Fig. 5. Schematic of the current generator that drives the heater

In order to drive the thin film resistor we have used a simple current generator driven by a Digital to Analog Converter (DAC). The schematic of this electronic board section is reported in Fig. 5.

The most of the current that flows in the heater comes from the collector of the transistor Q2 (BD245C from Bourns®) that is a NPN silicon power transistor with very high maximum continuous collector current (10 Amps) and a minimum forward current transfer ratio (h_{FE}) of 20. Taking into account this small value of the h_{FE}, we decided to use the Darlington configuration adding to the circuit the transistor Q1 (PN2222 from Fairchild Semiconductor), which is a general-purpose small signal transistor.

The operational amplifier is the TS921 from STMicroelectronic. This is a rail-to-rail single BiCMOS operational amplifier that exhibits very low noise, low distortion and low offset. The current provided to the heater is set by the MCP4821 converter (from Microchip), which is a single channel 12-bit DAC. The devices operate from a single 2.7–5.5 V supply. A Serial Peripheral Interface allows us to control the DAC through a PIC18F4550 microcontroller (also from Microchip). The device has a high precision internal voltage reference (V_{REF} = 2.048 V), and the user can configure the full-scale range to be 2.048 V or 4.096 V.

The value chosen for the sense resistance R_{sense} is 0.2 Ω, while the values of R_1 and R_2 are respectively 1 and 36 kΩ. With these values, we achieved a maximum driving current of 550 mA.

The same topology of circuit has been used to drive the fan that is necessary to quickly cool the LoC when thermal cycles are required.
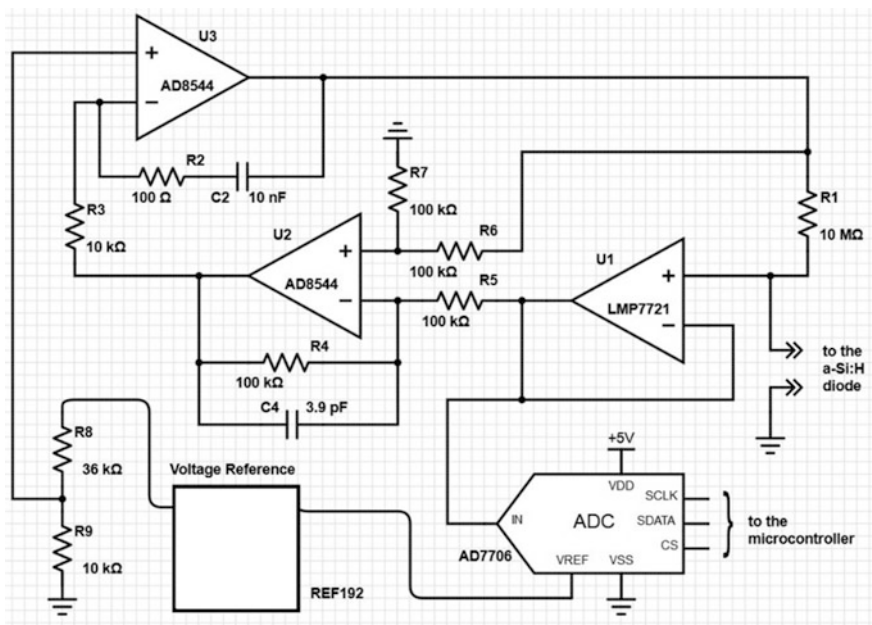
Fig. 6. Schematic of the circuit which senses the temperature biasing with a constant forward current the a-Si:H diode

The circuit that infers the heater temperature through the a-Si:H diode is instead depicted in Fig. 6. It drives the diode with a constant current in forward condition and at the same time reads the voltage across the diode. A detailed description of the circuit mode of operation was reported in [14].

Briefly, a voltage reference of 2.5 V (provided by the REF192 from Analog Devices) is partitioned with the resistances R_8 and R_9 obtaining a voltage reference for the circuit equal to

$$V_{ref} = 2.5\,\text{V} \cdot \frac{10\,\text{k}\Omega}{10\,\text{k}\Omega + 36\,\text{k}\Omega} \approx 0.543\,\text{V} \tag{1}$$

This voltage is reported, through the feedback loop, across the resistance R_1. In this way, the current that flows in the diode is

$$I_{diode} = \frac{V_{ref}}{10\,\text{M}\Omega} = 54.3\,\text{nA} \tag{2}$$

The same 2.5 V reference together with the ADC-gain of 4 were chosen for the DAC, obtaining a minimum detectable signal V_{min} equal to

$$V_{min} = \frac{2.5\,\text{V}}{(2^{16} \cdot 4)} \approx 9.5\,\mu\text{V} \tag{3}$$

All DA and AD Converters included on the board are driven by the PIC18F4550 microcontroller, which incorporate a fully featured Universal Serial Bus (USB) communications module that is compliant with the USB Specification Revision 2.0. This module allows us to control all the functionalities of the electronic board with a common personal computer equipped by the developed GUI.

3   Experimental Results

This section reports the performances of the whole system during the thermal cycles of a PCR experiment.

3.1   System Calibration

In order to control the temperature of the LoC system, we performed a preliminary calibration of the a-Si:H diodes combining the realized system and the FLIR A325. We monitored the temperature of the diode through the thermo-camera while the electronic board kept constant the temperature of the diode actuating the developed PID control on the heater and simultaneously recording the diode voltage.

Measurement results are reported for one diode in Fig. 7. Equation inside the figure is the linear fitting of the measured values. The slope of the fitting straight line (about
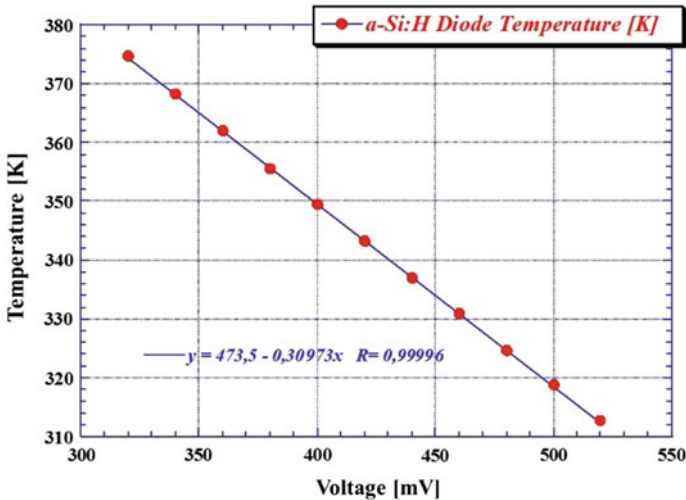

Fig. 7. Measured voltage-temperature characteristics of an a-Si:H diode integrated in the lab-on-chip

0.31 K/mV) represents the inverse of the diode thermal sensitivity, which is around 3.2 mV/K. Taking into account the minimum voltage variation that the ADC can discern (see Eq. (3)) and the diode sensitivities, the minimum temperature change that can be detected by our system is around 3 mK. This value satisfies the requirements of the routine biological applications, which demand, at mostly, to monitor temperature change of tens of degrees.

3.2 Testing of the Whole System

The performances of the developed system have been characterized through the implementation of a Polymerase Chain Reaction experiment, suitable for DNA amplification. In particular, the test has been accomplished carrying out the standard three-temperature cycling technique. In this approach, each PCR cycle consists of the melting of the double-stranded DNA (around 370 K), annealing of the specific primers
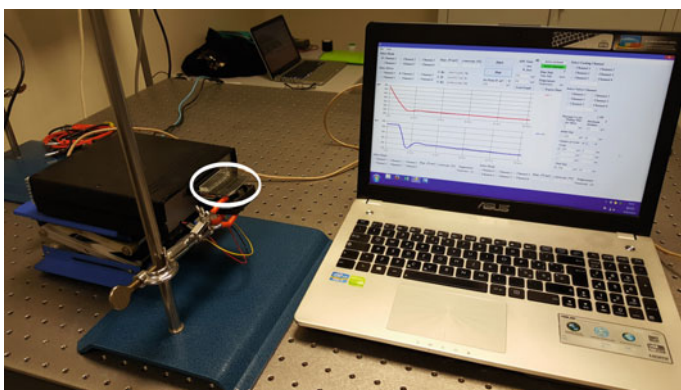

Fig. 8. Picture of the setup used for the PCR experiment. The *white circle* indicates the lab-on-chip, while the *black box* contains the electronic circuits (Color figure online)

to their target gene (usually between 323 and 338 K) and extension of primers with thermo-stable polymerase enzymes such as Taq polymerase (around 345 K).

In order to reproduce the operating conditions of a PCR experiment, the LoC has been thermally coupled with another glass hosting a microfluidic network made in polydimethilsiloxane (PDMS). In this way, apart from the few microliters of biological solution contained in the microfluidic network, this set-up includes all the elements to
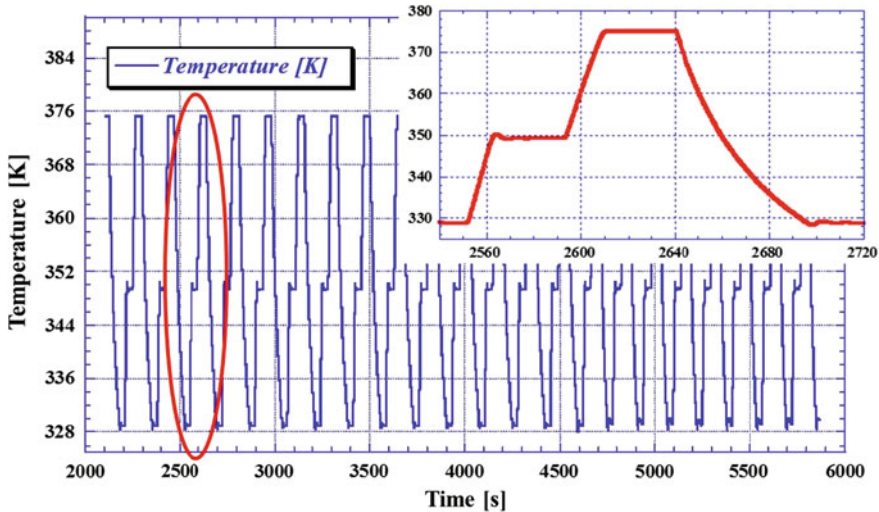
Fig. 9. Time evolution of the temperature during the PCR experiment. The zoom shows a detail of one PCR cycle

implement the DNA amplification through the PCR technique. A picture of the complete setup is shown in Fig. 8.

The sensor temperature during the PCR experiment is shown in Fig. 9. The inset shows a detail of one PCR cycle. Each cycle foresees 30 s at 329 K, 30 s at 349 K and 30 s at 375 K. The time evolution of the reported curves, and in particular the fall time, the rise time and the setting time, depends on the temperature control performed through the PID algorithm. We found that the rise rate was 2 K/s and that the fall rate, controlled by the fan, was 1 K/s. Furthermore, the curve showed absence of overshoot and a displacement from the set-point temperature below ±0.5 K.

These values meet the characteristics of the standard thermo-cyclers used for the PCR experiments in the biological laboratories and therefore demonstrate the suitability of the proposed LoC for thermal treatments of biomolecules.

4   Conclusions

This work has presented a very compact system able to perform controlled thermal treatments of biomoleculels. It is based on thin film technologies to avoid the use of bulky external metal block heaters. In particular, the realized lab-on-chip integrates on the same glass substrate thin film metal heaters on one side and amorphous silicon diodes, acting as temperature sensors, on the other side.

The experimental characterization of the single electronic devices (thin film heater and a-Si:H diodes) and of the whole system has demonstrated that the proposed LoC fully satisfies the requirements for the implementation of the PCR technique, the nowadays prevalent biological process for DNA amplification.

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