

Whole Blood Pumped by Laser Driven Micropump

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ABSTRACT

A novel laser driven peristaltic micro-pump for the manipulation of fluids in a micro system has been explored and validated on whole blood in saline solution. The pump is based on laser-induced *film-boiling* of the enclosed liquid, and works by forming a thermally graduated vapour-bubble, acting as a driving plug in the channel (figure 2-4).

The devised laser driven micro pump is ideally suited for injection moulded polymer disposables, as virtually no part of the technological components and means involved will have to be incorporated in or on the disposable itself, thus keeping the price of the disposable at an absolute minimum.

The CD-ROM R/W industry has been a driving factor in making available cheap and reliable infrared laser diodes that will provide the required levels of power.

Keywords: *micro-pump, whole blood, polymer disposable, lab-on-a-chip, film boiling.*

1 BACKGROUND

Numerous schemes for fluid manipulation in the micro domain, has been explored in the effort to find an alternative to the EOF pumping scheme or to the use of externally connected syringe pumps. The EOF pumping scheme has become popular due to factors such as *ease of use*, - just apply a DC voltage from one end of a channel to another, and *true micro-scalability*. EOF pumping is however hampered by a number of serious drawbacks: Ionic “relationship” between liquid and substrate material (apolar liquids cannot be pumped). EOF produces gasses and gas bubbles can inhibit or completely halt the flow irreversibly (gas bubbles will block the current path). The main drawback, when considering a scheme making full use of the before mentioned *true micro-scalability*, is the fact that each and every pump has to be accessed and addressed by electronic control systems. As a certain contact area is needed in order to supply a given voltage, the chip *real estate* used for electrical contact pads will be a limiting factor and *not* the size of the actual pump or the surrounding microfluidic circuit. As can be seen in fig. 1, the Nanogen cartridge [1] requires 90% of the (expensive!) silicon real estate for electrical connects, thus leaving only 10% for biochemical interactions.

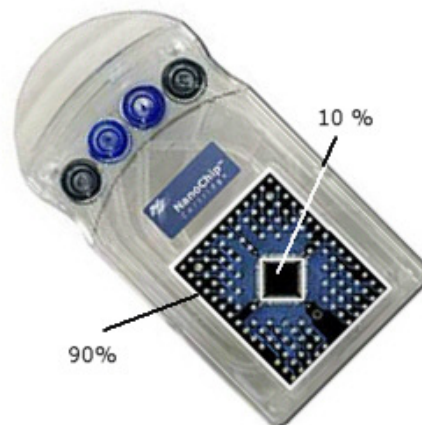


Figure 1. Nanogen™ chip: 90% contact area.

The obvious path of miniaturising existing “macro-World” –components, has been explored by numerous groups. Micro gear-pumps has been fabricated in silicon or metals [2] using silicon etching or LIGA technologies. Apart from the challenges in working with moving components, external means are still necessary in order to facilitate said movement. The diaphragm pump is another well known example of miniaturising existing technologies. Swiss company Debiotech [3] has developed a piezo-operated silicon micro pump based on the *displaced diaphragm* principle; however due to – amongst a number of reasons – the limited displacement capability of the diaphragm (in relation to area of same), the diaphragm pump will never become a true micro-pump used in lab-on-a-chip solutions.

The use of liquid-vapour phase as a driving force has previously been explored [4,5] but the suggested techniques has either been dependent on complicated geometries [5] and/or dependent on a high number of electrical connections from controlling equipment [4] as it is also the case with the EOF scheme.

Prosperetti et al. [5] produce a vapour bubble in a funnel-shaped microchannel. The vapour bubble will seek to expand in the direction where it will experience an expanding cross-section and the expanding bubble will induce a flow. The bubble is generated passing a current through the liquid, which will in turn experience a heat build-up, thus forming the vapour. Using the *bulk* of the liquid as a heating element may cause an undesired denaturing of biochemical components; also the pump is based on channel geometry, which means that one cannot

readily reverse the flow by e.g. reversing the current or similar means.

The work by C.J. Kim et al. [4] uses embedded micro heaters to produce a train of bubbles that will eventually produce a peristaltic motion and thus a pumping effect in the enclosed liquid. Kim et al. works at a relatively low heat flux, which causes an unnecessary long *bubble-life* as well as a bulk heating of the enclosed liquid. Also the set-up by Kim is dependent of encased micro heaters that will have to be individually accessed and controlled by external equipment.

We have sought a contact less solution whereby multiple pumping sites can be driven by the same external driving mechanism, - namely a laser scanning device.

2 TECHNOLOGY

Our technology is based on directing of optical energy into a microfluidic cartridge and *onto* a well defined surface part of a microfluidic circuit. The mechanisms in play are – by large – adopted from the *ink-jet printer cartridge*, which also makes use of implementing a tremendous heat flux at a minute area and for a very short period. In the ink-jet printer (a.k.a. *bubble-jet* printer) –cartridge a resistive heating element will induce a heat flux of around 500MW/m² which is around 2.5X that of the surface of the Sun. The ink-jet heater will experience a rise in temperature of around 100M°C/s and will be “on” for a period of only 2-3µs. The resulting vapor bubble will nucleate from a liquid layer that is less than 100nm thick and it will expand, cool and condense within 20-50µs. Upon the violent expansion it will displace a volume of the enclosed liquid which will eventually be expelled through the orifice.

We are using the focused laser diode beam as a heating element at a defined spot in a channel whereby we are able to influence and thus displace a part of the enclosed liquid.

2.1 Functionality

Upon directing the laser beam to a given spot; firing it up for a short period (2-4 µs) a vapor bubble will nucleate, expand, cool and contract as previously explained. However – as we are working with an enclosed liquid (no escaping *orifice*) there will be no net displacement of liquid after the bubble has collapsed. As the timing (bubble life) is relatively defined, we have the ability to produce another bubble adjacent to the previously formed bubble the second bubble will act as an “anchor” when the first bubble collapse. The void stemming from the collapse of the first bubble will thus be filled by liquid that stems from the opposing side of the second bubble.

What we have eventually realized is that due to the microscale channel dimensions, we are in fact able to produce a single bubble, thus stemming from a number of discrete and timely dispersed laser-shots along a given part of a channel. We thus get one single (elongated) vapor-bubble consisting of a “cold” end that is condensing and

contracting and a “hot” end of newly formed vapor that will thus still be in the expanding phase. The following figures 2, 3 and 4 - will illustrate the functionality; note: arrows indicate speed and direction of growth – respectively – collapse.

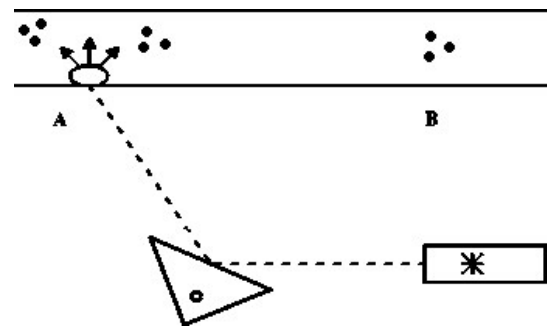


Figure 2. “First” bubble initiated.

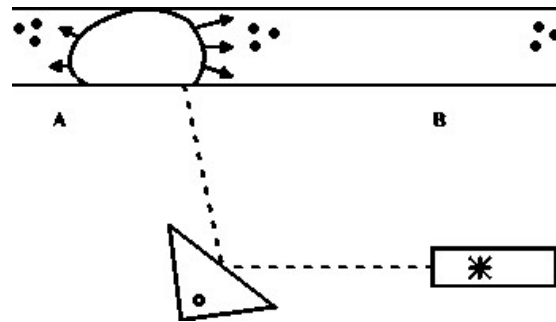


Figure 3. Driving bubble, channel filled.

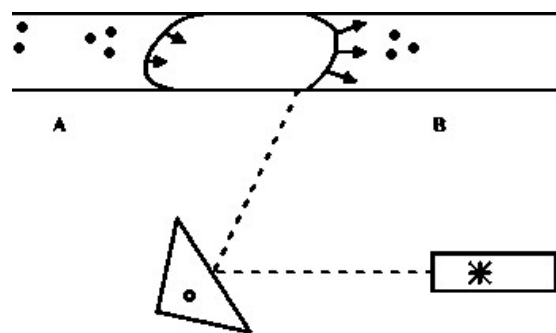


Figure 4. Driving bubble, “cold end” contracting.

As it is evident, the technology is independent of geometries such as e.g. constrictions or turns as it is often seen in for example “valve less” pumping schemes. It may also be evident that scanning the laser system from ‘B’ to ‘A’ will induce reverse pumping.

2.2 Fluid integrity, “the Leidenfrost effect”

As previously mentioned, concerning other vapor-phase pumping schemes [3, 4], it may present a problem that the bulk of – or substantial part of – the enclosed liquid is brought to a superheated state. Sensitive biochemical compounds may be denatured; cells may be lysed etc. The key issue of our technology is the immense heat-flux, which results in a *film-boiling* effect. From the ink-jet printer industry, we know that less than 100nm of liquid is brought to a super heated state. Considering a typical microfluidic channel having a height of 50 μ m, a mere 0.2% of the liquid is actually boiled. The effect is also known as the “Leidenfrost effect” after a Dutch researcher who performed experiments on droplet life in a heated silver spoon. Leidenfrost discovered that tap water droplets, placed in a silver spoon would evaporate within seconds if the spoon was heated to 120-150°C whereas a droplet would live for minutes if the spoon was heated to 250-300°C

Consequently – the key to preserving *liquid integrity* is to subject the liquid to immense heat fluxes!

2.3 Components

As mentioned we are *piggybacking* on the CD-ROM R/W -drive consumer industry. We are using a multimode 808nm (infrared) laser diode (figure 5). The laser-diode will deliver 500mW optical energy from a lasing aperture of 50X1 μ m. Theoretically we should thus be able to deliver a spot of similar size (~50 μ m²) and with 500mW of power. In reality the effective Gaussian spot that we can deliver is in the area of 60X15 μ m (~900 μ m²) with an optical power of around 250mW. Although we may thus be below the power flux of the ink-jet printer, we are still in that area and we are thus able to correlate with the vast number of investigations in that area.

We use a straightforward and thus well-known X-Y galvano scanner to address the chip area; we are able to access any given part of an area of our chip, and so we are obviously able to drive a large number of pumping sites.

The collimated laser beam is focused by a single plano convex AR coated lens. Beam quality over a larger scanning area may however be improved (from spherical aberration) by applying specialty optics such as e.g. an f-theta lens that is frequently used in the laser-machining industry.



Figure 5. - Laser diode, 808nm, 500mW (Ø9mm)

3 EXPERIMENTS

The laser pump has previously been validated on methanol (not published), thus underlining the postulated independence of driving liquid properties. Obviously viscosity, boiling point and hydrophobicity are influencing parameters, but pumping an *apolar* liquid with a boiling point below that of water, is possible right away with minor adjustments (such as laser power and scanning speed)

In order to evaluate the pumping scheme on a complex biochemical fluid and subsequently estimate the level of the postulated *liquid integrity* on same, we devised the following experiment:

A polymer substrate (PETG – Kodak Eastar) was machined using an Excimer laser. A channel of width 50 μ m and depth 25 μ m was machined. A lid was prepared with infrared absorbing dye (Avecia - 808nm peak absorption) implemented on one side. The lid was laser-welded onto the channel structure such that the absorbing dye –side, would face the polymer structure - consequently forming a fourth channel wall that (after the laser welding procedure) would thus be treated with the infrared absorbing dye.

A collimated infrared laser beam (808nm, 500mW, Sony – SLD322) was focussed, respectively scanned, along a micro-channel through the lid, effectively being absorbed by the dye layer in immediate connection with the enclosed liquid. A stepper motor driven galvanometer was used to position and scan the laser beam.

The microfluidic circuit was primed with whole blood (EDTA blood) suspended in isotonic saline (20/80% - blood/saline) -through external access ports, and the state of the enclosed liquid was recorded through a microscope with an attached digital camera.

The following screen-shots are taken from the recorded movie (figure 6, 7 and 8) Figure 6 shows the state of the channel with the liquid before being subjected to the *driving bubble*. Mainly erythrocytes (RBCs) are seen as they reflect incoming light. In figure 7, the driving bubble is approaching and the RBCs are violently displaced at a speed exceeding the camera capture rate. In figure 8, the driving plug I about to reach the centre of the frame and again the violent speed of the liquid should be apparent.

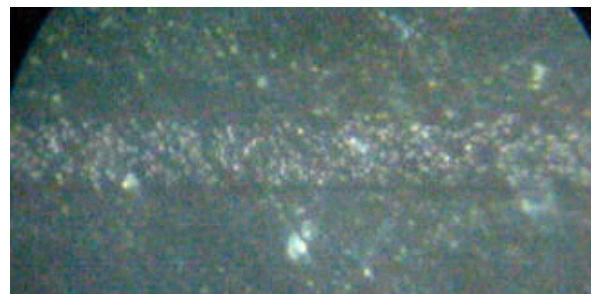


Figure 6. Erythrocytes in suspension

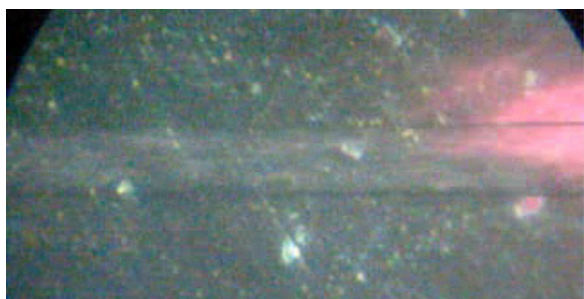


Figure 7. “Driving bubble” approaching.



Figure 8. Laser-beam/driving bubble reaching centre of frame

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From carefully examining the recorded footage (moving footage!) we are able to conclude that the liquid will follow the laser scanning speed. We worked with a scanning speed of 15mm/s and it appears that the liquid will thus move at 15mm/s; however – depending on scanning length versus overall channel length, some “back-lash” is present as can be seen when the laser-scanner returns to its original position. Further opto-mechanical optimisation may improve on this unwanted effect.

One object was to determine whether or not the violent pressure changes as well as the immense heat fluxes, would cause any serious denaturation of either RBCs or WBCs. After minutes of pumping we would examine the chip for haemolysed or fragmented RBCs, in a high NA microscope. We would repeat this procedure a number of times, and we never detected any bulk denaturation of the otherwise untreated (EDTA only) blood components.

4 CONCLUSIONS

We are certain that the pumping scheme in questioned, will tremendously enhance the flexibility of lab-on-a-chip systems. We envision a system where a *polymer disposable cartridge* will consist of only the molded microfluidic circuit, loaded with enzymes and reactants. Biological substances (blood, urine, wastewater etc.) will be added directly to the chip and the of-chip laser scanner system will thus enable complex handling of reactants in the chip only.