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A 3D printed microfluidic device for droplet-based cell encapsulation and study

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Summary:
This paper presents a 3D printed microfluidic chip for the encapsulation of biological cells in micro-droplets. The chip is capable of generating and trapping nanolitre-sized droplets of water-based cell culturing medium in the surrounding oil phase. Each droplet serves as an individual microincubator for cell culture study. The chip was fabricated using DLP 3D printing technology with a biocompatible GR-10 resin. The chip has successfully enabled the generation of droplets, the encapsulation of yeast cells and the real-time observation of their proliferation.

Keywords: microfluidics, cell encapsulation, droplet microfluidics, 3D printing, DLP, cell culture

Introduction

Miniaturization is a significant trend not only in technology but also in life science, where the development of miniature cell research devices is gaining prominence. Traditional cell culture on a static surface is laborious, time-consuming and often fails to replicate the dynamic *in vivo* conditions [1]. To address such limitations, microfluidic devices offer accurate control of proliferation environment, enable single-cell research and provide integration of various laboratory processes on a miniature lab-on-a-chip (LOC). Recently, many LOCs have been created using additive manufacturing with biocompatible resins. These 3D printed devices are a promising approach for life science applications, providing many benefits, such as rapid prototyping and cost-effectiveness [2]. The droplet-based cell culture method also offers many advantages, such as undisturbed and uniform culturing conditions, accurate flow control, easy parametrization of the experiment, and minimization of human error [3]. In this work, we present a fully 3D printed microfluidic device which enables the generation and trapping of droplets for cell encapsulation and culture.

Materials and Methods

The device was fabricated using the additive technology of Digital Light Processing (DLP) using Asiga MAX 3D printer. A biocompatible Printodent GR-10 resin (Pro3dure) was used due to its biocompatibility, high transparency, and mechanical stability. The microfluidic chip contains a flow-focusing droplet generator and a long main meandering channel with multiple droplet traps and perpendicularly connected bypass channels (Fig. 1). The operation principle is based on encapsulation of yeast cells in the generated water-in-oil droplets, which here play a role of miniature incubators for easy observation of the proliferation process.

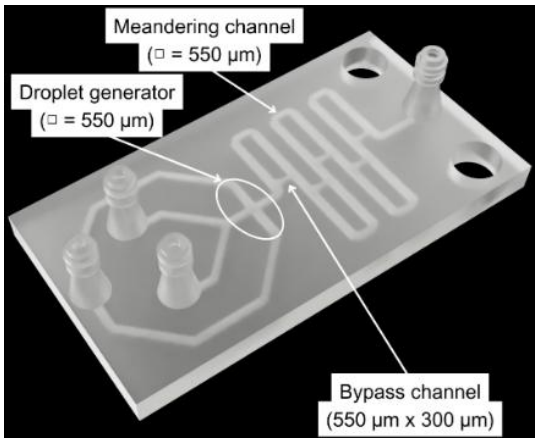

Fig. 1. 3D model of a microfluidic chip for cell encapsulation in water-based droplets

Cell encapsulation experiments were carried out with commercially available baker's yeast (*Saccharomyces cerevisiae*), as the model organism. Cells were suspended in yeast extract peptone dextrose broth medium (YPD) at a 1% w/v ratio and then incubated at 37°C for 10 minutes. The pressure-driven method was applied to control the flow of the yeast cell solution in the microfluidic device. The droplets were distributed in the meandering channel with controlled pressure of water (p_w = 9 mbar) and oil (p_o = 13 mbar). Next,

the pressure ratio p_w/p_o was adjusted to 0.42 to redirect the flow through the bypass channels and effectively immobilize the droplets in the traps (Fig. 2).

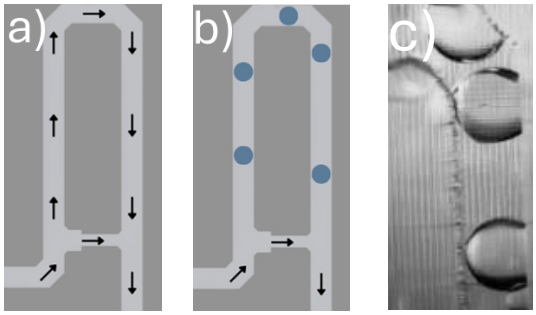

Fig. 2. Droplet flow control in the microfluidic device: a) droplets flowing alternately through the meandering and bypass channels, b) droplets trapped in the meandering channel while the flow is driven through the bypass channels, c) photo of trapped droplets with encapsulated yeast cells

Results

Experiments of encapsulating yeast cells in microdroplets with YPD medium showed successful cell proliferation within the controlled environment. Over a 2-hour observation period, cell proliferation was proven through visible budding over time, an increased number of cells, and noticeable gas production by yeasts, with bubbles forming within the droplets (Fig. 3). The number of yeast cells in the observation area increased by 75% (start: 797 cells, 2h: 1396 cells; Fig. 4).

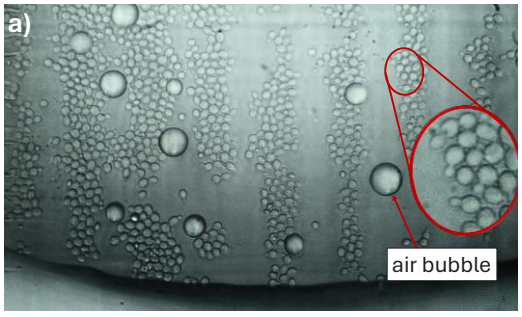

Fig. 3. Proliferation of yeast cells in droplet; red oval – yeast cells budding

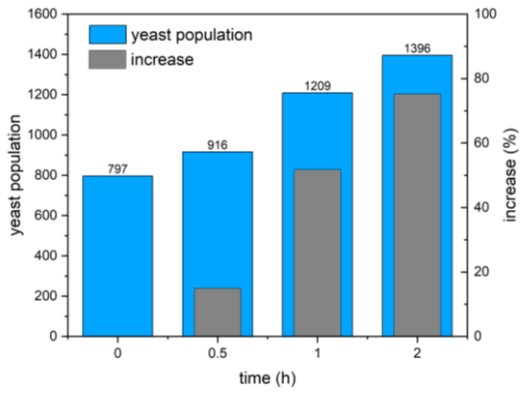

Fig. 4. Growth of the yeast population in droplets

Statistical analysis of droplet volume repeatability was also performed. For a group of 25 droplets, the measured volumes ranged from 71.5 to 129.1 nL, with a mean value of 92.3 nL (Fig. 5).

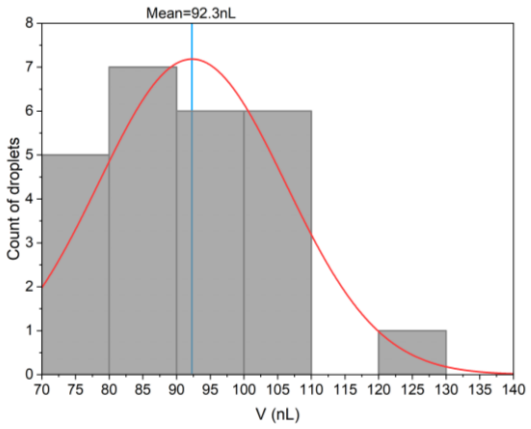

Fig. 5. Statistical analysis of droplet volume

Summary

The development of a 3D printed microfluidic device for droplet-based yeast cell encapsulation has demonstrated significant potential in cell culture research. The chip, fabricated using 3D printing technology with biocompatible resin, enabled generation and trapping of water-in-oil droplets that served as individual microincubators. The experiments confirmed the encapsulation of yeast cells in such droplets, with visible proliferation confirmed by budding, noticeable gas production, and increased cell number. The study demonstrated the potential of the combined 3D printing technology and droplet generation technique to enable controllable cell culture research in the microfluidic device.

References

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