# ENCAPSULATION OF BIOMOLECULES WITH PROGRAMMABLE CONCENTRATIONS IN MICRODROPLETS USING ELECTROKINETIC CONCENTRATOR

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## ABSTRACT

In this work, we describe a microfluidic device for the encapsulation of electrokinetically concentrated biomolecules in microdroplets and microparticles. We demonstrate the encapsulation of molecules and nanoparticles such as quantum dots into water-in-oil droplets and porous gel particles with on-the-fly adjustable concentrations by combining electrokinetic trapping and two-phase droplet generation in a single chip. Once in the droplets, the molecules and nanoparticles can then undergo chemical reactions or be delivered anywhere on the chip while maintaining programmed concentrations without dispersion loss over long time and distance scales.

**KEYWORDS:** Electrokinetic Concentration, Droplet, World-To-Chip Interface

## INTRODUCTION

Micro- and nanofluidic devices have inherently very low volumes (< 1nL). This can cause significant errors due to sampling noise and bias when handling very low concentration samples. We have earlier developed efficient electrokinetic concentrators [1,2] for charged species, which can act as world-to-chip interface by straining the species of interest from large initial volumes to very low volume plugs within a microchannel. However, diffusion and dispersion of the concentrated plug constrain its downstream manipulation. Here, we demonstrate the encapsulation of these plugs of species into water-in-oil droplets and porous gel plugs which can be used to maintain the programmed concentration while the molecules undergo reactions or are transported on the chip without dispersion loss over long time and distance scales. This is achieved by an integrated device, shown in Figure 1, which consists of an electrokinetic concentrator coupled to a two-phase flow channel via a T junction to encapsulate the sample plug inside a microdroplet after achieving the target molecule concentration. Using monomers and UV light exposure, even porous solid microparticles were made for easier handling while retaining the set concentration.

## EXPERIMENTAL

The device was realized in polydimethylsiloxane (PDMS), as shown in Figure 2. All the channels are 20μm high and 100μm wide. A high-aspect-ratio ion-selective membrane of Nafion™ (Sigma-Aldrich, St. Louis, MO ) was fabricated at the junc-



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tion between the buffer and sample channels by using a balance of capillary force and surface tension.

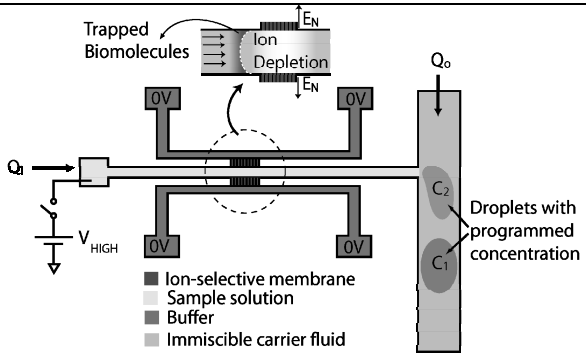


*Figure 1. Combined electrokinetic preconcentration and droplet generation in immiscible fluid via a T-junction. The middle channel is loaded with charged molecules or particles and the two side channels are filled with a common buffer solution. Applying a potential difference across the middle and the side channels, a concentrated sample plug is generated in front of the ion-selective membrane. The concentrated sample plug is then released into the immiscible fluid such as oil.*

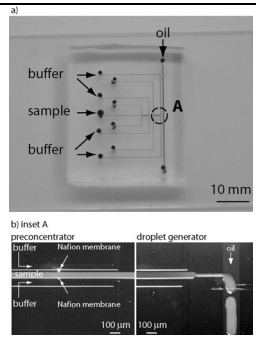


*Figure 2. a) Integrated PDMS concentration-encapsulation device. b) Nafion membranes at the junction. Two concentrators are connected in series to enhance the concentration efficiency.*

## RESULTS AND DISCUSSION

First, we concentrated 1µM FITC in 10mM phosphate buffer, by electrokinetic trapping at a flow rate of 100nL/min. After reaching the target concentration, we released the concentrated plug by turning off the voltage of electrokinetic trapping and sent it to an adjacent microchannel filled with an immiscible solution such as mineral oil. In this two-phase flow channel, the concentrated sample plug was encapsulated in a microdroplet, as shown in Figure 3. Using the concentrator, it was possible to vary the concentration of the sample within ~5 orders of magnitude. We demonstrated this capability with three concentration times, shown in Figure 4.

This encapsulation technique can be extended to any charged molecules such as DNA and proteins as well as nanoparticles, and even cells. Using the same approach, carboxylated quantum dots (Q-dot 525 ITK$^{TM}$, Invitrogen, CA) were successfully concentrated and encapsulated inside droplets. We also formed a porous gel microparticle by adding a UV-curable acrylamide mixture to the quantum dot solution and exposing the concentrated plug to UV light through a microscope objective. As shown in Figure 5, the quantum dots were encapsulated inside the gel particle whose porosity can be freely tuned with the composition of acrylamide solution.

## CONCLUSIONS

We have demonstrated an integrated microfluidic concentration-encapsulation device which can compartmentalize biomolecules and other charged species from

very low concentration solutions into droplets and particles with programmable concentrations to study reactions such as enzyme/binding assays or PCR amplification inside the droplets without dispersion loss. Furthermore, it offers an ideal way to store separated/preconcentrated samples in a micro container, to be analyzed later by other sensing techniques.

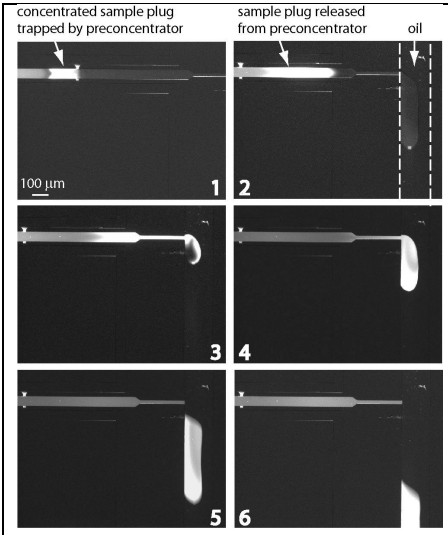


*Figure 3. 1. Electrokinetic trapping of the sample at $V_{high}$=500V. 2. Release of the plug after 5 min. preconcentration. 3. Plug is being injected into the immiscible oil with the pressure-driven flow via a T-junction. 4. Plug is completely encapsulated in the droplet. 5. Droplet break-off from the T junction. 6. Dispersion-free transport of the concentrated sample droplet.*

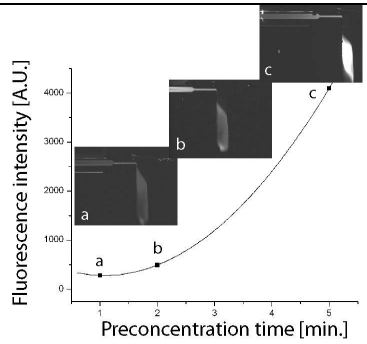


*Figure 4. Comparison of fluorescence intensity as a function of concentration time. This result demonstrates that we can vary sample concentrations on the fly for subsequent encapsulation*

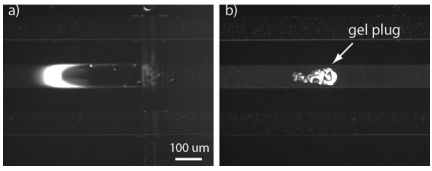


*Figure 5. a) Concentration of quantum dots in acrylamide solution, b) its encapsulation in polyacrylamide gel after UV polymerization*

**ACKNOWLEDGEMENTS**

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