A BIODYNAMIC MICROSYSTEM FOR FLUIDS VISCOSITY MEASUREMENTS

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Abstract. The purpose of this research was to model, design and fabricate a biodynamic analysis microsystem required for determination of various molecular transport properties of the biological fluids. In order to achieve this, a lab-on-a-chip device was fabricated. The microfluidic system developed satisfies the objectives for the study of microcirculation and characterization of cell rheological properties, functions and behaviour. The measurement principle of the viscosity of biological fluids is based on the detection of the rotation of a polysilicon gear-wheels system. The gear-wheels have external diameters of 250 μm, 200 μm, 160 μm and 3 μm thickness. The micromachining process combines the undercut and refill technique with pin-joint bearing permitting the fabrication of bushings that were used to elevate the rotor away from the silicon surface. The testing of the microfluidic dynamic system was performed using electromagnetic micropumps and magnetic controllers. Each device was fabricated by silicon micromachining technology and tested to obtain the specific characteristics.

Keywords: lab-on-a-chip, surface micromachining, biorheology.

1. INTRODUCTION

Biorheology represents the research undergone on the flow and deformation of biological systems and materials derived from living organisms. The goal of Biorheology is to relate the rheological properties of systems/ materials to their molecular, cellular and structural properties. This approach is meant to draw a link between the biochemical and the biophysical structure of biological systems and i) their supramolecular organization, ii) their mechanical response characteristics, iii) their function in the context of physiological requirements and constraints under which they are currently operating.

Blood rheology is highly relevant for both academic and practical purposes. The flow properties of blood have a direct impact on human health, from stenosis or hemolysis up to cardiac surgery. From the rheological point of view, blood is simply a complex fluid system, deformable particles (mostly red blood cells) suspended in plasma. The study of the flow behavior of blood, points especially on the existing relationship between its micro structural changes and rheology. The evolving knowledge is useful in the design of artificial organs, such as heart and lungs, or artificial tissues (bioreactor systems). Rheological properties of culture media (broth) strongly influence the bioreactor performance, and it is therefore important to understand this aspect in the microbial process accompanying its operation. Also, the morphology of cellular (both prokaryotic and eukaryotic)
cultures has an influence on the rheological properties of broth and the mass-transfer rate in the reactor.

Here we report the design and fabrication of a microfluidic dynamic system for the velocity and viscosity measurement of the biological fluids (e.g. blood in coronary arteries, cerebrospinal fluid). The potential of microfluidic technology for medical equipments and in scientific instrumentation is enormous. The opportunity of approaching this application with microdynamic tools was motivated by recent developments in micro- and nanotechnologies and silicon superficial micromachining [2; 3]. The benefits of this miniaturization microsystems are: (i) reducing the sensor elements to the scale of the target species and hence providing a higher sensitivity (single entity / molecule); (ii) reduced reagent volumes and associated costs; (iii) reduced time to result due to small volumes resulting in higher effective concentrations; (iv) amenability of portability and miniaturization of the entire system; (v) point – of – care diagnostic; (vi) multi – agent detection capability; (vii) potential for use in vitro as well as in vivo. There has been a large demand for the development of an easy-to-handle and inexpensive clinical diagnostic biochip using fully integrated microfluidic chips, which has the sampling/identifying capability of fast and reliable measurements of metabolic parameters from a human body with minimum invasion. We have investigated the use of a microdynamic gear wheels system as a sensing device.

2. THEORY
The flow properties of all materials are defined by the relationship between shearing stress and rate of shear. For Newtonian fluids the shearing stress is directly proportional to the rate of shear, but measured torque is not directly proportional to the angular velocity, \( \omega \).

\[
F = \eta D
\]  

(1)

The constant of proportionality, \( \eta \), is the viscosity coefficient, the dynamic viscosity, or simply the viscosity of the fluid.

![Fig.1. The viscosity of the fluid can be computed by considering the gear wheel is rotating](image)

Let’s consider the movement of fluid between a gear wheel and a cylinder, the gear wheel having the extreme radius \( a \) and the cylinder having the radius \( b \), just like in Figure 1, \( h \) being the width of the gear wheel. If \( \omega \) is the angular velocity of the fluid at distance \( r \) from the axis of rotation, and the shearing stress and rate of shear at this radius is \( \tau_r \) and \( D_r \), respectively [1].

\[
F_r = \frac{M}{2\pi^2 h} \\
D_r = \frac{d\omega}{dr} \\
M = \frac{4\pi a^2 b^2 h \eta \omega}{b^2 - a^2}
\]  

(2)

For a Newtonian fluid, \( \tau_r = \eta D_r \), and

\[
\frac{M}{2\pi^2 h} = \eta \frac{d\omega}{dr}
\]  

(4)
There are many biological fluids, particularly those in the form of more concentrated suspensions and emulsions that are non-Newtonian. These include the Bingham fluids, for which the rate of shear is zero if the shearing stress is less than or equal to a yield stress, \( f \), and is otherwise directly proportional to the shearing stress in excess of the yield stress \([4]\)

\[
F = f + \frac{1}{\mu} D
\]

The constant \( \mu \) is the mobility.

A family of materials of ever growing importance in the field of synthetic polymers is described as visco-elastic because they combine some of the properties of a viscous fluid with some of the properties of an elastic solid. Such materials require specialized techniques to elucidate the relationship between stress, rate of shear and amount of shear. A detailed consideration of visco-elastic biological materials is outside the scope of this paper.

The term viscosity of non-Newtonian fluids, \( \eta \), is defined as:

\[
\eta = \frac{1}{\mu} + \frac{f}{D}
\]

Rotational viscometer is consequently widely used for the study of the flow properties of non-Newtonian fluids. The rotational viscometer comprises two parts, separated by the fluid under test, which are able to rotate relative one to another about a common axis of symmetry. As a part rotates, the other tends to be dragged around with it, the test fluid transmits a torque to the second part. If the fluid obeys Bingham’s law, equation (5) can be calculated that:

(i) if \( M < 2 \pi a^2 hf \), the shearing stress throughout the fluid is less than the yield stress and no shear occurs;

(ii) if \( 2 \pi a^2 hf < M < 2 \pi b^2 hf \), the shearing stress exceeds the yield stress only in the region between the rotor and a critical radius \( r_c \), given by

\[
r_c = \sqrt{\frac{M}{2\pi hf}}
\]

(iii) if \( M > 2 \pi b^2 hf \), the shearing stress exceeds the yield value at all points. For this case, integration leads to the Reiner – Riwlin equation:

\[
\omega = \frac{M}{2\pi b \cdot \eta_B} \left( \frac{1}{a^2} - \frac{1}{b^2} \right) - \frac{f}{\eta_B} \ln \frac{b}{a}
\]

\( \eta_B \) is the viscosity of non-Newtonian Bingham fluid.

3. BIOANALYTICAL DEVICE FABRICATION

3.1. Microchannels fabrication

Microchannels are often used to mimic capillaries, which allow the observation of cells squeezing through the narrow passages of the vascular system. Meanwhile, single cell analysis and measurement of transit time, total flow rate of cell suspensions and cell component aggregation can be studied using microchannels. Photolithography techniques were also used to create hydrophilic and hydrophobic areas inside microchannels \([6]\) by patterning the interior of the protein-coated channels. The ultraviolet light actually cleaves exposed protein molecules, changing the proteins from hydrophobic to hydrophilic. When flow was then activated through the channels, the fluid wet only the patterned hydrophilic areas. For our device the channel length was chosen as 150 \( \mu m \) to allow enough length for cell travel and maintain a relatively low channel resistance. The channel depth was chosen 10 \( \mu m \) and was performed using a classical deep RIE (Bosch process) on Adixen AMS 100 equipment using a photoresist mask. The input and output fluid ports would be etched completely through the wafer thickness creating holes in the chip. The ports are 1mm² area for connection purpose. The ports are centered arbitrarily inside the reservoirs. The fluid reservoirs are simply a storage area for fluid before it is pushed into the channels and after it leaves the channels. In addition, a scale bar was drawn above and below each the channel device. The bar consists of 3 \( \mu m \) wide rectangles that are spaced 3 \( \mu m \) apart. This allows measurement of cell length and travel distance.
3.2. Gear Wheels System Fabrication

The fabrication processes of the gear-wheels system combines the undercut and refill techniques with pin-joints bearing permitting the fabrication of bushings that can be used to elevate the rotor away from the silicon surface. The basis for fabrication of movable parts is the use of SiO$_2$ sacrificial layers that act both as spacers and also keep the parts attached to the silicon wafer during fabrication. The main steps of the fabrication process are presented in Figure 4 and consist of:

- On a 4” silicon wafer with (100) crystallographic orientation and a resistivity in the range between 1 and 10 Ω cm a 2 μm-thick SiO$_2$ layer deposited followed by a 3 μm-thick polysilicon deposition in and horizontal furnace.
- The polysilicon layer is anisotropic patterned using a deep RIE process through a photoresist mask – Figure 4a - (such the body and the teeth of the microgearing wheels are defined). The etching process stops on the SiO$_2$ layer.
- Using a second photoresist mask the hole of the wheels was etched using the same deep RIE process –Figure 4b.
- The SiO$_2$ layer is etched through photoresist-polysilicon mask (Figure 4c) in BOE. The isotropic wet etching was preformed with an underetching of the polysilicon layer. This underetching generates a space that will be filled with SiO$_2$ and polysilicon in the next steps (required for the flange fabrication).
- After removing of the photoresist a new 1-μm LTO layer is deposited in furnace (for a conformal deposition)- Figure 4d. The thickness of this layer set the tolerance of the adjustment.
- Through a photoresist mask (deposited by spray coating for a better coverage) the oxide layer deposited on the bottom of hole is removed in and ICP deep RIE - Figure 4e. The step is absolutely necessary for a mechanical contact of the flange on the silicon substrate.
- A second polysilicon layer (3 μm-thick) is deposited in a horizontal furnace – Figure 4f. The conformal deposition assures the filing of the gap under the wheel generated during the previous steps.
- The second layer of polysilicon is pattern (dry etch) through a photoresist mask in order to define the shape of the flange –Figure 4g.
- In the last step –Figure 4h- the SiO$_2$ molding layers are removed in HF 49% and the gear-heel structure is released.
In order to avoid the bending of the polysilicon layer the stress in this layer was adjust by annealing – method suggested by Chen et al in [11]. The measurement of the stress value was performed on test wafer using a KLA-Tencor stress measurement system. The sticking effect of the polysilicon layer on silicon surface was avoided by a methanol rinse after dissolving the latter sacrificial layer follow by drying process with CO$_2$ in a Critical Point Dryer (Baltec).

On the backside of the chip a Ti-Pt heater was microfabricated using a classical lift-of process in order to study the variation in temperature of the viscosity coefficient.

4. MEASUREMENT SET-UP

The measuring system is an electro-mechanic momentum changing device, based on the relative rotation of the gear wheel coupled with the rally axis. A dynamometer, tied in a bridge with a potentiometer, measures the relative rotation such that the signal obtained is proportional with the momentum which acts on the indicator. Switching to different positions on the dynamometer allows us to change the torque.

For each experimental point, calculate the geometric mean shearing stress $F_g$ using equation (9) and plot the values of angular velocity, $\omega$, against $\ln M$.

$$F_g = \sqrt{F_1 \cdot F_2} = \frac{M}{2\pi \cdot a \cdot b \cdot h}$$

The true shear rate corresponding to $F_g$ is then obtain using Krieger and Elrod formula:

![Fig. 4. The main technological process steps for fabrication of the gear wheels system](image)

![Fig. 5. The gear-wheel system](image)
A concentrated slurry in a Newtonian liquid may exhibit Bingham properties. The flow curves for two slurry fluids, fluid B more slurry concentrated then fluid A, are shown in Figure 6. The non-linear flow curves observed for the two fluids can be explained by interaction between particles, interaction with the continuous phase, and particle deformation.

Bingham’s law of plastic flow gives us

\[
D = \frac{\omega}{k} + \frac{k}{6} \frac{d^2 \omega}{d(lnM)^2} + \frac{7k^3}{360} \frac{d^4 \omega}{d(lnM)^4}
\]

(10)

\[
k = \ln \left( \frac{b}{a} \right)
\]

The rate of shear at the rotor is determined for the straight portion of the flow curve. This is achieved by solving equation (8) for \( \eta_B \) from equation (11). The shear rate is plotted against the shear stress at the rotor from the measured torque. The slope of this plot is \( \frac{d\eta}{dt} \), by definition.

5. CONCLUSIONS

The purpose of this research is to design and fabricate a microfluidic biodynamic system to measure the velocity and viscosity of biological non-Newtonian fluids (e.g. blood in coronary arteries, cerebrospinal fluid). The flow microsensor was designed and fabricated from polysilicon thin films through silicon surface micromachining and sacrificial layers technique. The microfluidic sensor consists of three driving gear wheels with external diameters of 250μm, 200μm and 160μm and 3μm thickness. The wheels need clearances to guarantee the motion and bearings for centering. The microsensor design has a flow channel to guide the fluid across the rotor, causing a velocity gradient which is necessary to make the gear wheels system turn. This microdevice enjoys the advantage of being compatible with silicon IC fabrication technology. The device was designed for asymmetrical forces to act on the rotor. Fluidic parameters such as dynamic contact angle or capillarity were taken into account for optimizing the microfluidic system performance. For the achievement of the micromechanic parts, either static or dynamic, of the microfluidic system the technique of sacrificial layer is used, the sacrifice material being etched in a solution that doesn’t attack microstructures.

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