RAPID λ BACTERIOPHAGE DETECTION VIA CO-CULTURE OF HOST CELL ESCHERICHIA COLI BY DROPLET OPTOFLUIDIC SYSTEM

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ABSTRACT
This paper focuses on the design and fabrication of a droplet-based optofluidic system to detect bacteriophages via measuring the growth of the host cell infected by the bacteriophages in a microdroplet carrier. The growth of the host cell *Escherichia coli* (*E. coli*) is detected by the scattering pattern of the microdroplet carrier and the pattern is analyzed using the mean power frequency. The growth curve of *E. coli* co-cultured with λ bacteriophage is portrayed using the detection method.

KEYWORDS: Optofluidic, Scattering, Bacteriophage

INTRODUCTION
To reduce human health risks from viral infection, drinking water sources have to be constantly monitored to avoid viral contamination [1]. Bacteriophages are viruses that infect bacterial cells. They have long been considered as attractive indicators for determining drinking water quality since the concentration of bacteriophages is significantly correlated with virus concentrations in water samples [2-4]. Current bacteriophage detection are adapted from the clinical applications such as plague assay method by using host cells combined with molecular biology based assay polymerase chain reaction (PCR) methods, which include long processing time for culture assay and complicated pre-concentration step before target detection can be achieved [5-7]. These techniques required complex fabrication process and the detection device can detect only target bacteriophage. It is difficult to realize rapid, sensitive and low-cost detection techniques for various types of bacteriophages of low concentration in water samples.

PRINCIPLE
The principle of the droplet-based optofluidic system for bacteriophage is shown in Fig. 1. The bacteriophage sample is first mixed with host cell *E. coli* culture medium and then divided into large number of droplets. After an incubation period, the host cell growth in the bacteriophage containing microdroplet will be obvious different with the microdroplet with only host cell. The final concentration of the host cell will affects the scattering patter of the microdroplet carrier, which can be used to detect the existence of the bacteriophage.

**Figure 1:** Principle of optofluidic system for bacteriophage detection.

**Figure 2:** Schematic of optofluidic chip design.
EXPERIMENTAL RESULTS

The design of the optofluidic chip is shown in Fig. 2. The sample is mixed with high concentration of host cells in the microfluidic channel then divided into microdroplets. As the droplet flowing downstream, the content in the is mixed. The microdroplets are incubated in a microchamber and after the incubation period, the valve towards optical detection area is open and the incubated droplets go through the light scattering area successively.

The optical density at wavelength of 600 nm (O.D. 600), which is the general measurement method of cultured bacteria concentration, of E. coli cultured individually or co-cultured with λ phage in culture flask is shown in Fig. 3 [5]. The E. coli cultured individually grows as a typical bacterial growth curve. When co-cultured with λ bacteriophage, the infection process last for approximately 2 hours. After the second hour, the population of the E. coli cell decrease obviously since most of the bacteria is infected by the phage after several lytic cycle and finally broke up during the phage release period.

Figure 4 (a-b) shows the scattering pattern of microdroplets containing different concentration of E. coli. Compare the two groups of graphs, it can be seen that at the higher concentration, the scattering pattern of the whole microdroplet has higher level of disorder. The intensity distribution of the same order of the droplet diffraction pattern split into more individual peaks. The mean power frequency value of the single microdroplet scattering pattern increases with the incensement of the concentration of E. coli in the microdroplet as shown in Fig. 4(c).

Figure 3: The transmitted optical density of E-coli culture individually or co-culture with λ phage.

Figure 4: Scattering pattern analysis with mean power frequency of microdroplets containing different concentration of E. coli (a) the scattering pattern of E. coli of 10^9 cell/ml (100 cell/droplet) (b) of E. coli of 10^7 cell/ml (0-1 cell/droplet) and (c) the mean power frequency changed by the E. coli concentration in the microdroplet.
The concentration varies of *E. coli* cultured individually or co-cultured with *λ* in the droplet measured based on the mean power frequency of the scattering pattern is shown in Fig. 5. The initial infection period is shorter than the traditional method in flask. It is mainly because in the droplet picoliter microenvironment, the contact probability between *λ* bacteriophage and its host cell of *E. coli* is higher than in a large open environment.

**CONCLUSIONS**

In this paper, the *λ* bacteriophage is detected, which is co-cultured with the host cell *E. coli* using a droplet-based optofluidic system. The system is in advantages of a real-time, label-free and high sensitivity quantification of bacteriophage through measurement of host cell growth with high accuracy and stability.

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**REFERENCES:**


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