LIGHT-DRIVEN MICROFLUIDICS TOWARDS SOLAR-POWERED POINT-OF-CARE DIAGNOSTICS

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ABSTRACT

Point-of-care diagnostics for resource limited settings is a much-researched application of microfluidics technology due to its great potential. Unfortunately, one of the current limitations is the difficulty in creating tools that are both inexpensive and simple to use but also able to perform complex tasks. Light-governed microfluidic systems are of interest because, in principle, sunlight could provide the power source to operate these tools, potentially allowing for increased functionality with minimal device complexity. Here, we study the use of light to perform both the fundamental function of fluid actuation and valving and the more sophisticated process of on-chip polymerase chain reaction (PCR). To facilitate light-driven flow, we use poly(N-isopropylacrylamide) (PNIPAAm), a "smart" polymer that changes wettability as a function of temperature. It is grafted onto a carbon black-polydimethylsiloxane (PDMS) surface, which absorbs light and converts it to heat, to produce various temperature profiles. We use this to create switchable hydrophobic and hydrophilic regions that respectively stop and activate flow and show that light can valve off flow within 4 s after illumination. We also perform continuous-flow PCR by fabricating PDMS lenses that concentrate light onto a carbon black layer to produce the necessary heat pattern, and demonstrate amplification of a 43bp segment of genomic DNA. These investigations show the potential for development of light-operated microfluidics to provide both the simple architecture and advanced functionality needed in point-of-care devices for low resource environments.

KEYWORDS

Optofluidics, Point-of-Care Diagnostics, Liquid Handling, Solar Energy, Polymerase Chain Reaction

INTRODUCTION

For point-of-care diagnostics to become widely adopted in the developing world, devices must be low-cost, easy to use, multifunctional and capable of processing complex samples. [1, 2] Thus far it has been difficult to bridge these goals, partly due to the dichotomy between the approaches that researchers have taken. On one hand, disposable and low-cost devices [1, 3] are excellent for performing detection assays on relatively simple samples such as urine. [4] They cannot however work with more complex sample matrices to detect rarer targets. [5] Conversely, sophisticated nanotechnology/microfluidics-based systems have been developed that can manage complex tasks such as target amplification through polymerase chain reaction (PCR). [6, 7] Unfortunately, the addition of multiple steps in one device is mainly enabled through the integration of pumps, valves and electrical components and controllers, which increases their expense and operational complexity. To solve this problem, microfluidic methods must be developed that are simple to use yet able to perform complex functions. Here, we report separately the development of light-governed flow and light-powered PCR in microfluidic devices.

As Figure 1 shows, our simple flow valving device passively pumps fluid at room temperature and actively stops its motion based on photo-thermal heating, thereby eliminating the need for external pumps, integrated valves or complex fabrication steps. To do this, we graft poly(N-isopropylacrylamide) (PNIPAAm) via UV polymerization on PDMS microfluidic devices. PNIPAAm is a frequently used "smart" polymer due to its strong response to temperature, in that it transitions between expanded coils and compact globules as the temperature is varied around its lower critical solution temperature (LCST) of 32°C. [8] This is caused by the formation of H-bond networks below the LCST and the breakdown of those networks above the LCST, thereby making PNIPAAm hydrophilic at low temperatures and hydrophobic at high temperatures. This allows for passive pumping of flow via capillary action at room temperature, while above 40°C, it becomes hydrophobic and impedes further flow. To show its potential applicability towards integrated point-of-care devices, we present a bifurcating microfluidic design in Figure 1a, b, where the inlet channel splits into two large chambers, with
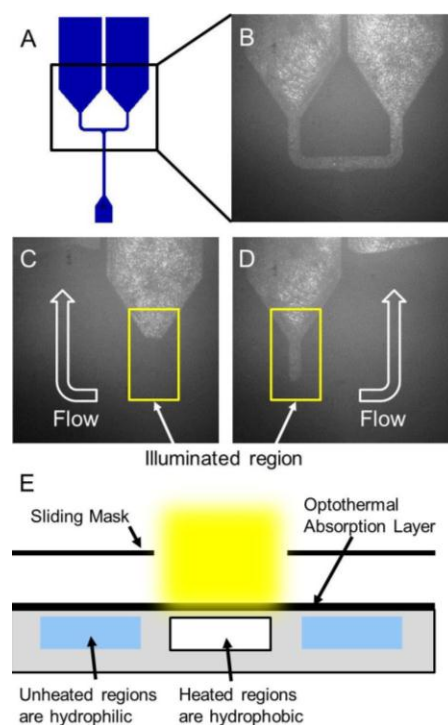

Figure 1. Light-driven flow valving. (a)Schematic and (b) image of bifurcating channel. When light is used to heat the (c) right or (d) left channel, that region becomes hydrophobic, preventing flow from entering the connected chamber. (e) Schematic demonstrating how this can be used in the field with a movable mask to define heated regions.

each chamber representing a separate step of a multistage process. In step one, projector light is incident on the right (Figure 1c) or left (Figure 1d) channel, heating that region and valving off the flow, while flow continues down the adjacent hydrophilic path. In step two, the light is removed at a user-defined time, allowing flow to penetrate into the previously closed chamber. Our light-controlled capillary flow technique is capable of performing multiple flowing steps without the need for complex fabrication, external syringe pumps, integrated valves or modification of the fluid. Further, the broadband absorption capability of carbon black should allow for sunlight to be used as the light source (Figure 1e), which in essence would afford power-free actuation and valving control.

We also demonstrate successful amplification of a 43bp segment of genomic DNA using light-powered continuous-flow PCR. Here, projector light was used such that we could maintain control over the intensity and uniformity of the incident image. In principle, this could be extended to work with sunlight, shown schematically in Figure 2. A lens would concentrate solar energy to the required intensity to produce high enough temperatures for the denaturation step (95°C) (Figure 2a). A carbon black layer of varying absorbance would then also produce the correct temperatures for annealing (65°C) and extension (72°C) (Figure 2b). This technique would address the significant energy requirements of PCR, facilitating its implementation in low-resource settings.
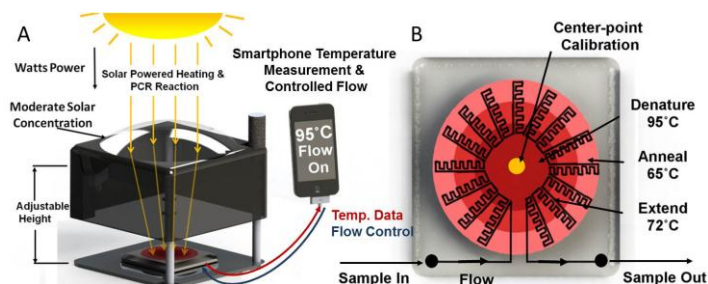

Figure 2. Schematic of solar-PCR device. (a) A lens is used to focus sunlight to the required intensity to produce high enough temperatures for PCR. Temperature and flow regulation is controlled by a cell phone "app." (b) Schematic of circular PCR device, in which the reagent repeatedly cycles through the three temperature zones to amplify the target.

EXPERIMENT

Light-Governed Capillary Flow

The base of the device consists of first spin coating a 200 μm layer of clear PDMS onto a glass slide. Above this, a mixture of carbon black and PDMS in a 0.01:1 ratio was spin coated to produce a 50 μm thick film to act as the absorber layer. Finally, another 50 μm thick film of clear PDMS was spun on top of this. These steps were required because we found that PNIPAAm could not graft directly onto a carbon black-PDMS surface.

The grafting method, based on the UV photopolymerization technique developed by Schneider *et al*. [9], is modified here to produce uniform PNIPAAm-grafted surfaces. Briefly, a solution of 10 wt % benzophenone (BP) in acetone was first run through the channel to allow BP to absorb into the PDMS. Then, a degassed monomer solution of 20 wt % NIPAAm in DI water was loaded into the channel and exposed under a 100 W mercury arc lamp for 15 min. Finally, the channel was washed with ethanol for 1 h and water for 2 h.

Using the grafted channel, we demonstrate actuation and valving of flow with light (Figure 3). As Figure 3a shows, initially light is shuttered off and flow moves into the channel. At 20 s, the shutter is opened and flow progression stops. At 50 s, light is again shuttered off and flow moves once again. The flow rate is measured through a series of on/off switches to demonstrate repeatability (Figure 3b). Also, the switching on and off speeds are characterized in Figure 3c, d, which show that flow is valved off in less than 4 s and that it takes about 10 s for flow to reach a steady rate when valved on. These values are comparable to other PNIPAAm-based valves, which require more than 6 s to close and 3 s to open. [10, 11] Unlike our device, these previous techniques utilized a swelling property of PNIAAm instead of changing the surface chemistry and achieved valving by building porous monoliths inside the channel. The monoliths are swollen at room temperature, clogging the channel, and shrink when heated, opening the pores to allow flow to pass through. The disadvantage of using swelling-based valving is that due to heating, the opened pores would also be hydrophobic, making it mandatory to use a syringe pump to drive flow. Therefore, even though the opening time is slower for our technique, it does not require any external pumping mechanism due to the capillary pumping capability.
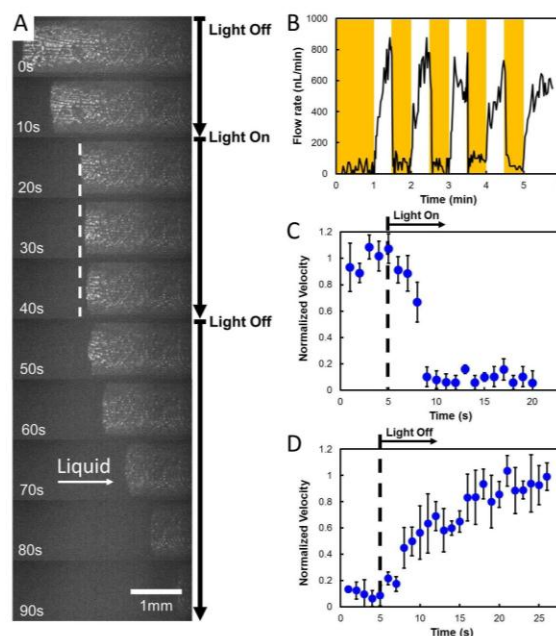

Figure 3. Valving speed characterization. (a) Images of liquid interface in 10 s intervals, demonstrating the cessation of flow when light is on. (b) A series of on/off valving shows repeatability and quick response (orange bars represent when light is on). (c) After light is turned on, flow is valved off within 4 s. (d) After light is turned off, it takes about 10 s for flow to reach a steady flow rate.

Light-Powered PCR

We demonstrate light-powered on-chip DNA amplification by using a PDMS lens system to create a specific thermal profile that facilitates the steps of PCR. Figure 4a shows the experimental setup, in which a projector light is collimated through a glass lens onto the PDMS lens. The PDMS lens system, shown in Figure 4b, is molded from a laser-cut acrylic glass frame. The light through lens 1 is focused the most to enable the denaturation step (95°C), lens 2 enables elongation (75°C) and the flat region facilitates annealing (60°C). The temperatures at various locations under the lenses are measured with a thermocouple and compared with Comsol simulations, (Figure 4c). Figure 4d shows this lens system combined with a microfluidic channel, which is designed for flow to pass through 20 cycles of the denaturation, annealing and elongation steps in a time ratio of 4:4:9, respectively.
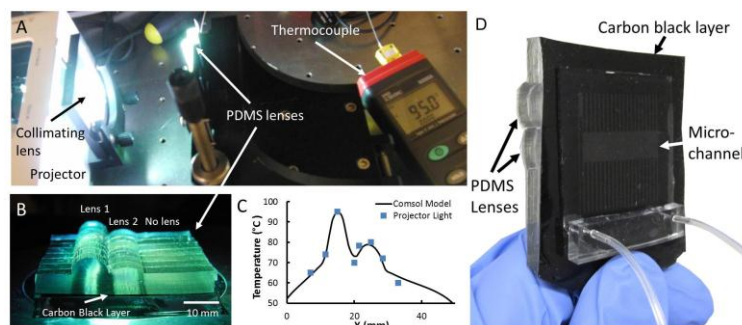

Figure 4. Light-driven PCR chip. (a) A projector image shines through a collimating lens onto the microfluidic PCR chip. (b) The PDMS lens device focuses a uniform light source to different intensities, creating the temperatures needed for the different steps of PCR. (c) Temperatures measured from the chip compares well with Comsol simulations. (d) The integrated PCR device, combining the lenses and microfluidics.

Genomic DNA extracted from Kaposi's sarcoma herpes virus (KSHV) was used as the template for performing PCR in this chip. As figure 5 shows, we successfully amplified a 43bp segment of the DNA after running the sample through our chip twice for a total of 40 cycles. The result is compared to PCR using a conventional thermocycler. As can be seen, amplification using the light-powered PCR is not as significant as with the thermocycler. We believe this is because the temperature varies across the chip and along the length of each lens, preventing some of the 20 cycles from operating optimally. This becomes quite significant due to the exponential rate of amplification of the PCR process, as each cycle that does not run correctly reduces the final DNA concentration by an order of magnitude. In the future, we plan to develop a radial microfluidic design so that the temperature would remain constant along the azimuthal direction, allowing all cycles to run optimally under a uniform light source such as sunlight.
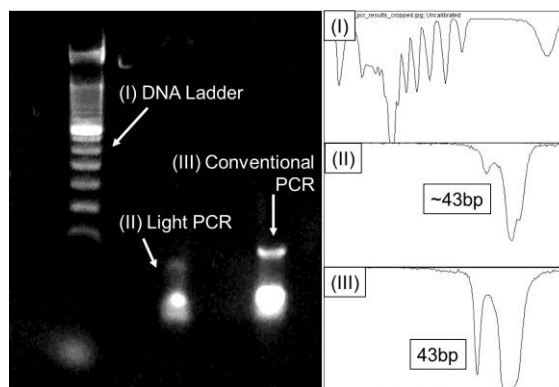

Figure 5. Demonstration of light-driven PCR. A 43bp segment of genomic DNA is run through the microfluidic device and a thermocycler. While we do see amplification using light-driven PCR, it is not as significant as through the thermocycler, and several improvements can be made.

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