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Study of blood flow behaviour in microchannels

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Abstract

Microfluidic (also known as lab-on-a-chip) devices offer the capability of manipulating very low volumes of fluids (of the order of micro litres) for several applications including medical diagnostics. This property makes microfluidic devices very attractive when the fluid, such as blood, has a limited supply because the patients cannot easily and frequently provide a large sample. This is typically the case for aged, diseased patients that do require frequent sampling during acute care or of older people that have the option of being treated and cared for at home [1].

Prototype lab-on-a-chip devices for medical diagnostics comprise a number of elements which separately perform different functions within the system. Activity within the research community is focusing on the better integration of device functionalities with the long term goal of creating fully integrated, portable, affordable clinical devices. However, engineering these solutions for the large volume production of lab-on-a-chip devices requires design rules which are not yet entirely available.

This paper describes the results obtained from a set of experiments run to draw generic design rules for the manufacture of a cells/plasma micro separator [2]. The cells/plasma micro separator was selected for investigation because it is a strategic element required in the preparation of blood samples for many different analytical devices. The experiments focused on the study of the behaviour of whole blood passing through micro constrictions which are required for enhancing the separation effect [3].

The test microfluidic device was an aluminium specimen designed and manufactured to incorporate micro constrictions of different width and length. The

metallic aluminium test device was designed for manufacturing by micromilling and diamond cutting processes in view of applying these techniques to the manufacture of micro-moulds for the high-volume production of plastic microfluidic devices via micro-injection moulding.

The widths of the constrictions were 23, 53 and 93µm and the lengths were 300 and 700µm. The blood flow pattern and the level of haemolysis generated in the whole blood were determined for flow rates between 0.2 and 1 ml/min. Initial results suggested that the above conditions generate a stable flow and do not cause blood haemolysis following passage through the narrow constrictions. This result implies that constrictions as narrow as 23 µm and as long as 700µm can be safely used in blood microfluidic devices under appropriate flow conditions without the risk of damaging the blood components.

1. Introduction

Blood separation is a strategic preliminary step in the preparation of biological samples for on-chip analysis. Conventional batch technologies for removal of blood component (cells) are centrifugation and membrane filtration. New technologies such as CD-like platforms have been developed as continuous processes; however they are complex and require expensive instrumentation. To overcome these limits a new blood/plasma separator was designed to perform high-efficiency plasma separation in a simple way. No filtration is used at any stage of the process reducing any tendency for the blood flow to clog.

The solid model cross section of the novel polymer microfluidic device is shown in Figure 1. The device has a functional cavity composed of an inlet channel, a constriction, a set of channels for plasma collection, a central channel for the cell enriched blood collection and two outlets. The separation efficiency of the device is governed by the cell/blood channels width-ratio and the length of the constrictions. The interested readers are referred to [2],[3]; however there are currently no definitive design rules for determining the exact channel dimensions

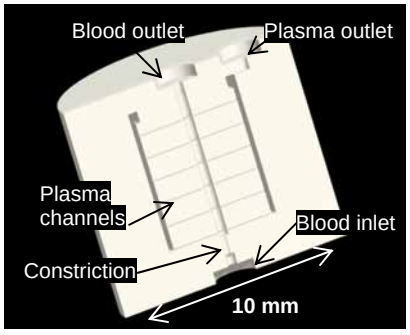

Fig.1: Novel microfluidic blood separation device

required for achieving efficient separation without inducing damage in any of the blood components. In particular the effect of narrow, long channels (and therefore high shear rate) on blood composition remains to be investigated.

2. Device fabrication

The test device shown in Figure 2 and 3 was fabricated in Aluminium 6061-T6 in two steps: a) micromilling and b) diamond planing. The first step, which was planned to create the channels reservoirs, was carried out with a KERN micromilling machine. The second step was performed on a CUPE 7-axis grinding machine to generate the precision constrictions bridging the reservoirs. The cutting process generating the constrictions was performed using single crystal diamond cutting tools with flat nose ends. The nominal nose sizes were 20, 50 and 100µm (measured nose sizes were 23, 53 and 95µm).

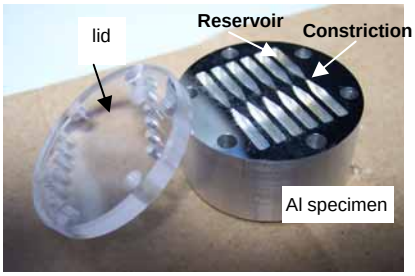

Fig. 2: Aluminum test device and plastic lid

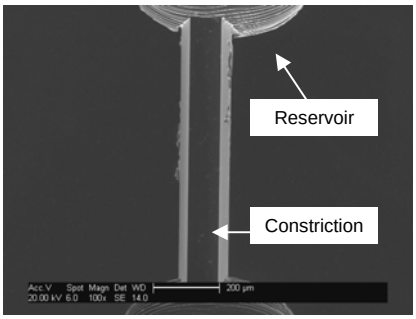

Fig. 3: SEM micrograph of one of the 95µm constriction. A reservoir is at the top of the micrograph

The diamond planing process was inspected with a microcamera and monitored with a Kistler dynamometer with the aim of detecting the cutting forces involved in the planing process, hence optimising the cutting strategy to achieve smooth surfaces [5]. In table 1 the nominal dimensions of the 6 constrictions are listed. The cutting strategy was determined by experimental trials and simulations of the cutting process [5]. For example the 95µm deep groove was fabricated in 12 passes: 8 of 10µm cutting depth followed by 4 final steps of 5µm depth to achieve a high quality surface. In all cases ethanol was used to lubricate the surface and produce smooth cutting. The Al test

Table 1: Nominal dimensions of the 6constrictions

Constriction	1	2	3	4	5	6
Length (µm)	300	700	300	700	300	700
Width (µm)	23	23	53	53	95	95

piece was covered with a plastic lid and mechanically bolted to avoid leakages at the lid-device interface during testing.

3. Device testing

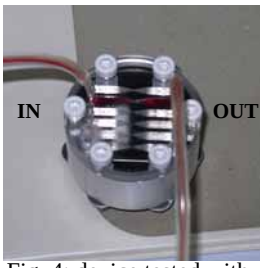

Fig. 4: device tested with whole horse blood

The device was tested using defebrinated equine whole blood (TCS Biosciences ltd). Blood was pumped through the channels using a micro-peristaltic pump varying the flow rate between 0.2 and 1 $ml \cdot min^{-1}$ with intervals of 0.2 $ml \cdot min^{-1}$ (Figure 4). The general flow pattern in the channels was visually inspected with an optical microscope. The haemolysis caused on the equine blood by the constriction at each flow rate was determined by collecting a blood sample before and after the constriction. The samples were then analysed using a reverse optical microscope by counting the red blood cells which appeared damaged following the high shear flow within the constriction.

4. Results

Initial results suggested that a stable flow can be achieved through all six constrictions under the above mentioned flow rate conditions. Moreover no blood haemolysis was observed at the constrictions outlet. This result implies that constrictions as narrow as 23 µm and as long as 700µm can be safely used in blood microfluidic devices under appropriate flow conditions without the risk of damaging the components of blood.

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