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Method Article

A hand-held, power-free microfluidic device for monodisperse droplet generation

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A B S T R A C T

Here we develop a microfluidic device to generate monodispersion sub-nanoliter size droplets. Our system reaches steady state within 3 s after the flow starts and generates 100,000 droplets in 28 s with high size consistency (CV < 8%). This low cost device is composed with a microfluidic chip, 2 tubings, a collection vial, a syringe and a station; and is in the size of an iPad Mini (4" × 6" × 3/4"). In this system, all incoming reagents share the same pressure drop across the fluidic passage to generator droplets. A single source negative pressure is applied to the fluids to create the flow by a vacuum at the exit end of the device. The vacuum is generated on-site by pulling the plunger of a syringe. The position of the plunger before and after pulling determines the degree of vacuum. A fixture is used to hold the plunger after it is pulled to maintain its vacuum. Although this system loses vacuum gradually as the liquid filling in, it maintains a flow rates with the changes less than 10% and droplet sizes changes less than 2% during the course of generating 150,000 droplets. The pressure drop across the chip, the flow rates of all reagents, the droplet size and generation frequency are predictable, programmable, and reproducible. This device is designed for generating droplets for single cell genome profiling application but can be also used for digital PCR or other droplet-based applications.

A R T I C L E I N F O

Keywords: Droplet generation, Emulsion, Monodisperse, Single cell sequencing, Digital PCR, Portable device
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Specifications Table

Subject area	*Engineering*
More specific subject area	*Microfluidic Device*
Method name	*Monodisperse droplet generation using a passive setup*
Name and reference of original method	1. *Droplet generation using 3 individual pumps, Highly Parallel Genome-wide Expression Profilingof Individual Cells Using Nanoliter Droplets, Macosko EZ, et. al., Cell. 2015 May 21;161 (5):1202-1214.* 2. *Droplet generation using 1 pump, W Stephenson, et. al., NATURE COMMUNICATIONS (2018) 9:791.*
Resource availability	*ImageJ, an open source image processing software.* https://imagej.nih.gov/ij/

Background

Droplet-based technologies catch a lot of interests during the past decades for its capability of screening very large numbers of samples simultaneously (usually tens of thousands). By dividing the sample and reaction reagents into separate small volume reactors, each sample is expressed individually. Such kind of platform can be used to quantify and qualify cellular genomic information at individual cell level (such as digital PCR, single cells genome profiling).

In a droplet-based system, two or more reagents are loaded in the reservoirs at the inlet of this device. The reservoirs are connected via microfluidic channels which intercept at least once at junction(s). An exit channel connects the junction and the exit port and allows fluid to exit the device. As the fluids traveling though the channels and intercept at the junction, continuous phase reagent pinches the discret phase reagent either by focusing flow (a cross-junction setting) or concurrent flow (a T-junction setting). The balance between the inertia of discret phase solution, surface tension between discret and continuous phase and viscosity enable continuous phase reagent to encapsulate the discret phase reagent and form droplets of discret phase solution. The dimension of the droplets are determined by the flow rates of all reagents (Q), surface tension (σ) between these two immiscible phases, viscosity (μ) of the continuous phase, density (ρ) of the continuous phase, the channel height (h), channel hydraulic diameter (d) at the junction and the channel width (w) at the exit of the junction are the junction. The correlation is expressed as below in Eqs. (1a) and (1b) [1]

$$R_{droplet} = \frac{3.7\mu_o w_{down} h}{4\rho_o Q_o} e^{\frac{-4}{3w_{down}}\left[\frac{6\mu_o Q_o \pi^2 d_j^2}{\pi^2 d_j^3 \sigma - 4\rho_w Q_w^2} + \beta h\right]}, \quad R_{droplet} > h/2 \tag{1a}$$

$$R_{droplet} = \frac{w_{down} h(\pi^2 d_j^3 \sigma - 4\rho_w Q_w^2)}{6\mu_o Q_o \pi^2 d_j^2 + 2\beta h(\pi^2 d_j^3 \sigma - 4\rho_w Q_w^2)}, \quad R_{droplet} < h/2 \tag{1b}$$

In this research, we adopted the parameters of generating nanoliter size droplets by keeping the flow rate of 3 liquids at 5, 5 and 10 mL/h (water/water/oil) [2]. However, instead of using three individual syringe pumps to drive the liquid, we develop a microfluidic device, of which all three incoming reagents share the same pressure drop (ΔP) through the fluidic passage. The channel length, width and height and liquid viscosity determine the resistance (R) of each channel, as showed in the equations below in Eq. (2). The channel height of this device is 120 μm. The system therefore generate flows at the flow rate ratio at 1:1:2. The design of the chip is showed in Fig. 1a. The AutoCAD file is available upon request.

$$Q = \Delta\Pi / R; \quad \Delta\Pi = P_{atm} - P_{syringe}; \quad R_{rec} = \frac{12}{(w/h) - 0.63}\frac{\eta L}{h^4} \text{for } w > h \tag{2}$$