DESIGNING OF LAB-ON-A-CHIP FOR THE THERAPEUTIC DRUG MONITORING OF ERLOTINIB HYDROCHLORIDE

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Contents :

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Introduction

- **Chemotherapy** is one of the treatment approaches used to kill malignant cells, which prevent invasions and metastasis.
- Chemotherapy treatment have several **side effects.**
- In order to avoid such side effects, **Therapeutic Drug Monitoring** (TDM) techniques are necessary.
- **Analytical techniques** available to perform TDM includes, **spectrophotometry, TLC, HPLC ,GLC**, etc.
- These techniques have various **drawbacks**, as an alternative to such analytical techniques, an **Electrochemical sensor** is required to perform real time monitoring.

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- The rapid development of Lab-On-a-Chip (LOC) is greatly impacted by the incorporation of **microfluidics-related** techniques and concepts.
- An **LOC** device is an instrument for scaling down laboratory functions onto a chip in **micrometre** scale.
- Primarily through the manufacture of progressively smaller sensors with greater sensitivity and selectivity as well as cheaper production and maintenance costs.
- The challenges in integrating and fabricating active mixers make passive micromixers a suitable substitute.
- Main **advantages** includes:-
  - *Cost effectiveness*
  - *Ergonomics*
  - *Diagnostic speed*
  - *Sensitivity*

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- Main **fabrication** methods of LOC are lithography, glass etching, etc
- Also these fabrication methods are
  - *Expensive*
  - *Time consuming*
  - *Manual work needed*
  - *More number of microchannel has to made for studies.*
- Due to this drawback, simulation software came into action, they are used to validate the design structure of microchannel with suitable physics interfaces.
- **COMSOL Multiphysics software** is a finite element analysis, solver, and simulation software package for various physics and engineering applications, especially coupled phenomena and different physics interfaces.

Literature Review :

- M. Itomlenskis et al,2008
  - *Using COMSOL multi-physics packages and chemical engineering modules explore the possibility of enhancing the mixing efficiency of two fluids in a micro channel. Flow field modelling, mixing and numerical analysis was done in COMSOL.*
- A. Pradeep et al,2016
  - *Studies about microchannel with various geometry to improve the efficiency of the passive micromixers and was further optimized for best mixing performance. The optimized design was fabricated using direct laser write lithography.*
- D. S. Dkhar et al,2023
  - *Different fabrication methods of LOC and additionally the detection of analytes like small molecules, macromolecules and cell bodies are also reviewed in this paper.*

Design

- **Homogeneous mixing** of the fluids passing through the microchannel is one of the major challenges to design LOC devices.
- Effective mixing can be achieved using either an **active mixer** or a **passive mixer**.
- In passive mixing, no external energy source is required for mixing the fluids moving through the microchannel.
- In this case, the extent of mixing is influenced by channel geometry and pressure gradient.

❖ Mixing efficiency of passive mixers can be improved by altering the channel geometry. Passive micromixer was designed using COMSOL Multiphysics software.

❖ COMSOL Multiphysics permits to use **PDEs** to simulate and evaluate Multiphysics phenomena.

OPTIMIZATION OF PARAMETERS

- Inlet channel parameters
  1. *Angle of inclination (ø) (30°, 45°, & 60°)*
  2. *Entry length (3mm, 4mm & 5mm)*
  3. *Shape of entry channel (T & Y channel)*

- Mixing channel parameters
  1. *Straight channel*
  2. *Curved channel*
     - Normal meander
     - Modified meander

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MICROMIXERS DESIGN PARAMETERS

- Binary system with inlet streams as ‘X’ and ‘Y’.
- Height and depth of microchannel H & D respectively
- Angle of inclination (ø) of inlet stream
- Outlet stream indicated by ‘S’
- Microchannel length (L)
- Length of inlet channel (L1)

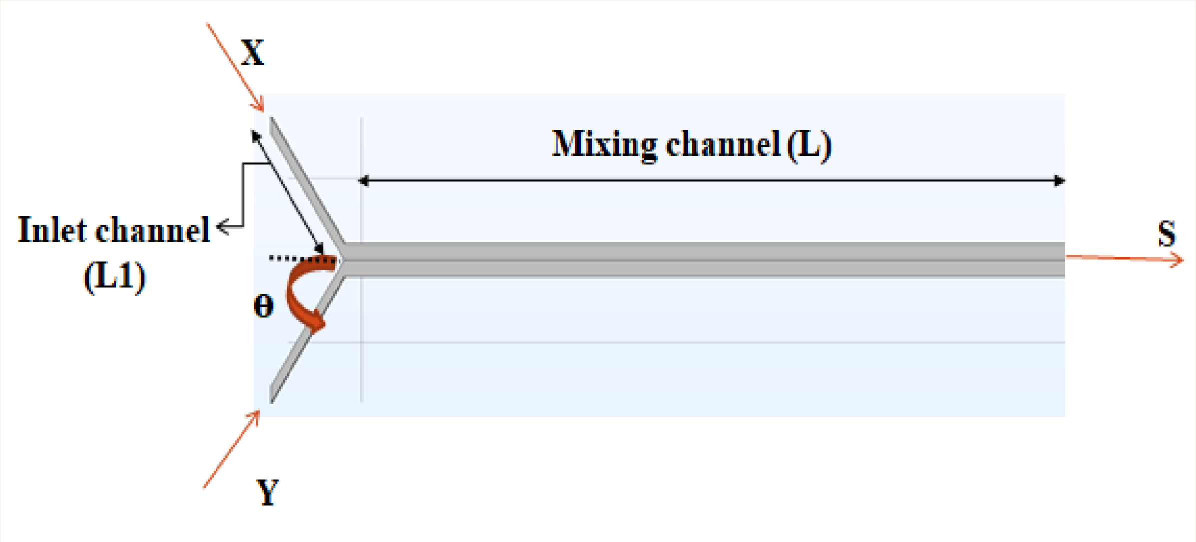


Fig. 1 : Dimensions parameters of Y-channels

INLET STRAIGHT CHANNEL DIMENSIONS

- L = 45 mm
- H = 1.4 mm
- D = 0.1 mm

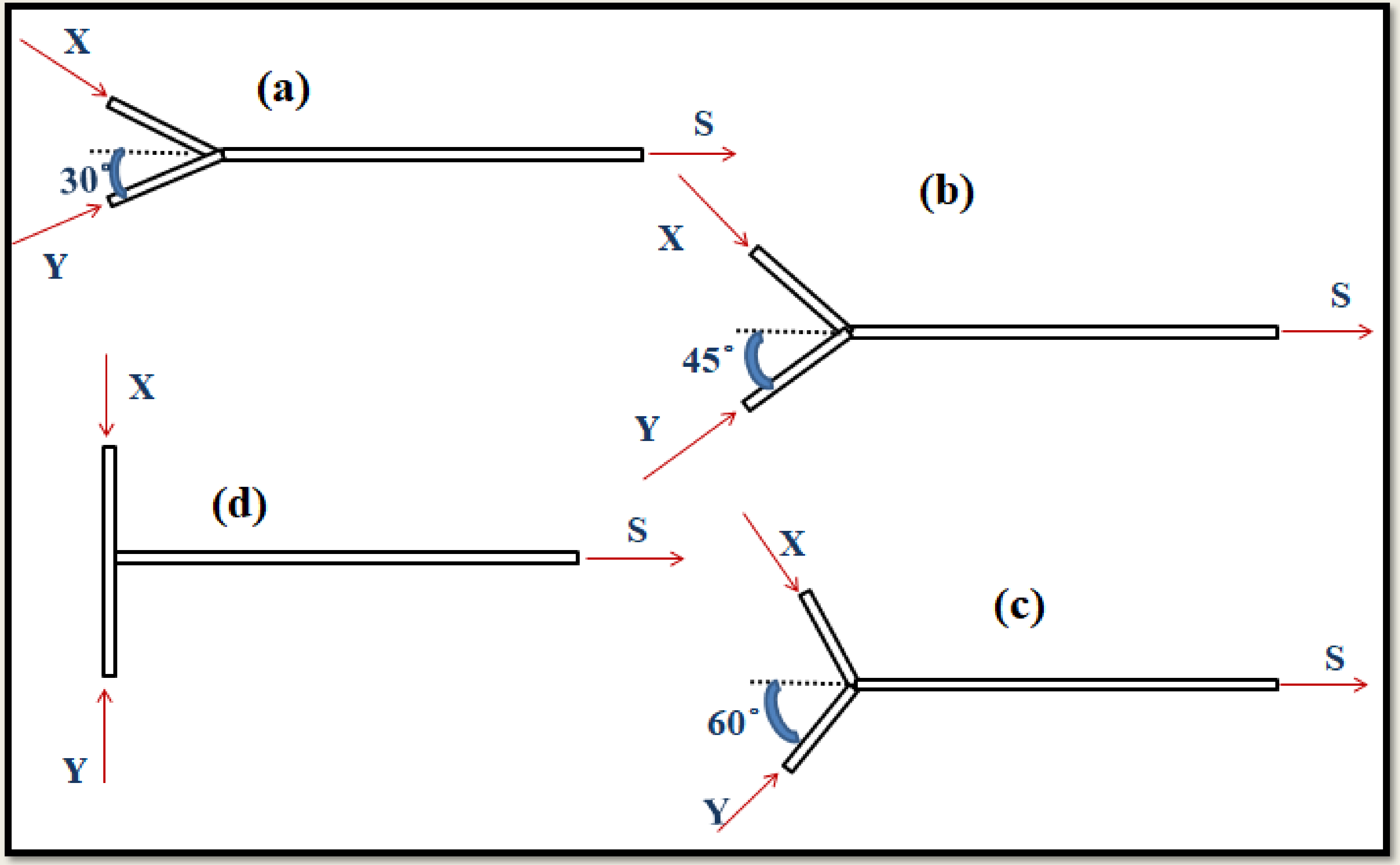
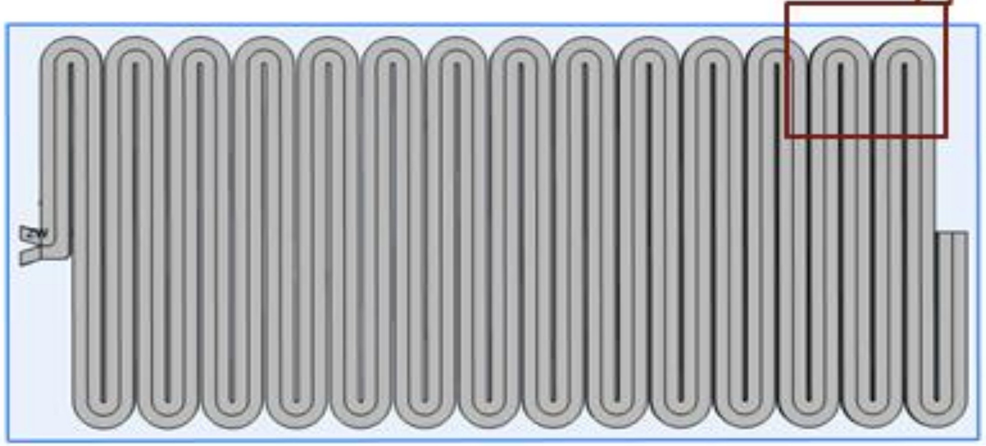
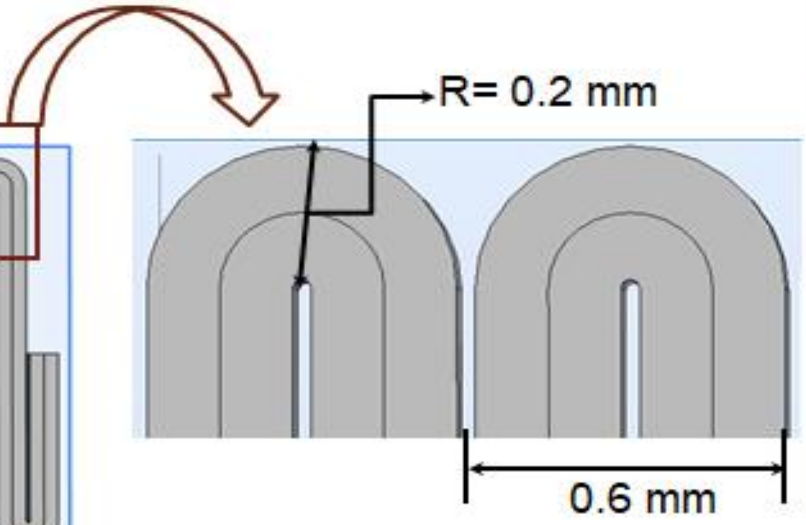


Fig. 2 : Dimensions of Y-channels a) 30°, b) 45°and c) 60° and d) T-channel

CURVED MIXING CHANNEL DIMENSIONS – NORMAL MEANDER

- No. of meanders = 14
- Radius = 0.2 mm
- Height = 1.4mm

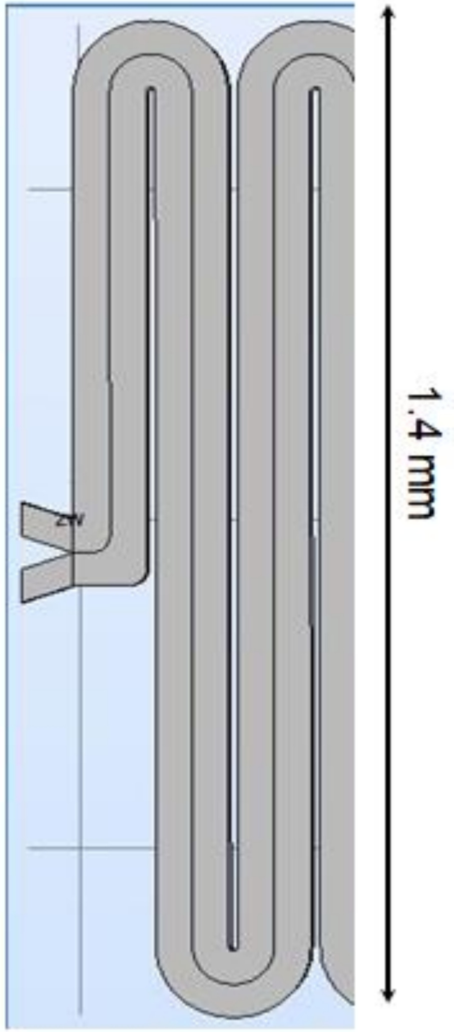


Fig. 3 : Dimensions of normal meander

CURVED MIXING CHANNEL DIMENSIONS – MODIFIED MEANDER

- No. of meanders = 14
- No. of smaller curved surface per meander = 15
- Radius = 0.1 mm
- Height = 1.4 mm

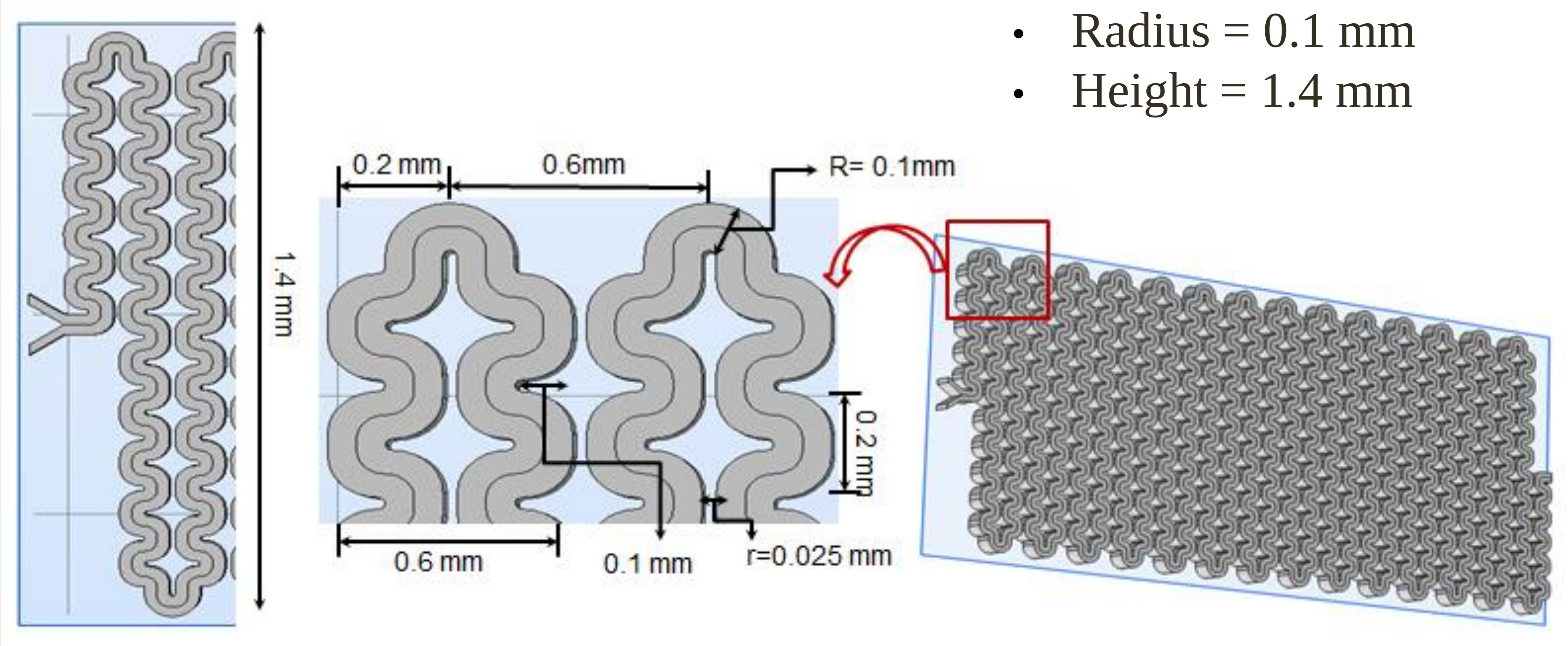


Fig. 4 : Dimensions of modified meander

Simulation

- Optimization of parameters
- Geometry design
- Material selection

Fluid	Density (Kg m^{-3})	Viscosity (Kg m^{-1} s^{-1})	Diffusivity (m^2 s^{-1})
Water	9.998×10^2	0.9×10^{-3}	1.2×10^{-9}
Ethanol	7.89×10^2	1.2×10^{-3}	1.2×10^{-9}

Table. 1 : Properties of model fluid at 20 ^0C

- **Selection of physics interfaces :**

  Laminar flow interface; Navier Stokes equation

  Transport of Diluted species; Convection- Diffusion model equation

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Results and Discussion

- EFFECT OF INLET CHANNEL – ANGLE OF INCLINATION

Y-channels with different 'θ'	Inlet centre velocity(ms^{-1})
60°	1.6828
45°	1.8334
30°	2.2217

Table. 2 : Inlet centre velocity at different angles

- ✔ The inlet channel with 45° inclination have **normal velocity profile and residence time** compared to others.
- ✔ Hence, 45° inclination of inlet channel is chosen for further simulation studies.
- ✓ For 60° inclination - covers more area, increase in the size of microchannel - increase in fabrication cost - longer time to attain fully developed flow due to smaller velocity.
- ✓ And 30°, inlet stream angle attained the fully developed flow in shorter time, because of greater velocity.

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- From the velocity profile, it shows that 45° have significant impact on homogeneous mixing due to **moderate velocity component** in the direction of flow
- Compare to the structure wise fabrication the 45° required **intermediate area** and velocity compared to others.
- It will **reduce the size** of the LOC.

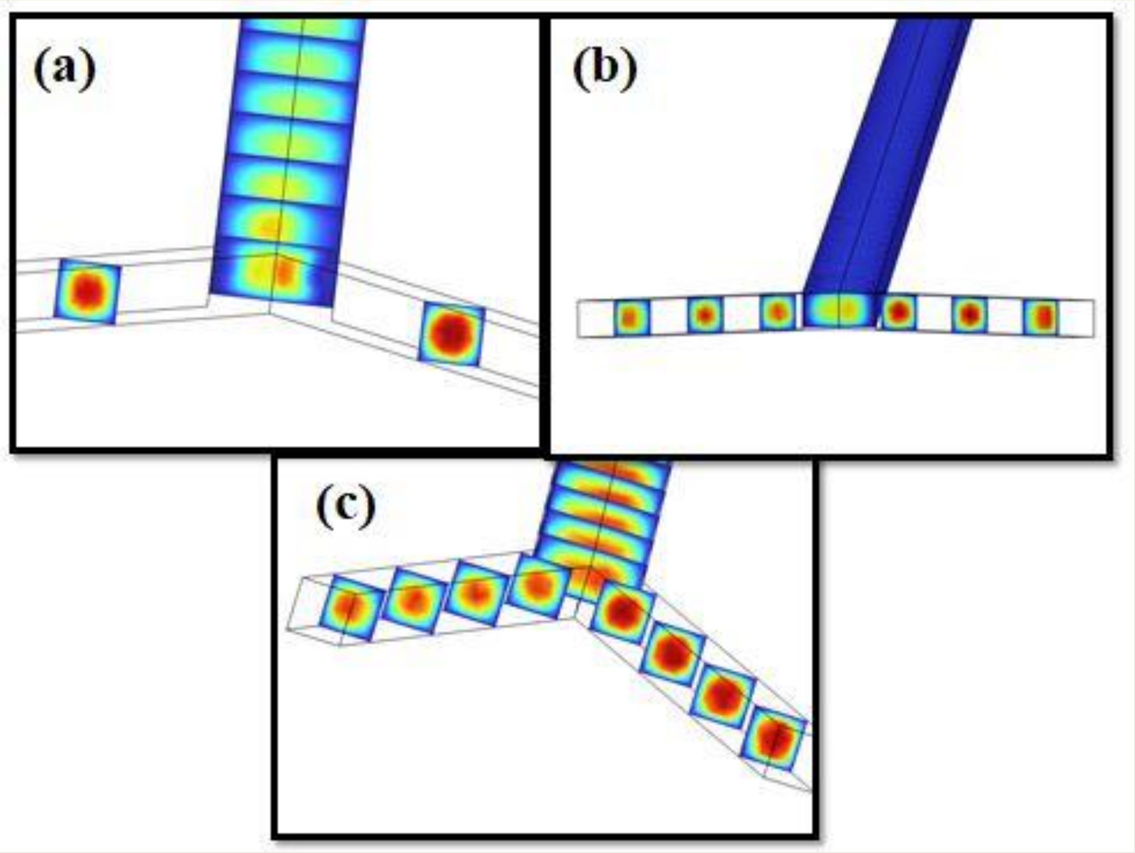

Fig. 5 :Inlet velocity profile for different angles of inclination a) 30°, b) 45°and c) 60

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- EFFECT OF INLET CHANNEL – ENTRY LENGTH

- ✔ Straight channel with 45° inclination and entry stream with various length (3, 4 and 5 mm) was studied
- ✔ Compared to other entry length, 5mm have more effect on mixing due to **increase in residence time**
- ✔ When residence time increase, the fluids have **more contact** and **maximum mixing**.

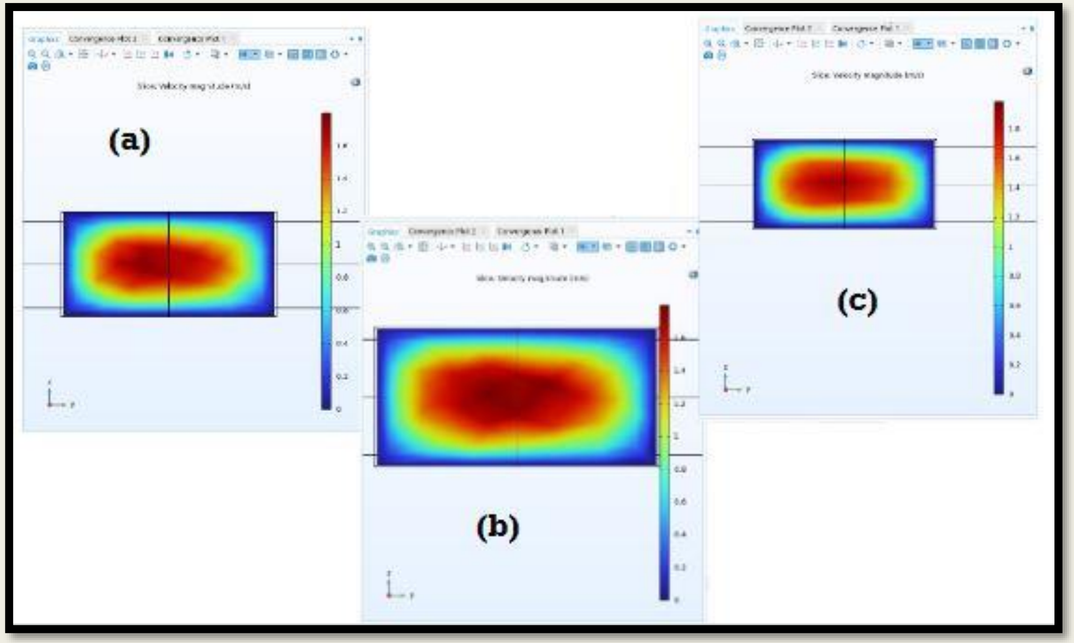

Fig.6 : velocity profile for different entry length at angle of inclination 45° (a)4mm, (b) 5mm, (c) 3mm

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- EFFECT OF MIXING CHANNEL

- ✔ Mixing efficiency of straight and curved channel was studied
- ✔ Its observed that straight mixing channel have complete mixing at **40mm & 32mm for T & Y – channel respectively**.
- ✔ And in case of **normal meander** the homogeneous mixing starts at **19mm**.

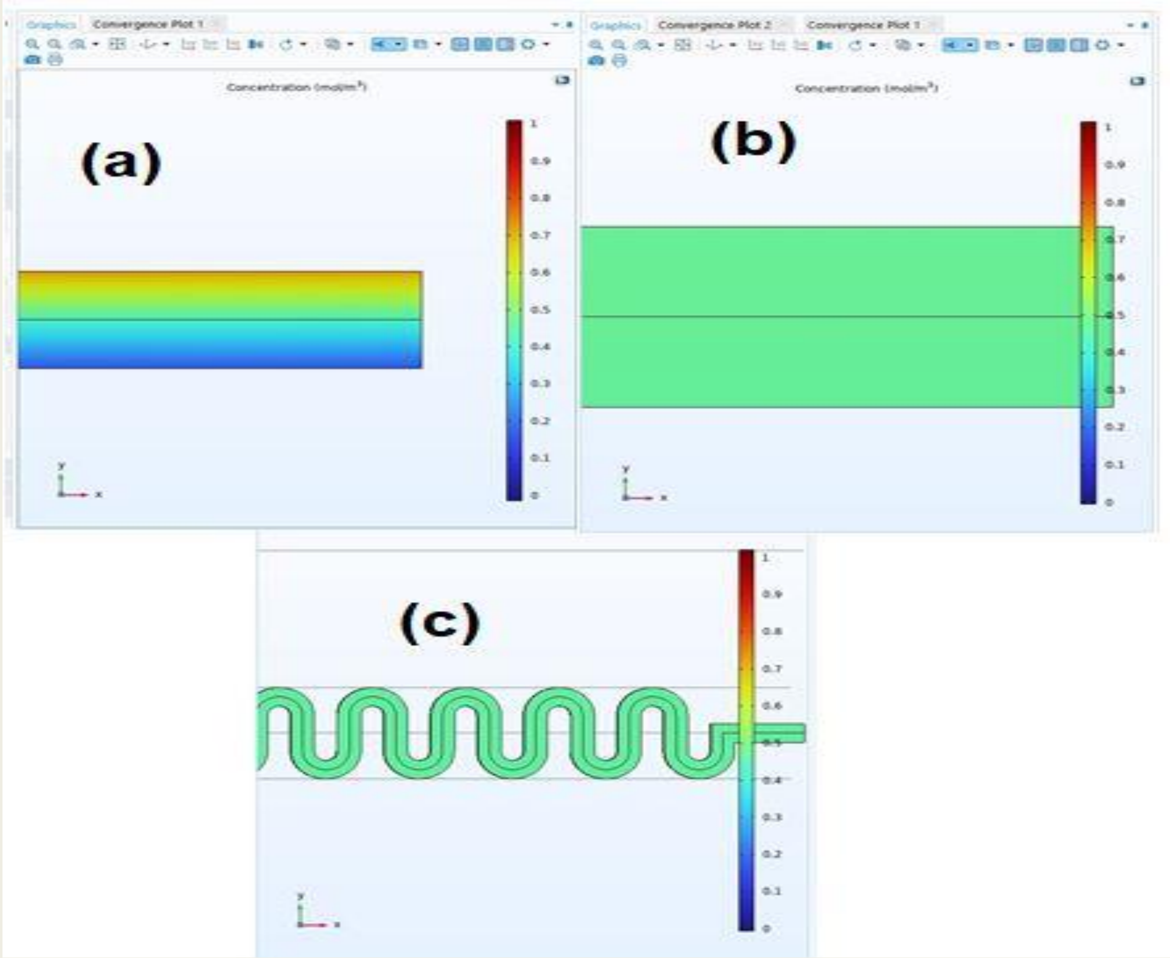

Fig.7 : XY plan Concentration profile of; a) T-channel, b) Y-channel with 45◦ inclination and 5mm entry length and c) normal meander

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EFFECT OF CURVED MIXING CHANNEL

- Comparing with normal meander, the modified is prone to **more chaotic advection**.
- Due **continuous change in the flow path**, increase in the mixing of fluids.
- Deviation in the path also led to **greater residence time**.
- With in one meander, **15 subunits of smaller meander** are introduced.

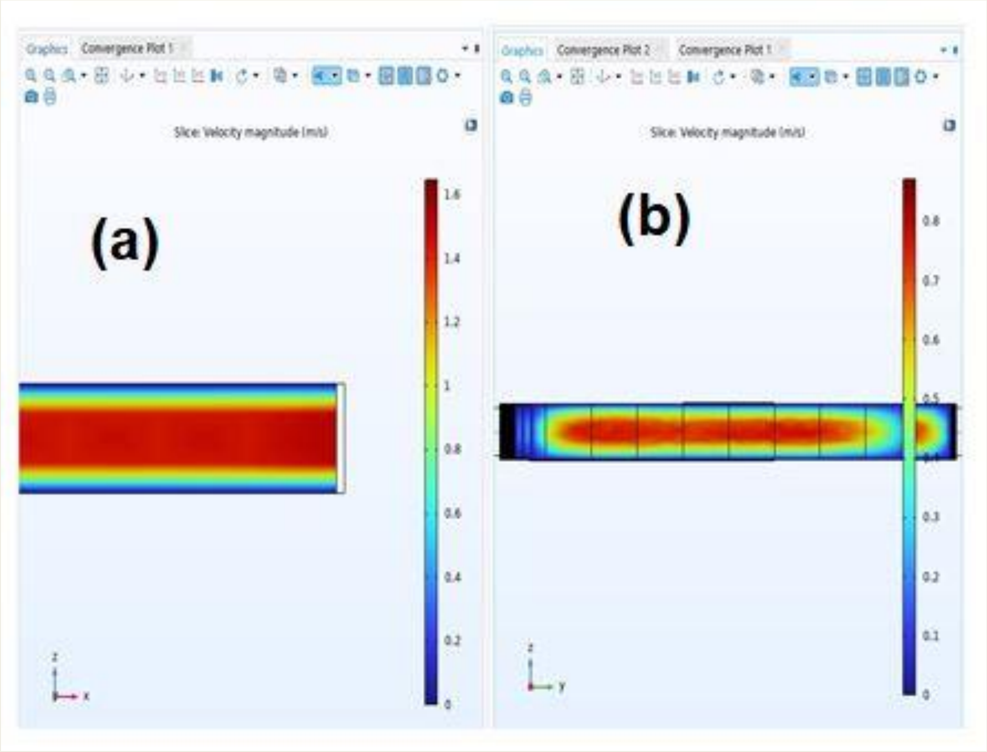

Fig.8 : YZ plane Concentration profile a) normal meander and b) modified meander

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OVERALL DATA OF THE SIMULATION

Design analyzed	Outlet concentration(mol m^{-3})
T-channel	0.38700
Y-channel with ‘θ’ 60°	0.42065
Y-channel with ‘θ’ 45°	0.46635
Y-channel with ‘θ’ 30°	0.47281
Normal meander	0.47346
Modified meander	0.49863

Table. 3: Outlet Concentration profile for different Geometry

Maximum homogeneous mixing is observed in the modified meander

Design analyzed	Standard deviation(mol m^{-3})
T-channel	0.325
Y-channel	0.210
Normal meander	0.080
Modified meander	0.002

Table. 4: Standard deviation of each geometry

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- The modified form have less deviation from effective efficiency.
- Modified meander have homogeneous mixing at 10 mm.

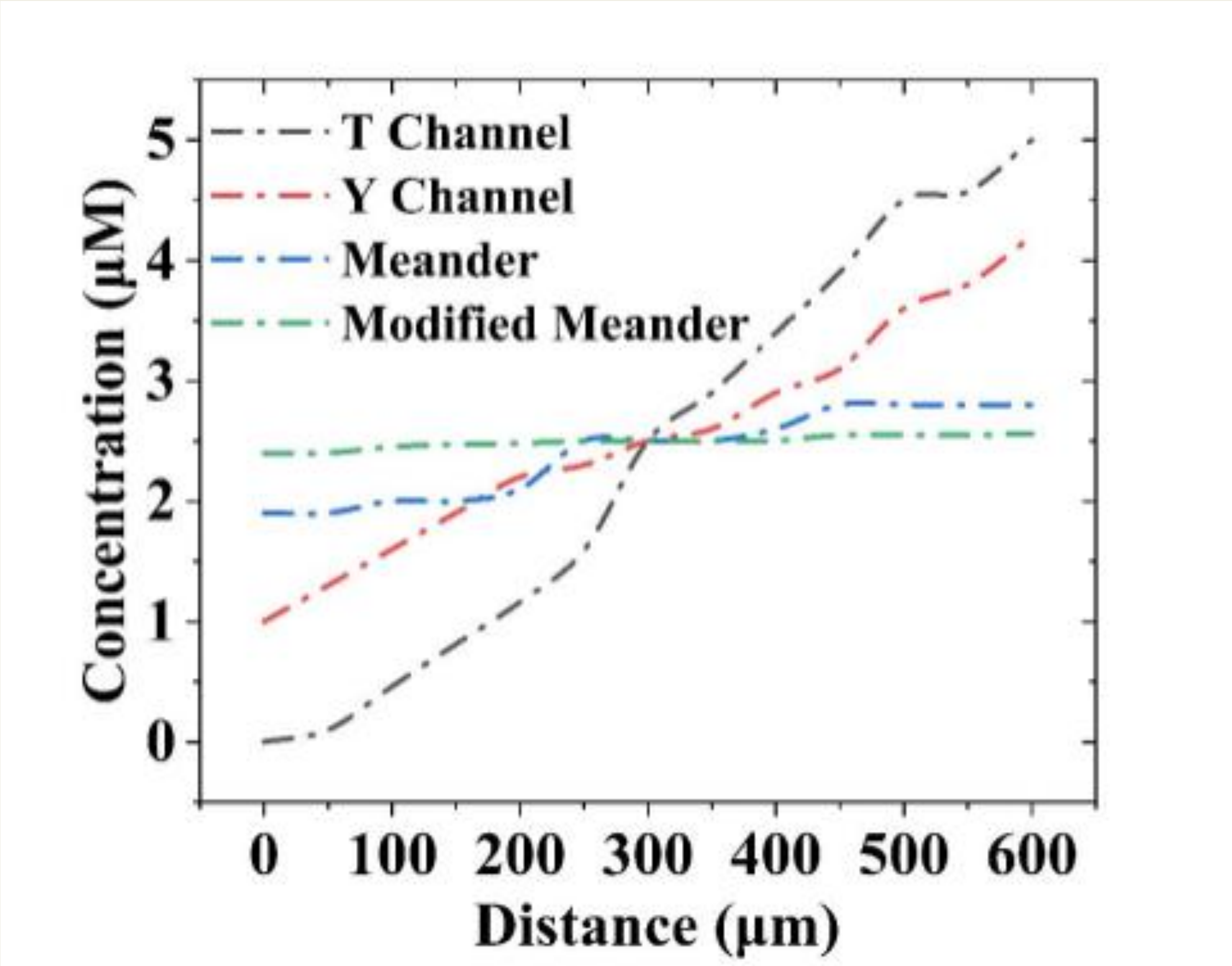

Fig.9: Concentration plot of various geometries at 30mm cut-line

Conclusion

- Parameter optimization was done successfully.
- **Simulation results of geometry**
    - Modified meander have higher efficiency in homogeneous mixing due to smooth curved structure, more chaotic advection, residence time and centripetal force.
    - So the LOC having modified meanders microchannel is highly portable, and provides homogeneous mixing with great accuracy.

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THANK YOU

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