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Design and Simulation Study Analyses of Flux Based LOC Regulator Cum Mixer For drug Delivery System

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ABSTRCT

A novel lab on chip system is proposed in this paper for the delivery of combinational drugs to a micro Drug delivery system. The lab on chip mixer system proposed is designed to deliver the few selective drugs in combinations in suitable proportions. Model proposed in this article is used to deliver combination drugs after mixing in mixer chamber and flow rate of the fluid is maintained with a flux based regulator positioned at chamber bottom. The system proposed here is used to serve complex drug delivery, which will be attached to the inlet of delivery needle. The mixer system proposed is designed with a polymer material suitable to handle the Combinational drugs for the Therapy, and the COMSOL multiphysics tool is used for the Fluidic simulation of the mixer setup.

Keywords: Comsol Multiphysics, combinational drugs, PDMS, Laminar flow, Naviers Strokes, Slip condition, Incompressible flow.

Introduction

The Micro electro mechanical system finds application in various biomedical, automotive, food processing, agriculture, defense and aerospace industries. The MEMS based sensors and actuators are widely deployed in recently developed Drug delivery LOC system for various treatments and Research purposes. The one such system Proposed in this article is MEMS based fluidic mixer and regulator. The system proposed is designed to specifically deliver the combinational drug for the delivery system. In fluid science, for various applications enormous number of MEMS based mixers are proposed for applications meeting both industrial and domestic standards. The combinational type of drugs is in specifically used for certain medications and such a combinational drugs has to be delivered in suitable Proportions. The regulation of such drugs in suitable combinations can be done with suitable mixer kit for the Micro scaling Drug delivery system and also in the fluidic regulators. The any mixer kit in general will be composed of a fluidic channel and injectors part either of Mechanical or flux based actuation systems. The fluidic flow in this model experiences two type of flow at two phases, the flow at phase 1 be the laminar type of flow and the phase 2 the flow will be a Turbulence type of flow. The drugs actuated with the flux regulators will not experience any field changes so the phenomenon of drug delivered is preserved and the flux based system actuators are more efficient when compared with the MHD, CO polymeric mixers.

μ-TAS mixers

The MEMS based fluidic mixers finds application in both Industrial and Research standards, the Mixer systems proposed conventionally follows various actuation mechanisms, designs, the Aspect ratio and geometry aspects. MEMS based μ-TAS mixers find various biomedical applications like DNA, RNA polymerase reactions, Glucose sample analyzers, Assay formations, Stem cell culture analyzed, Drug delivery systems etc. The MEMS based fluidic mixers are generally devised with poly materials to achieve a relatively better compatible with the bio elements.

Design Specifications

The lab on chip system to drive a combinational drug for a biomedical application is proposed in this article. The system is devised in the micron to mm scaling to enable a proper delivery system to the needle. The system is incorporated with the additional flux point at the base of mixer chamber to improve the fluid outflow to needle.

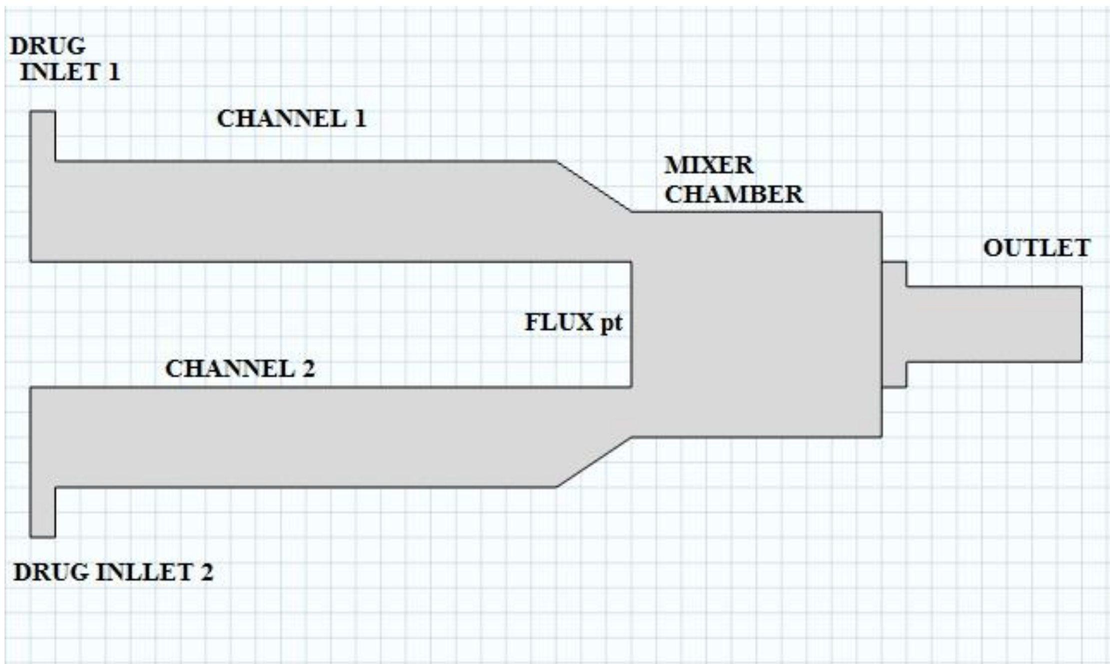


Figure 1: Design Sketch of Mixer

The proposed lab on chip system is designed the two inlets to fed two different drugs, equipped with a flux induction system, a fluid (Drug) regulator. The system proposed in this article is a fluid regulator and mixer system connected to the inlet of Delivery part. The device aspect ratio of the system simulated in this article as follows.

Table 1: Device Aspect Ratio (All in microns)

S.No	Parameter	Dimension
1	INLET Channels a. Hydraulic Depth b. Length	 1000 2500
2	Delivery Channels a. Hydraulic Depth b. Length	 2000 5000
3	Mixer Chamber a. Mixer Inlet b. Chamber Dimension	 1000 3000 * 3000
4	Outlet a. Primary Notch b. Secondary Notch	 2000 1200
5	Delivery System Inlet	1200
6	Flux Area	~1600 - 1900

The primary notch and secondary notch are designed to reduce the system diameter periodically and to increase the fluid flow velocity which conservatively reduces the fluid back flow. And the fluid in the chamber experiences a 0 slip boundary condition along the walls.

Polymerized Mixer

The regulator cum mixer system proposed in this article is devised with the polymer material. The Polymer materials are considered to be the most likely compatible material for any biomedical applications because of inert nature towards the biomedical elements and Biological components. The system proposed in this article is devised with Polypropylene material which can be fabricated with the Rapid prototyping or laser sintering technique. The poly propylene material being proposed for our system because of its intermediate density suitable to regulate the fluid flow. The poly propylene material being used for our system can be machined with laser beam cutting, ensuring the smoothness in the channel. The poly propylene material case data sheet for our material be

Table 2: Material Specification

S. No	Parameter	Value
1	Molecular Formula	$\sim(C_2H_6O\ Si)_n$
2	Density	$0.965 g/cm^3$
3	Melting Point	Liquid State at Room Temperature
4	Polymer Type	Thermoplastic polymer
6	Curing Agent	Ethanol.

In The PDMS material proposed for our system will bubble formations will be observed and same should be reduced.

Operation Specification

The µ-Lab on chip system devised to deliver combinational drugs to the delivery Needle of entire medication setup is proposed. The system designed in this article is used to mix the two different drugs in proportions and to regulate its flow towards delivery needle system. The drugs fed in the inlets are driven with suitable force\Pressure in two different channels. The flow injected in the channels follow the laminar type of flow and when the flow mixes in the mixer, a state of unsteady is absorbed in the fluids following a turbulent state of flow. The state of unsteady also followed due to the flux inhibitor equipped at the Mixer chamber bottom phase and the flux based inhibitor is used to increase the fluid outflow to delivery needle.

Flow Modeling In Rectangular Channel

The type of flow exhibited by the fluid till the mixer chamber will be a Laminar flow and the velocity of fluid will be maximum at the centre with '0' Velocity observed at the walls, where the fluid molecules experiences No slip. The fluid flow modeling by Navier- Strokes Equation is as

$$\rho\left(\frac{\partial v}{\partial t} + v.\nabla v\right) = -\nabla p + \nabla.T + f.$$

Where V is Velocity of flow, p be pressure at inlet, ∇ *be* fluid stress.

The type of fluid flow predicted with a measureless quantity called Reynolds number in fluid dynamics. The flow in the channel before mixer is predicted to follow a laminar type of flow and it will be having Reynolds number of Re<<2100 and the flow after mixer is a turbulence due to mixing and disturbance caused by flux regulators. The Reynolds number for the fluid flow in notch outlets will be Re>>4300.

The fluid flow in a linear channel is modeled with a Reynolds number as follows,

$$Re=\frac{\rho V\ Dh}{v}=\frac{QDh}{va}.$$

Where D_h be the fluid hydraulic diameter of channel, Q be volume of flow rate, a be cross sectional area, ρ be density. Flow of fluids in the channel is considered to be a Laminar flow and any flow in the rectangular channel is considered to be a continuum flow mechanics with low flow rate profile. The Average flow rate of fluid across the channel is given by Q which is

$$Q=\frac{4ba3}{3\mu}\left(-\frac{dp}{dx}\right)\left[1-\frac{192a}{\pi 5b}\right]\sum\frac{\tanh\left(\frac{i\pi b}{2a}\right)}{i5}.$$

Here$\frac{dp}{dx}$be changes in pressure gradient with respect to the Distance factor x, with a, b be the length of channel and walls length. The Changes in pressure gradient can be represented by

$$-\frac{dp}{dx}=\ \Delta p.$$

The ∇p is given by -$\frac{4\tau}{D}$ where τ be the Shear stress experienced by the rectangular channel.

The fluid flow inside the rectangular channel is considered to be an In Compressible fluid, since the densities of the most used drugs will be unchanged with respect to the applied potential, and at the chamber of mixing.

The fluid flowing inside the channel will experience a certain loss between the inlet and outlet and the loss may be due to friction factors observed in the outer layer of Laminar flow fluid, Fluid back flow due to the hinge structures in channel. The flow modeling can be presented by calculating the Pressure loss across channel and dividing by channel Cross sectional area, or channel Diagonal in case of rectangular channel. The shear stress of wall by fanning friction factor is as follows, Shear Stress of the fluid is given by

$$\tau=\ \frac{f\rho v2}{2}.$$

Fanning friction factor for the fluid is given as one fourth of the Darcy friction factor flow and it is given as

$$f=\frac{16}{Re},$$

where Re be the Reynolds number of the system and fanning friction factor with respect to Pressure loss in a rectangular channel is given as

$$F=\frac{\Delta PR}{L\rho v2}.$$

The Flow of fluid after the mixer chamber follows the turbulent flow profile and such a relation can be given by Colebrook equations.

$$\frac{1}{\sqrt{f}} = -2\log_{10}\left(\frac{\sum}{3.7Dh} + \frac{2.51}{Re\sqrt{f}}\right).$$

Where f is Darcy friction factor, D_h be Hydraulic Diameter, Re be Reynolds number, ∑Heightof Roughness.

Here ∑can be neglected since surface considered is a smooth one.

Micro Channel Fabrication

The entire mixer part of the system can be prepared with PDMS and Silicon wafer mold. ***PDMS Curing:*** The PDMS fluid mixed with suitable curing agent is properly stirred to remove the air bubble formation with PDMS solution and Curing agent in the ratio of 1:10, the properly mixed solution is kept in the Vacuum Desiccator followed by Thermal treatment to remove the air bubbles. The bubble free solution is then poured on to the mold with silanization treatment to prevent the sticky nature and wafer breakage. Once the PDMS with suitable channels and chamber has been prepared then PDMS and glass is bonded with Plasma treatment until the appearance of pale Violet Hue.

Wafer Processing

The Silicon wafer of N type is selected for the mold preparation, where the wafer is subjected to the several processes Like Deposition, Patterning with UV radiation, Etching for mold preparation. After the wafer level mold is prepared the silanization agents are used for removal of PDMS layer without breakage of Silicon Wafer. The Silanization material of Pluronic F127 or 1H, 1H, 2H, 2H-Perfluorodecy ltrichlorosilane is used for proper peel off.

Simulation Analyses

The COMSOL multiphysics Simulation tool used for our simulation of the fluidic regulator cum mixers. The simulation is carried out in the Stationary environment for both fluid flow and chemical Species concentration analyses. The two types of physics selected to carry out the flow and concentration gradient mixing simulation simultaneously. Laminar flow, Turbulent flow selected for fluid simulation and Chemical Species Transport selected for concentration gradient analyses. The entire simulation is carried out with poly propylene as device material. The simulation of the system is carried out under three different constraints as follows:

Case 1:

The fluid flow simulation carried out is shown with respect to the varying velocity of fluid at each individual point. The Simulation result epics that the velocity strain of fluid is maximum at the curvature and linearized in the straight away channels, the simulation results shows that the fluid flow takes up the laminar type of flow in the channels with acquiring ‘0’ slip at the sliding walls and maximum flow at the middle of flow cross section.

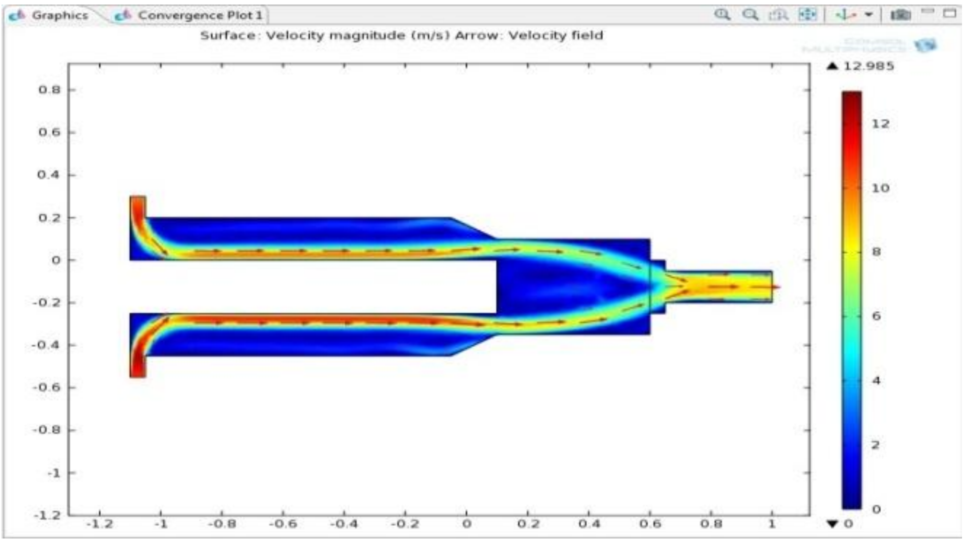


Figure 2: Fluid Flow & Velocity Modeling

Case 2

The pressure exerted by the fluid flow in the channel is simulated. The simulation output shows the maximum pressure exerted by fluid at the low flow Notch outlets and the potential pressure exerted on fluid at the bottom of mixer tank due to the flux point.

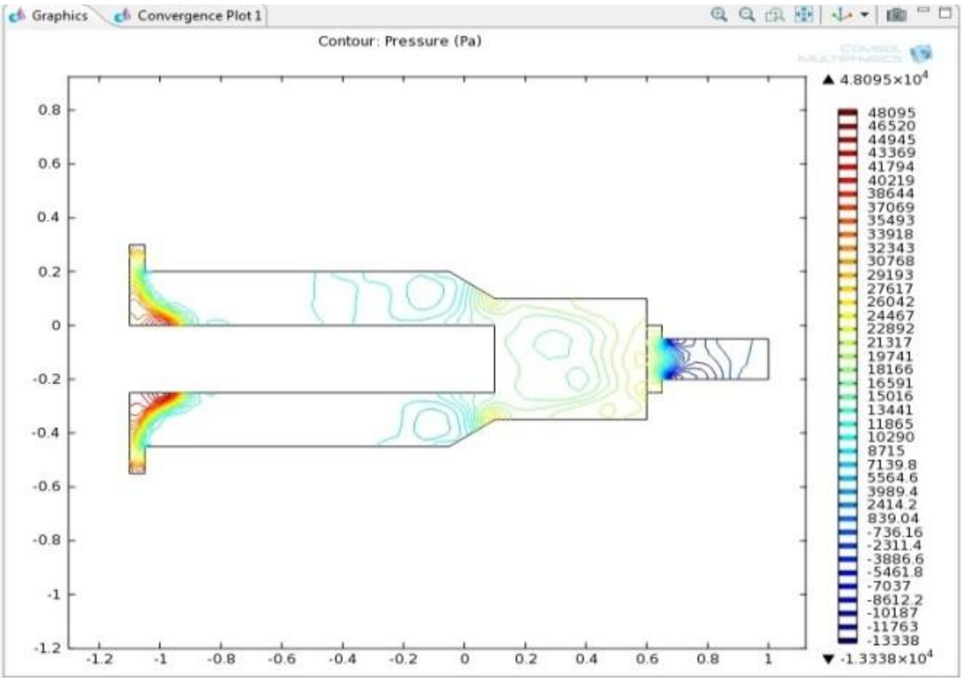


Figure 3: Fluid Flow & Pressure Modeling

Case 3:

System simulated for the concentration gradient analyses is discussed where inert concentration of the liquid at the inlets will be maximum and as the fluid approaches mixer chamber the native inert concentration of fluid starts to decrease and at the outlet notch, the combination drugs concentration is high indicating the proper combination outflow.

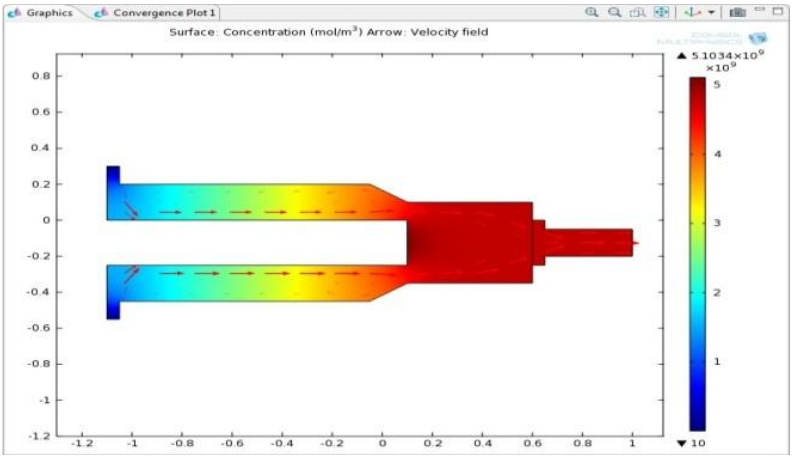
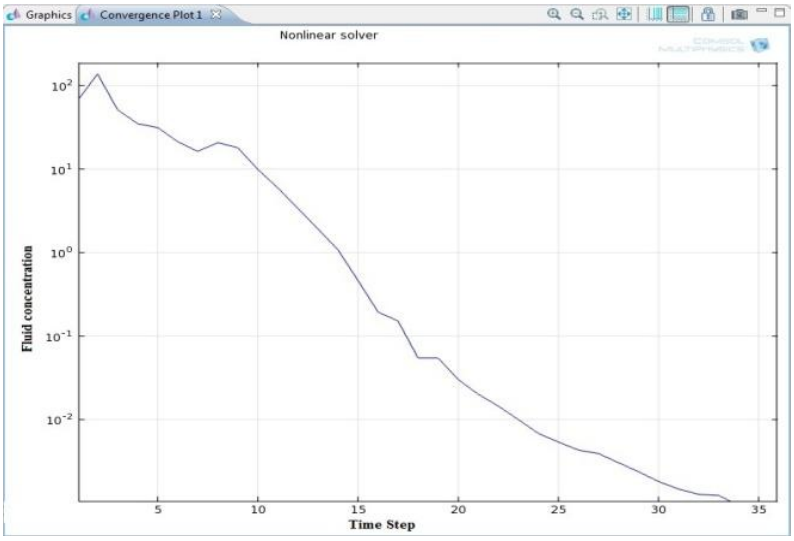


Figure 4: Mixing Concentration Modeling

Graphical Analyses

The 2 Dimensional fluid flow simulation is carried out between applied fluid flow concentrationsover a period of time. The graph epics the decreases ininitial concentration of fluids at the mixer chamberwhich may results in the turbulent flow.



Plot 1: Fluid Concentration Vs Time Stamp.

Conclusion

The MEMS based fluidic mixers finds efficient applications in the field of chemical and bio µ-TAS systems. The system designed and modeled in this article is used to efficiently deliver the drug in suitable combinations and the fluid flow in the channel is regulated continuously with flux based actuation system. The fluid at inlets is driven with a velocity of 15 – 20µl/s. The system is proposed to specifically serve as input for the micro fluidic needles in case of combinational drug injections.

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