# SOLUTION CONCENTRATION CHANGE OF PICOLITER-SIZED MICRODROPLET REACTORS

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## ABSTRACT

We achieved solution concentration change of a picoliter-sized water-in-oil (w/o) microdroplet reactor based on electrofusion and hydrodynamic breakup of microdroplets in a microfluidic channel (Fig. 1). A carrier droplet changes the solution concentration of a reactor droplet by electrofusion of them, and then they are divided without changing their reaction volume before and after the fusion-fission event. We found that this system realized high-speed concentration change of the reactor droplet (< 1 s even for complete exchange of solution). We believe that this system will be useful for analysis of dynamic chemical reactions (e.g., dynamic structural change of motor proteins, enzymatic reactions, etc.).

**KEYWORDS:** Microdroplets, Microreactors, Microfluidics

## INTRODUCTION

In recent years, microreactors based on w/o microdroplets have attracted attention as powerful tools that achieve miniaturization of chemical experiments, high-throughput and quantitative chemical experiments, etc. [1-3]. However, a w/o microdroplet reactor is a chemically closed system; thus, it is unfavorable for chemical reactions requiring solution exchange. Therefore, the realization of a chemically-open system in a w/o microdroplet reactor is highly required. To date, microfluidic devices based on electrowetting-on-dielectric (EWOD) have achieved a chemically-open system by fusion, fission, and transport of microdroplets, but this device has limitations in downsizing of microdroplet volume (> several dozen nanoliters). Here, we propose a microfluidic system that achieves changing the solution concentration of a picoliter-sized w/o microdroplet in a microfluidic channel based on electrofusion and hydrodynamic breakup of microdroplets. It enables a chemically-open system in a picoliter-sized w/o microdroplet reactor.

## EXPERIMENTAL METHODS

This microfluidic system is composed of a reactor droplet fixed in a microchamber, and a carrier droplet delivering chemicals in different concentrations (Fig. 2). These microdroplets electrically fuse and then the solution concentration of the reactor droplet is changed. After that, the carrier droplet is divided from the reactor droplet. The volume of each droplet before and after the fusion-fission event is kept constant.

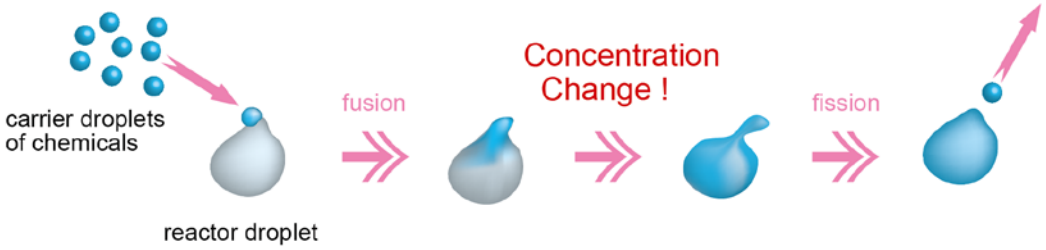


*Figure 1: Concept of solution concentration change of a w/o microdroplet*

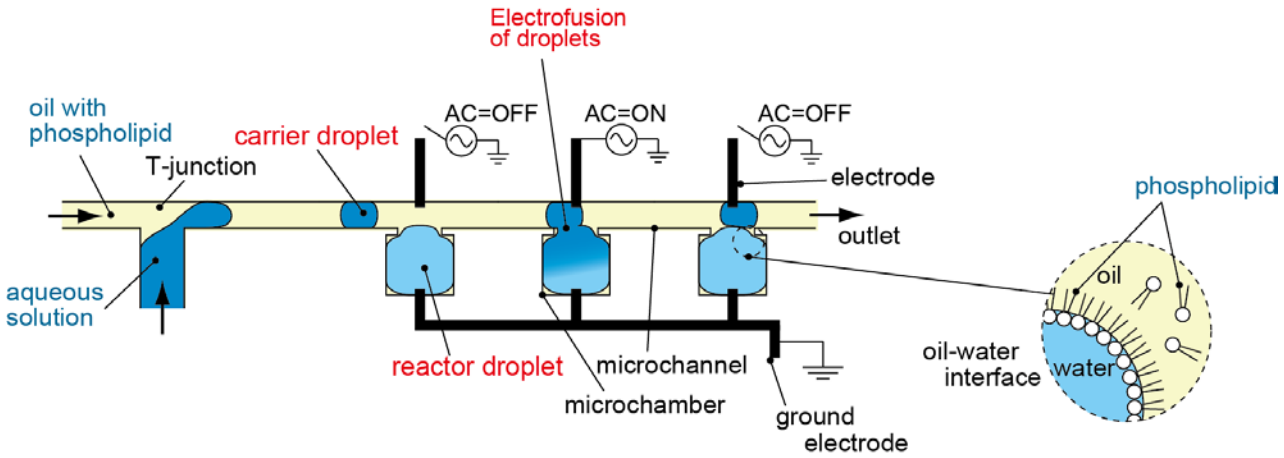


*Figure 2: Schematic illustration of solution concentration change of based on fusion and fission of w/o microdroplets.*

The microfluidic system is schematically illustrated in Fig. 2. Reactor droplets and carrier droplets are picoliter-sized w/o microdroplets surrounded with a biological surfactant, lecithin (phospholipid). A reactor droplet is trapped in a square microchamber located on one side of the microchannel; carrier droplets are produced monodispersely and periodically at the T-junction, and they carry aqueous solution containing different chemicals to the reactor droplet through the microchannel. A carrier droplet is not fused with the reactor droplet without applying voltage, even if they come in mutual contact (Fig. 3a). In contrast, they are fused when an alternating-current (AC) voltage is applied to the reactor droplet (Fig. 3b). The fusion is caused by the electric-field-induced destabilization of the interface between them. At the moment of the fusion, the solution concentration of the reactor droplet is changed by the diffusion of chemicals from the carrier droplet. Immediately after the fusion, the carrier droplet is ejected from the fused droplet and released from the reactor droplet. This fission event results from the competition between the surface tension of the fused droplet and the fluid resistance of the oil flow around the fused droplet, just like the mechanism of a microfluidic T-junction. Figure 4 presents the design of the microfluidic system and its microscope image. Three microchambers that can be independently controlled by applying voltage were built in the system. The microchannel and microchambers were made of poly(dimethylsiloxane) (PDMS) on a glass slide where indium tin oxide (ITO) electrodes were patterned to apply voltage. The inside walls of the microchannel and microchambers were coated with the perfluoropolymer, CYTOP™ (Asahi Glass).

## RESULTS AND DISCUSSION

Figures 5a and 5b demonstrate that the microdroplets fused only when AC voltage was applied. The fusion probability depended on the concentration of a surfactant (phospholipid) and the strength of applied voltage: the proper condition for this system was that phospholipid concentration is 0.5% and applied voltage is 30 V (Fig. 5c). Under the condition, we investigated the process of concentration change of the reactor droplet by fluorescence imaging (Fig. 6). We found that the concentration was changed within 0.7 s by continuous multiple fusion-fission events (Figs. 6a and 6b) and the mixing time for a single fusion-fission event was only about 0.2 s (Fig. 6c and 6d). And also, we succeeded in the stepwise changing of concentration.

The microfluidic system we developed has achieved high-speed solution concentration change of a picoliter-sized w/o microdroplet reactor in a microfluidic channel. We believe that the system will expand the ability and usage of existing picoliter-sized microdroplet-based microfluidic systems, and achieve several experiments for more complex and dynami cal chemical reaction systems.

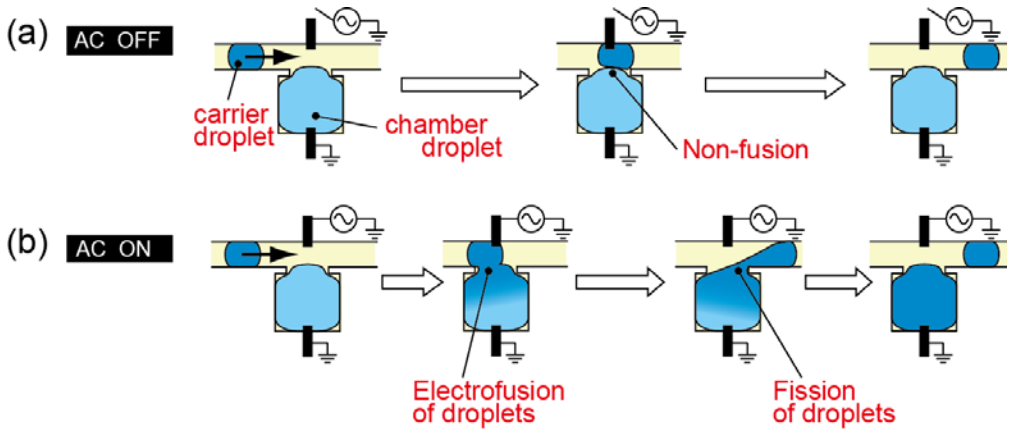


*Figure 3: Mechanism of electrofusion and hydrodynamic fission*

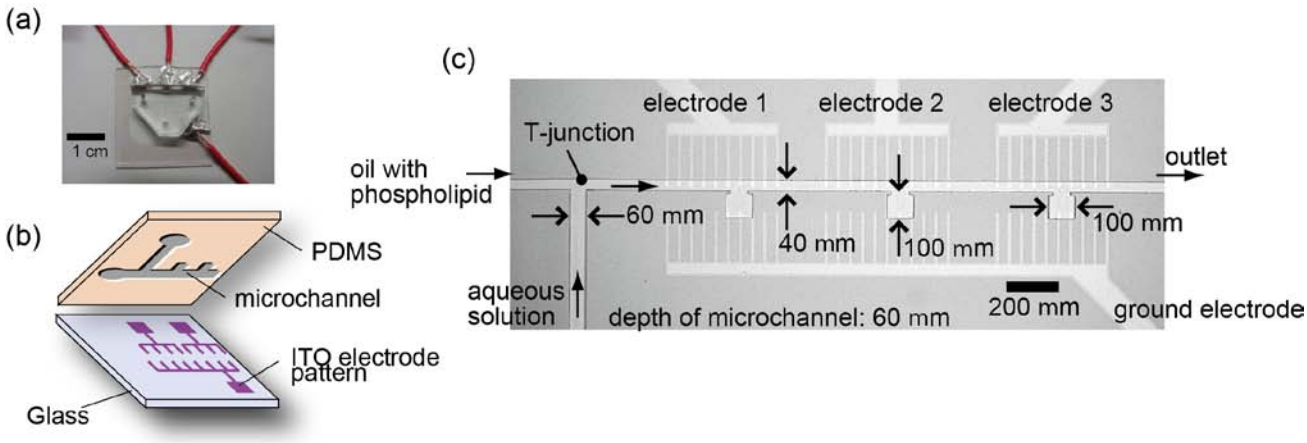


*Figure 4: Microfluidic device for solution concentration change of w/o microdroplets*

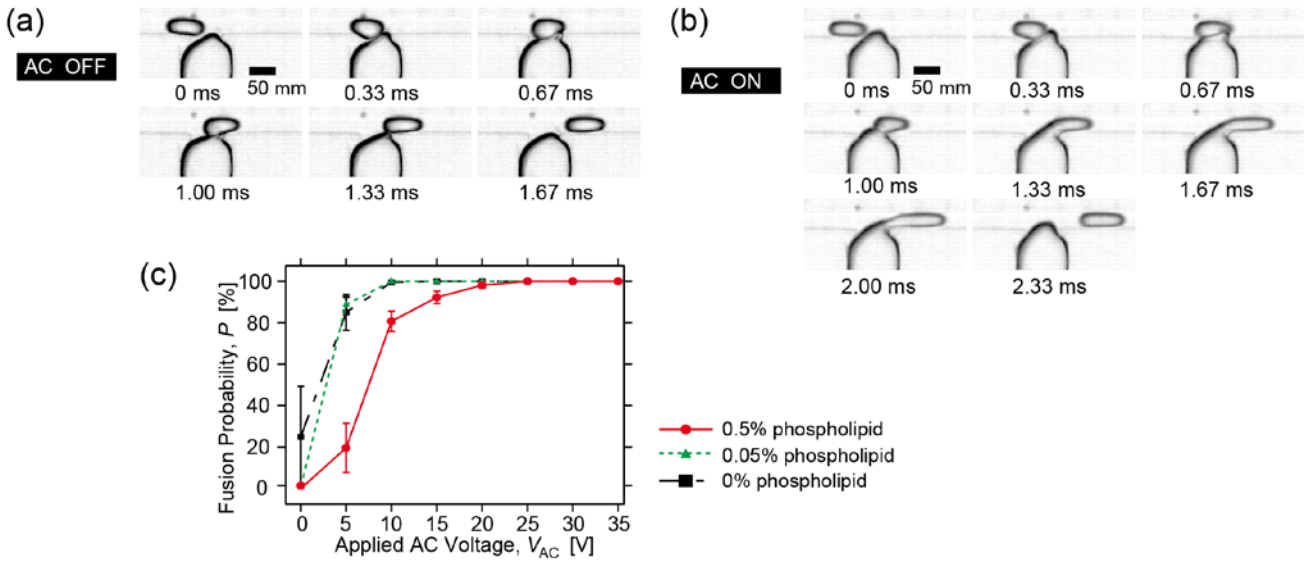


*Figure 5: High-speed images of electrofusion and hydrodynamic fission in the microfluidic device.*

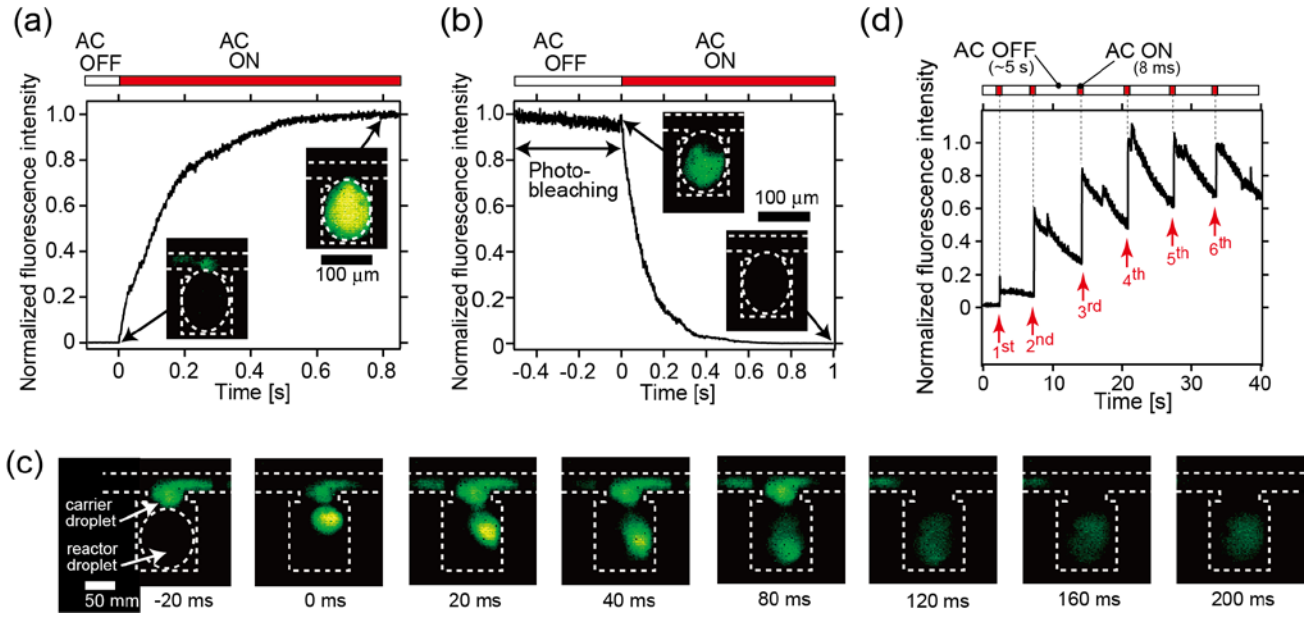


*Figure 6: Fluorescence images of solution concentration change by the fusion-fission device.*

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**REFERENCES**

[1] "Droplet microfluidics", S.-Y. Teh, R. Lin, L.-H. Hung, A. P Lee, Lab Chip 8, 198 (2008).

[2] "Reactions in droplets in microfluidic channels", H. Song, D. L. Chen, R. F. Ismagilov, Angew. Chem. Int. Ed. 45, 7336 (2006)

[3] "Droplets as microreactors for high-throughput biology", V. Taly, B. T. Kelly, A. D. Griffiths, ChemBioChem 8, 263 (2007).

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