Statistical Modeling on Cell Encapsulation

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Introduction

The encapsulation of a single target cell in a microfluidic droplet through a droplet generation system is a biomedical engineering technology that contributes to a variety of medical practices and research. Cell encapsulation is a mechanism to keep cells viable as a potential tool for the treatment of human illnesses, such as cancer, diabetes, and Parkinson's disease.

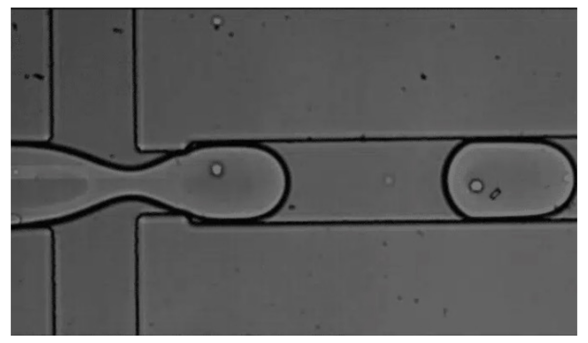

Figure 1. Image from *Microfluidic Droplet Production Method* by Fluigent, captures high droplet generation frequency and the low volume of the microfluidic system.

Due to the randomness and uncertainty in the cell encapsulation process, an understanding of the physical and statistical parameters of the process contribute to its optimization. The statistical modeling of the process is a way to understand the random probability distribution and optimize the single target cell per microfluidic droplet.

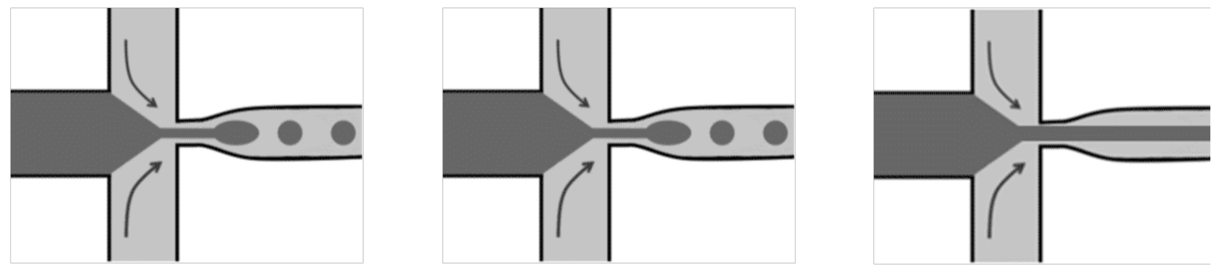

Figure 2. Image reference from *Microfluidic Droplet Production Method* by Fluigent, captures varying regime formation of droplet generation system, ranging dripping, jetting, and stable co-flow regime.

The broad application of the cell encapsulation process contributes to the importance of understanding the dynamics within the process. There are two foundational concepts behind the understanding of the dynamics in cell encapsulation: the physical understanding of microfluidics and the statistical modeling of cell encapsulation.

Methods

In order to create a statistical model of the cell encapsulation process, we assumed that the microfluidic channel of a droplet generation system had some considerations before statistical analysis. These factors included inertial, capillary, and viscous forces that deal with the two fluids in the droplet generation systems. Once a foundational understanding of the system was established, the statistical analysis of this process was accredited to the statistical concept of Poisson distribution.

$$P(X = k) = \frac{\lambda^k e^{-\lambda}}{k!}$$

Figure 3. Poisson distribution formula, where λ is the mean number of events within a given interval of time or space, e is Euler's constant, and k is the number of times an event occurs in an interval.

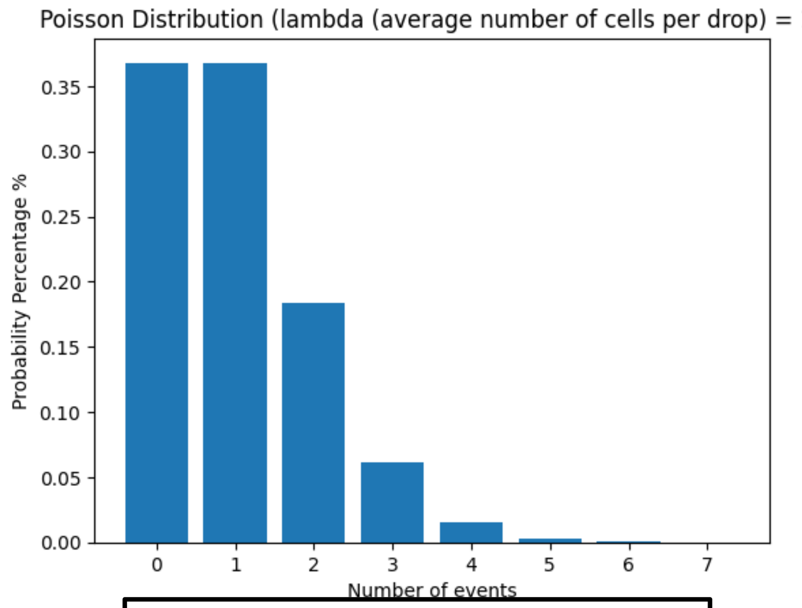

Figure 4. Python code for Poisson distribution.

Poisson distribution was best fit for this model because it is a probability distribution that deals with a number of events that occur in a fixed interval of time or space being that each event is independent of one another just like the randomness of the cell encapsulation process. Using Poisson distribution, we had to relate the average number of cells per droplet to flow rate and drop size which came down to the volume of one drop and cell flow in the formula. While taking into consideration these factors and plugging them into the Poisson distribution formula, we were able to find droplet size in terms of varying parameters in a droplet generation system.

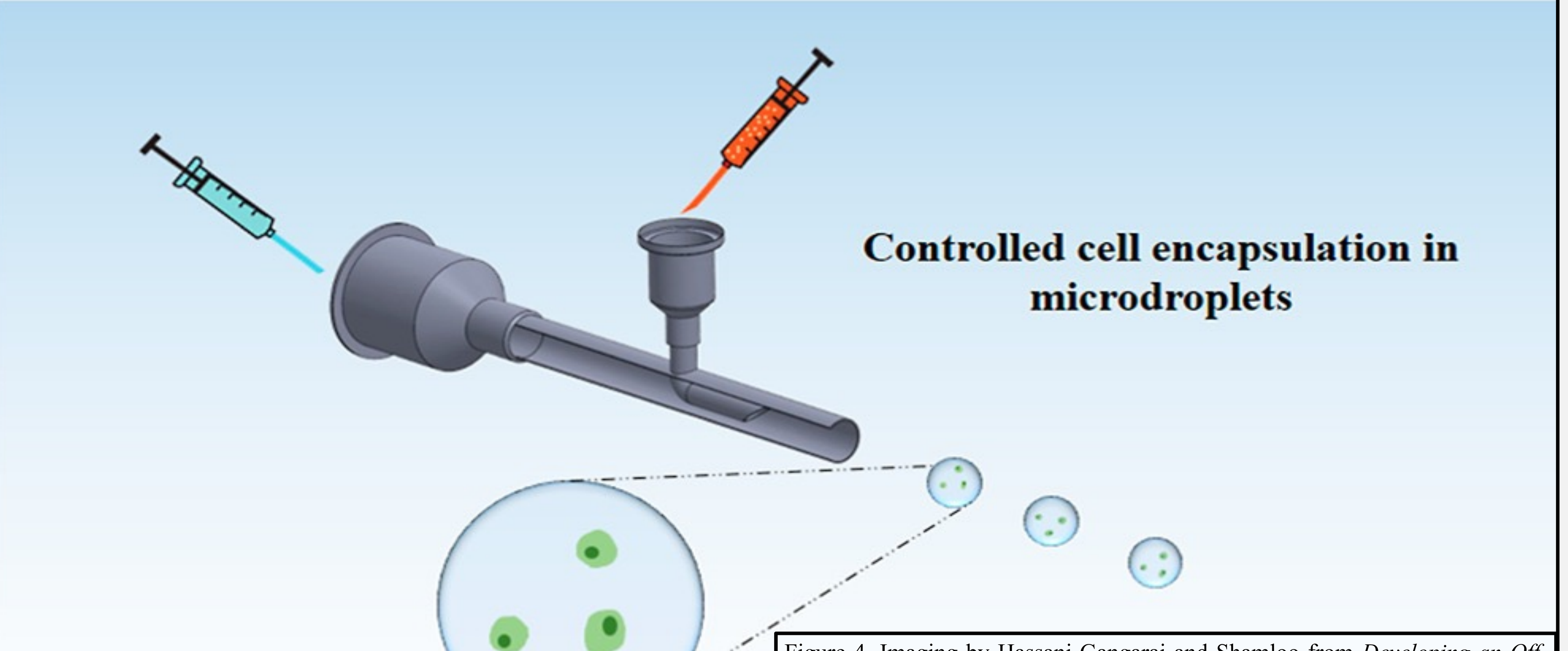

Figure 4. Imaging by Hassani-Gangaraj and Shamloo from *Developing an Off-the-Shelf Microfluidic Droplet Generation Device for Cell Encapsulation* visualizes the controlled cell encapsulation process into microfluidic droplets.

Results and Conclusion

A statistical analysis and model using the discrete probability distribution, Poisson distribution, was used to aid in the optimization of the cell encapsulation process. With this model, the parameters of fluidity, flow, geometry and cell count per volume of the process make up the distribution which attribute to its optimization.

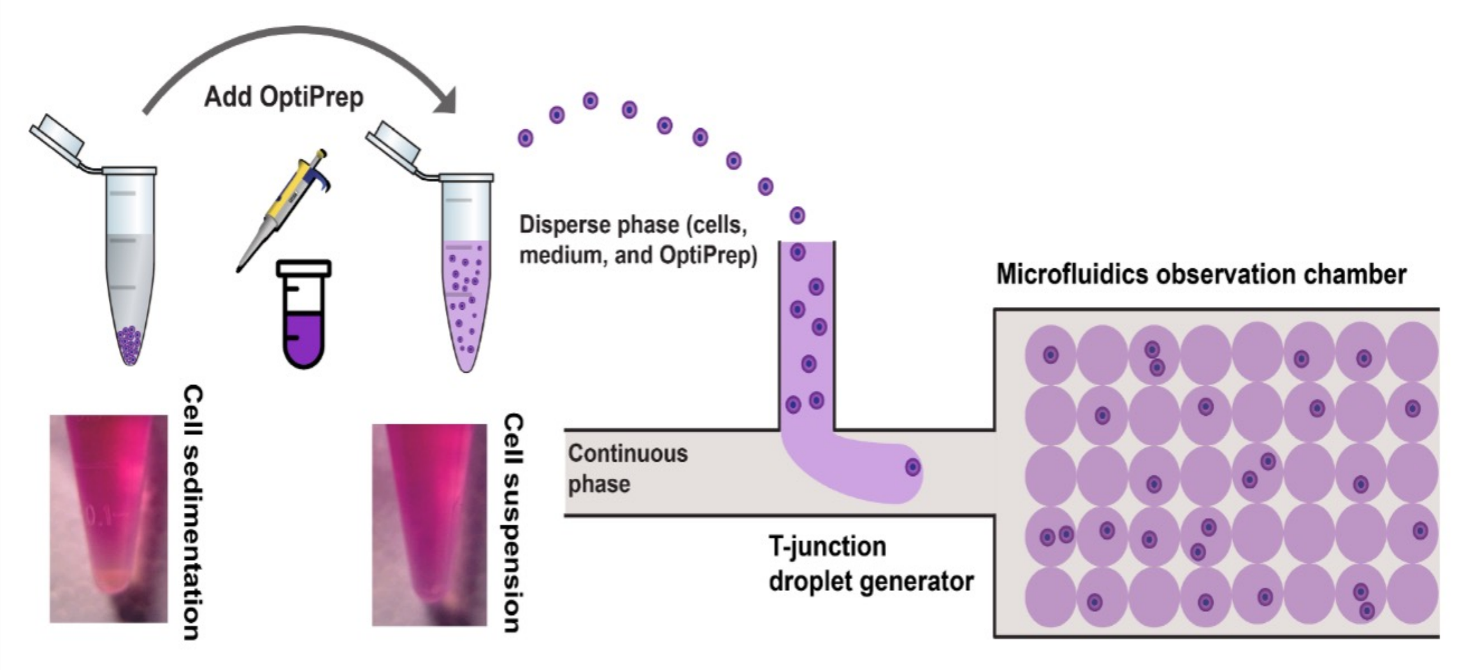

Figure 5. Image by Liu *et al.* in *Improving Single Cell Efficiency and Reliability through Neutral Buoyancy of Suspension* shows single-cell encapsulation process with human monocytic OptiPrep™ to create a neutral buoyancy of suspension.

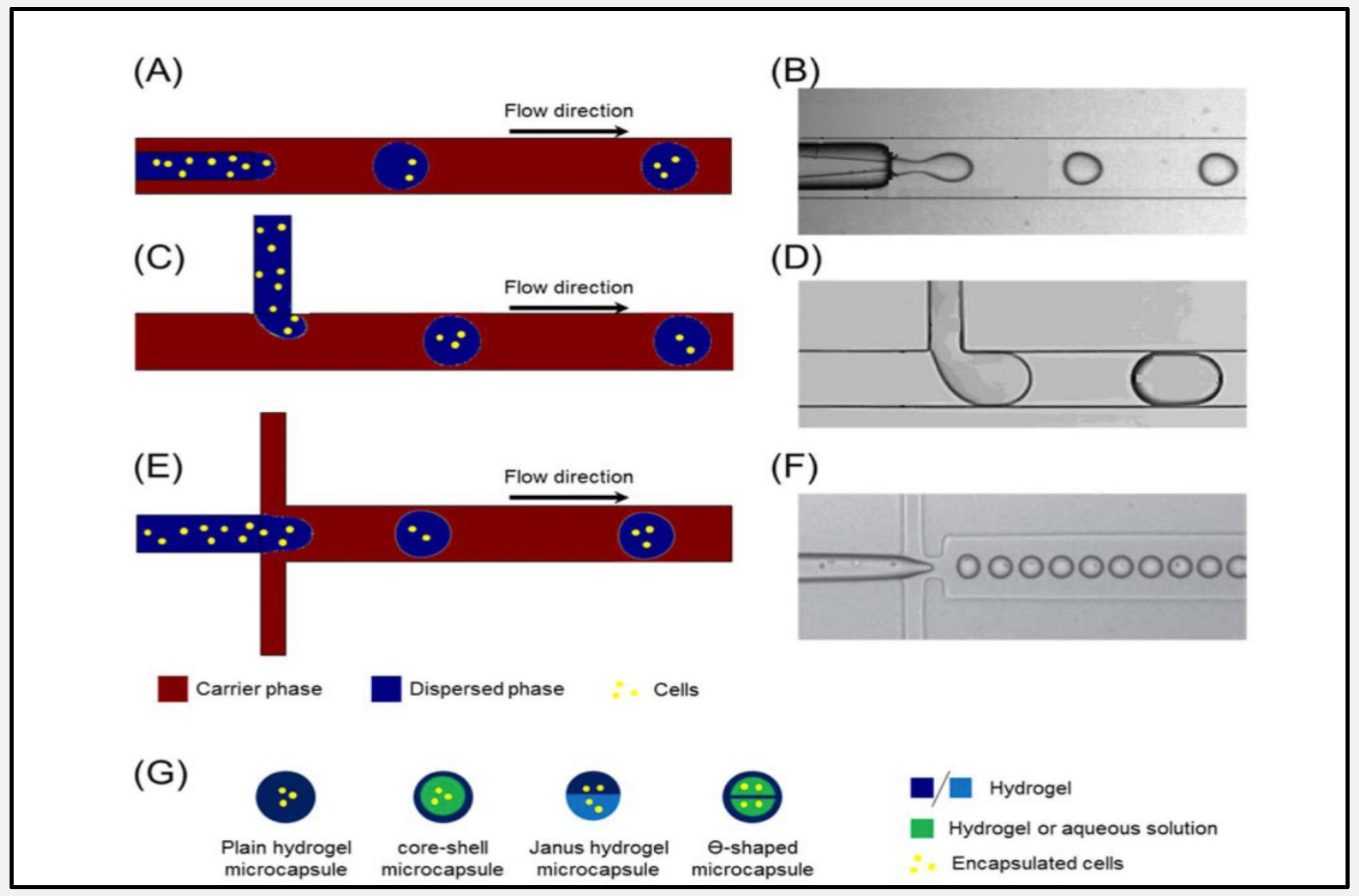

Figure 6. Image by Huang *et al.* in *Generation and Manipulation of Hydrogel Microcapsules by Droplet-Based Microfluidics by Droplet-Based Microfluidics on Mammalian Cell Culture* shows the three different basic microfluidic devices that are used for cell encapsulation with a variation in the schematics of the generation system.

References

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