DOUBLE DROPLET AS A SENSOR FOR MOLECULAR TRANSPORT THROUGH ORGANIC LIQUID MEMBRANE

Mao Fukuyama[1] and Akihide Hibara[1]

[1] *Institute of Industrial Science, The University of Tokyo, Japan*

ABSTRACT

This paper reports a novel method for molecular transport thorough an organic liquid membrane by using water-in-oil-in-water (W/O/W) double droplets. The double droplet encapsulating small inner droplets with detection reagents is dipped in analyte solution. The inner droplets change their fluorescence subject to outer analyte composition. The membrane transports of several substances can be investigated simultaneously. Here, in order to demonstrate feasibility of the novel method, we prepared double droplets encapsulating two kinds of inner droplets containing Cl^- selective reagent (MQAE) and an internal standard substance (Fluorescein) and observed their responses $CaCl_2$ solution.

KEYWORDS

Double droplet, liquid membrane

INTRODUCTION

Organic-liquid-membrane permeability of drugs is sometime used for evaluation of transdermal absorption. For instance, 1-octanol/water system is often used as a model for biological membranes because of the solubility parameter of 1-octanol is close to that of the biological membranes, such as humane skin [1]. By utilizing a microfluidic channel, molecular transport in a water-oil-water three-phase laminar flow was reported [2]. In that system, one aqueous phase (donor phase) contained analyte before contact, and its transportation to another aqueous phase (acceptor phase) through the organic phase was observed. Because of the short diffusion distance of the system, the investigation time was dramatically shortened. In this paper, a novel method for molecular transport thorough an organic liquid membrane by using water-in-oil-in-water (W/O/W) double droplets is reported.

CONCEPT

Here, we propose a new method for investigating the membrane transport by using a W/O/W microdroplet (Figure 1). In the concept, the outer aqueous phase (W_o) and small inner aqueous droplets (W_i) work as the donor and acceptor phases, respectively. The molecular transport from W_o to W_i is investigated. The double droplets encapsulate several inner droplets with different functions. By applying multivariate analysis to fluorescence changes, simultaneous multi-component membrane transports can be investigated. In order to demonstrate the concept, we prepared double droplets encapsulating two kinds of W_i droplets containing a detection reagent and an internal standard substance, respectively, and observed the performance.

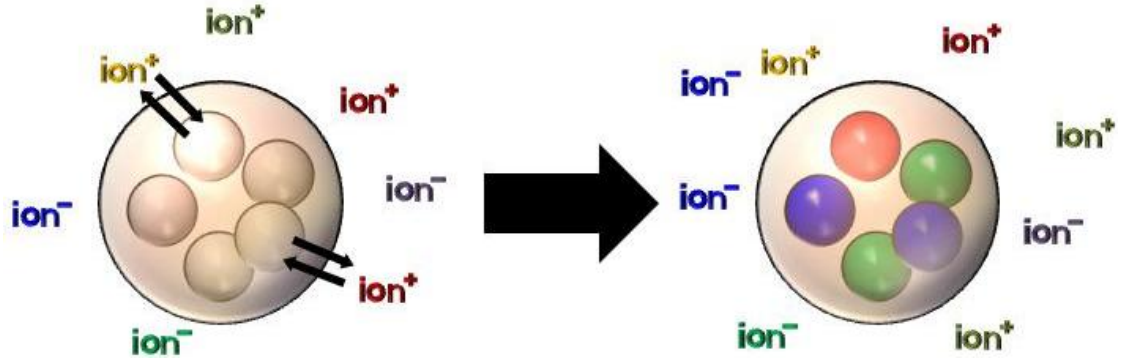

Figure 1. Concept of a new investigation method for molecular transport through an organic liquid membrane by using W/O/W double droplets. The double droplet encapsulating small inner droplets with several detection reagents is dipped in analyte solution, and, then, fluorescent intensities change. The transport of several substances can be investigated simultaneously.

EXPERIMENT

Figure 2 shows the preparation method for the double droplets. Briefly, the W_i/O droplets were prepared in a glass microchip, and the W_i/O/W_o droplets were formed at the exit of the capillary tube dipped in W_o phase.

The glass microdevice was fabricated by a two-step photolighographic wet etching method. In this device, the W_i/O droplets are formed at the T-junction between the deep main and shallow branch channels. The main channel has a 220 μm width and a 42 μm depth, and the branch channel has a 70 μm width and a 2 μm depth. By using the two T-junctions, two kinds of W_i/O droplets are formed; the droplets from the lower side contain 1 mM MQAE, a fluorescent dye quenched by Cl^-, and the droplets from the upper side contain 1 mM Fluorescein as an internal standard substance. Bromoethane containing 1% w/w Span 80 was used as an organic continuous phase.

A PEEK capillary tube having a glass capillary tip was used to form O/W_o droplet. The hydrophilic glass

978-0-9798064-5-2/μTAS 2012/$20©12CBMS-0001

capillary was attached to the tip of the PEEK tube by epoxy resin in order to prevent the organic phase from wetting the tip of the tube. For W_o phase, 0.2 mM sodium dodecylsulfate (SDS) aqueous solution was used.

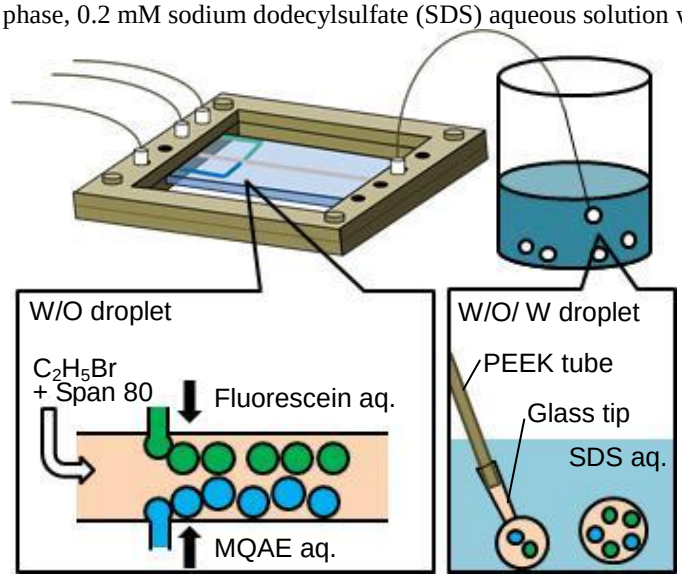

Figure 2. Setup for preparation of W/O/W double droplets. Two kind of W/O droplet, which contained MQAE (Cl- ion selective dye) and Fluorescein (an internal standard substance), respectively, were prepared by two T-junction in a glass microchip. W/O/W droplets formed at the exit of the capillary tube.

RESULTS AND DISCUSSIONS

By flowing W_i and the organic phase at the rate of 0.5 μL/min and 4 μL/min, respectively, 600-μm-sized O/W_o droplets encapsulating 80-μm-sized W_i droplets were prepared (Figure 3).

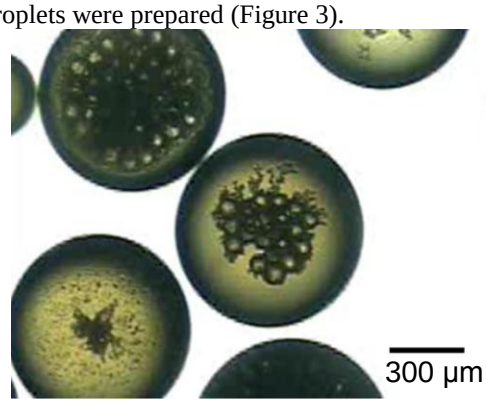

Figure 3. Micrograph of W/O/W double droplets.

Figure 4 shows fluorescent micrographs of the $W_i/O/W_o$ droplets. In case of 0.1M $CaCl_2$, the blue fluorescence of MQAE gradually weakened by Cl^- transport (Figure 4a). Eventually, the color of the droplet became green originated from Fluorescein. Contrastively, both the blue and green fluorescence kept their intensities without Cl^- ion (Figure 4b). The tendency is clearly seen in the time course of the ratio of MQAE blue fluorescence to the total fluorescence (Figure 5).

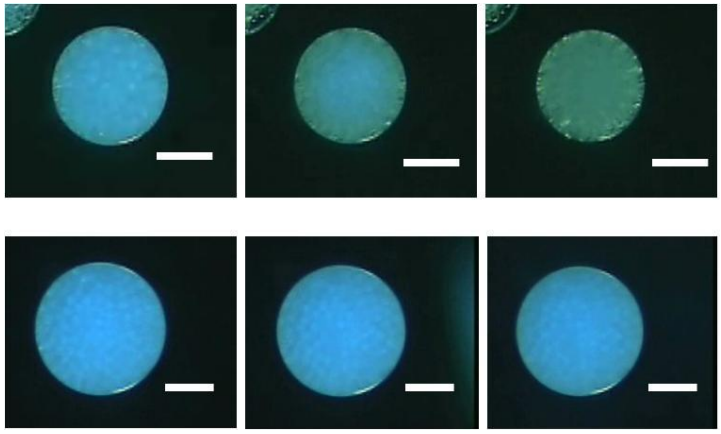

Figure 4. Fluorescence micrographs of prepared W/O/W droplet. (a) The outer aqueous phase contained 0.1M $CaCl_2$. (b) The outer aqueous phase without Cl^- ion.

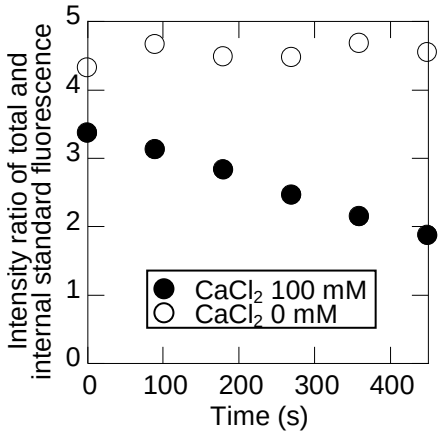

Figure 5. Time variation of the total fluorescent intensity of MQAE and Fluorescein.

CONCLUSION

We have successfully demonstrated feasibility of the new method for molecular transport measurement through the organic liquid membrane by using the double droplets. By applying multivariate analysis to the fluorescent changes, simultaneous multi-component membrane transports can be investigated. We expect that this method will be a powerful tool for rapid evaluation of drugs' characteristics.

AQKNOWLWDGEMENT

This work was partially supported by KAKENHI (Grant 24350038), and by the Food Nanotechnology Project of the Ministry of Agriculture, Forestry and Fisheries of Japan. MF acknowledges the Global COE Program, Chemistry Innovation through Cooperation of Science and Engineering, MEXT, Japan.s

REFERENCES

[1] C. Hansch and W. J. Dunn, *J. Pharm. Sci.* 61, pp. 1-18 (1972).
[2] M. Surmeian, M. N. Slyadnev, H. Hisamoto, A. Hibara, K. Uchiyama and T. Kitamori. *Anal. Chem*. 74, pp. 2014-2020 (2002).

CONTACT

Akihide Hibara TEL +81-3-5452-6341, hibara@iis.u-tokyo.ac.jp