Fibrin Droplet Production Using Step Emulsification

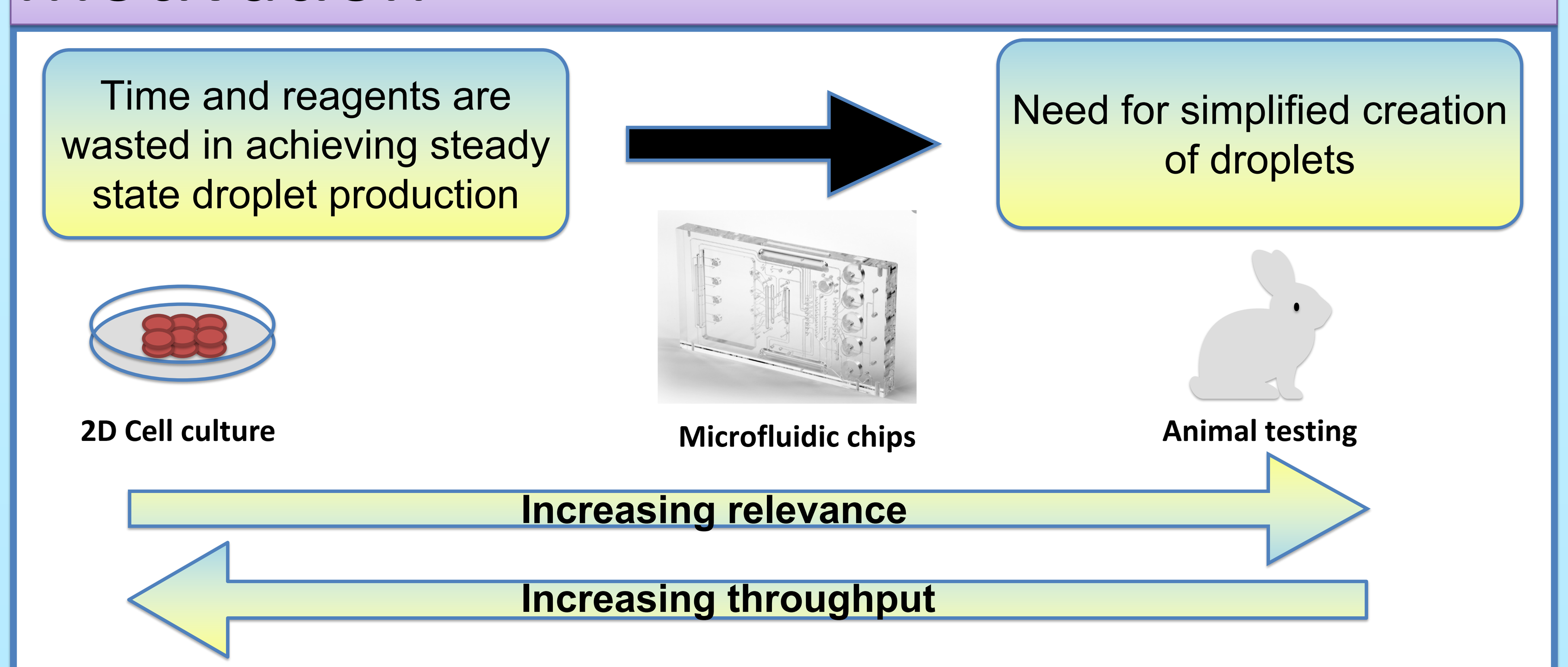
Priyanka Sreeram, Tomas Jimenez , Dr. Melinda Simon

Department of Biomedical Engineering San José State University, San José, CA

Abstract

Step emulsification is a microfluidic technique which is a streamlined method to produce monodisperse droplets, offering several advantages. The droplet size is independent of the continuous phase flow rate, which minimizes time and reagents wasted in achieving steady flow between two immiscible fluids. In step emulsification, droplet break-off is driven by a rapid change in the height of the channel. This induces a pressure imbalance according to the Young-Laplace equation. Published step emulsification schemes are limited to the creation of droplets from a single phase of aqueous material, reducing their application space. Emerging technologies for the creation of tumor spheroids increasingly include two or more materials, but balancing multiple flow rates can result in unsteady droplet production and long start-up times. Therefore, there is a need to simplify the creation of monodisperse droplets using multiple aqueous phases. Without these simplified techniques, rapid production of consistent and stable droplets becomes difficult. However here we will show it is possible to produce fibrin droplets using step emulsification. The research problem addressed, is to use two aqueous channels, containing fibrinogen and thrombin to produce fibrin droplets. We anticipate this will lead to more consistent droplet production using two aqueous phases.

Motivation

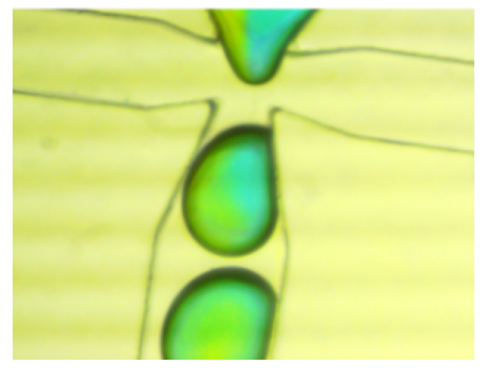


Fibrin

Mimics ***in vivo* conditions**, **biodegradable** and provides **cell attachments**

Background

Previously



Flow focused

Flow rates	1.Dispersed 2.Continuous
Droplet formation	Shear Force

Now

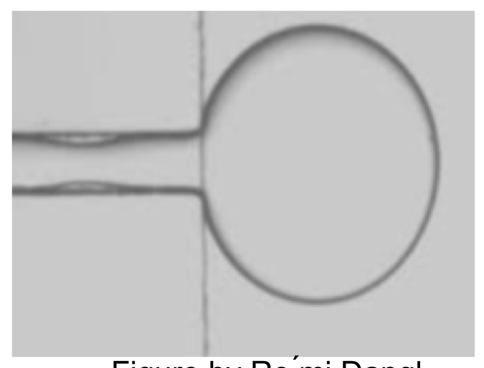
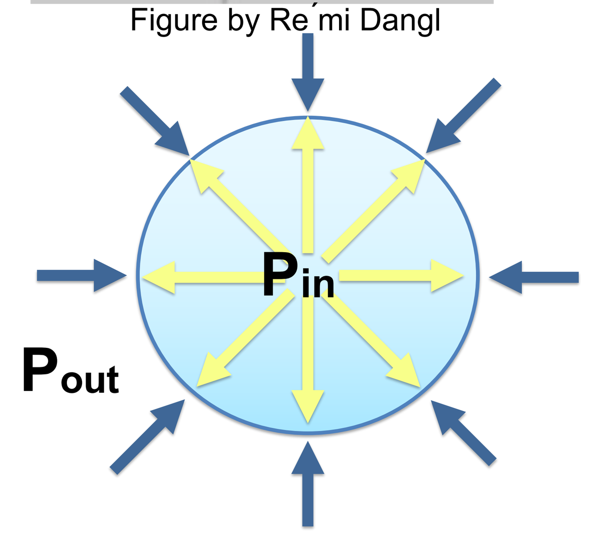


Figure by Re´mi Dangl

Step Emulsification

Flow rates	1.Dispersed
Droplet formation	Interfacial Tension

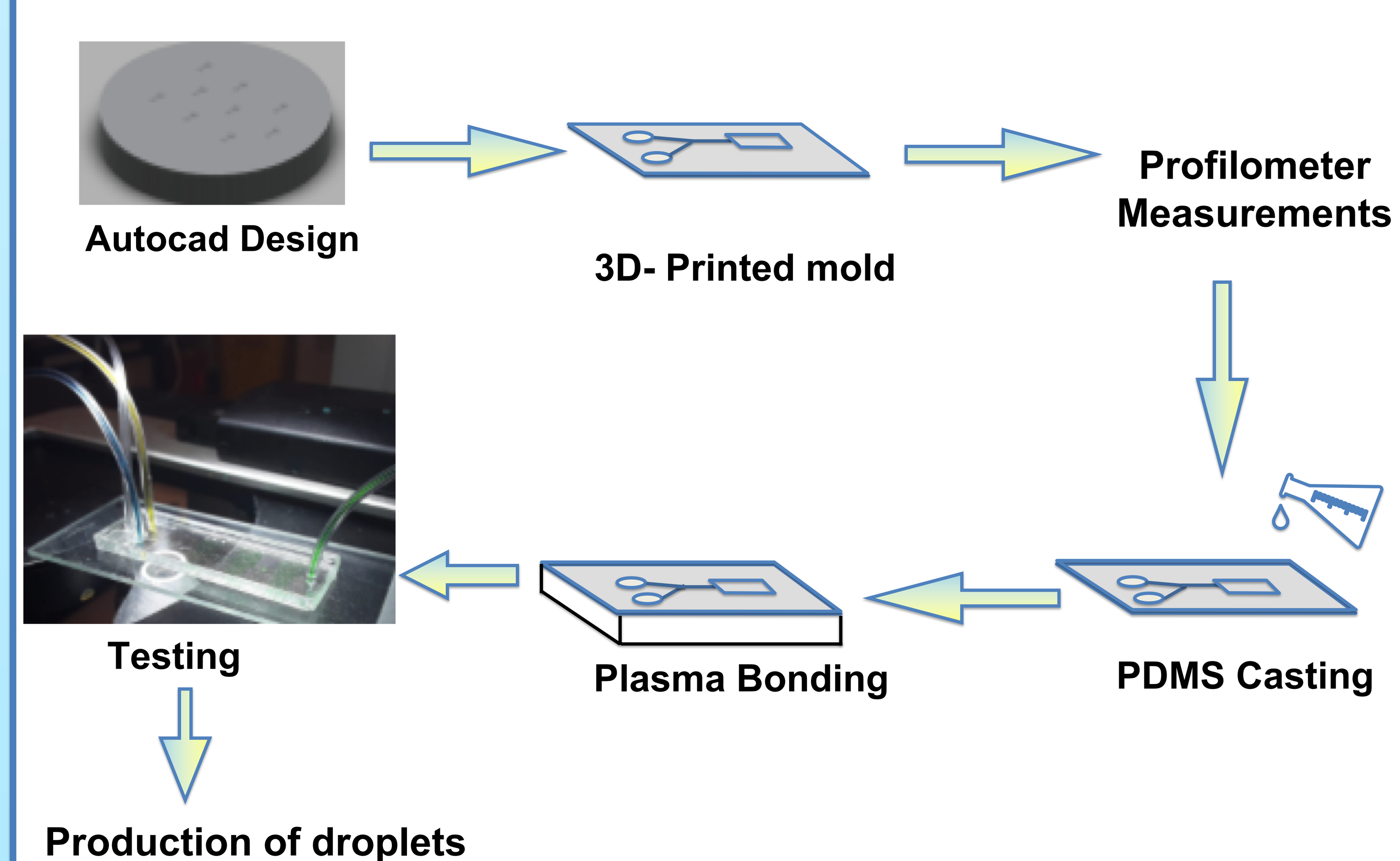


Laplace Equation

$$\Delta P = \gamma\left(\frac{1}{R1} + \frac{1}{R2}\right)$$

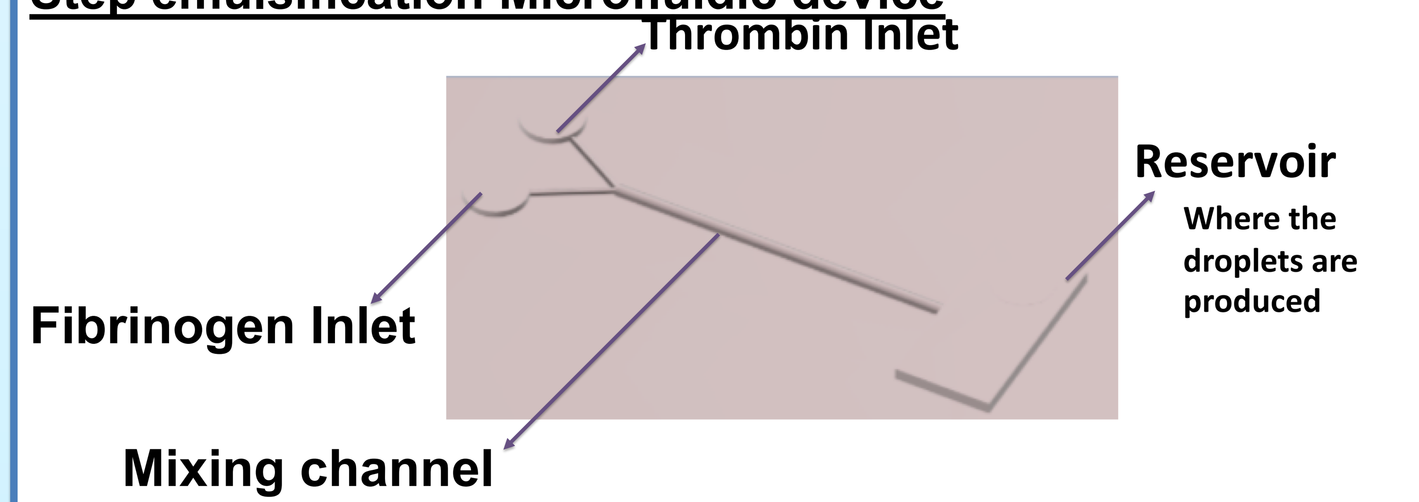
P - Pressure
ϒ - Interfacial Tension
R_1 & R_2 - Radius of curvature

Methodology



Results

Step emulsification Microfluidic device



Trial	Results	Modifications
1	Mixing channels and inlet channels not clearly printed	Change diameter to 70
2	In progress	-

Trial 3 No.	Inlet channel	Mixing channel	Reservoir
1	Diameter: 90 Length: 1650	Diameter: 190 Length: 3500	Length: 2000 Width: 1000 Height : 125
2	Diameter: 100 Length: 1650	Diameter: 200 Length: 3500	Length: 2000 Width: 1000 Height : 125
3	Diameter: 110 Length: 1650	Diameter: 210 Length: 3500	Length: 2000 Width: 1000 Height : 125
4	Diameter: 90 Length: 1650	Diameter: 190 Length: 3500	Length: 2000 Width: 1000 Height : 220
5	Diameter: 100 Length: 1650	Diameter: 200 Length: 3500	Length: 2000 Width: 1000 Height : 225
6	Diameter: 110 Length: 1650	Diameter: 210 Length: 3500	Length: 2000 Width: 1000 Height : 230

Conclusion & Next Steps

- This project will allow fibrin droplets to be created which can be used for cyto-toxicity testing.
- The next steps would be to fabricate the current design and test for droplet production

References

Eberhardt, A., Bošković, D., Loebbecke, S., Panić, S., & Winter, Y. (2019). Customized Design of Scalable Microfluidic Droplet Generators Using Step-Emulsification Methods. *Chemical Engineering and Technology*. https://doi.org/10.1002/ceat.201900143

Eggersdorfer, M. L., Seybold, H., Ofner, A., Weitz, D. A., & Studart, A. R. (2018). Wetting controls of droplet formation in step emulsification. *Proceedings of the National Academy of Sciences of the United States of America*.

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