

HIGH PRESSURE EWOD DIGITAL MICROFLUIDICS

W. C. Nelson¹, M. Yen¹, P. Y. Keng^{2,3}, R. M. van Dam^{2,3} and C.-J. Kim¹

¹Mechanical and Aerospace Engineering Department

²Department of Molecular and Medical Pharmacology; ³Crump Institute for Molecular Imaging
University of California, Los Angeles (UCLA), USA

ABSTRACT

We are developing new electrowetting-on-dielectric (EWOD) digital microfluidic systems for operating at non-atmospheric conditions. The first generation is a compact pressure chamber with an electric feed-through, enabling EWOD operation within a gaseous medium of well-controlled pressure and composition. EWOD performance is insensitive to chamber pressure because the chip is of open-channel architecture. We demonstrate two different types of previously unachievable processes – (i) controlling evaporation rates of common solvents (water, methanol, acetonitrile) by adjusting the pressure of an inert gaseous medium (N₂), and (ii) controlling the reaction rate of a solid-liquid-gas-phase reaction by adjusting the pressure of a gas-phase reagent (H₂).

KEYWORDS

Electrowetting-on-dielectric (EWOD), digital microfluidics, pressure chamber, evaporation, diffusion

INTRODUCTION

Since off-chip pumps and valves are not needed for their operation, EWOD-based digital microfluidic chips can be implemented in highly compact and portable systems. In this work, the fact that EWOD chips require only electrical connections has enabled the design of a very simple, yet effective high pressure system, which has only one electrical feed-through and one gas port.

In digital EWOD, droplets slide on or between planar substrates that have digitized surface electrodes [1]. Droplet routes are determined by the sequence in which electrodes are activated rather than physical channels. As long as the electrical driving force overcomes the drag imparted by the surface(s), EWOD chip operation is straightforward – it is the simplicity and re-configurability of this actuation mechanism that makes EWOD-based systems attractive for a wide range of applications from bio-analyses to optical displays.

Two important consequences of EWOD are: (i) droplets are exposed to a secondary fluid, e.g., an immiscible liquid or a gas, and (ii) droplet actuation is insensitive to the pressure of the surrounding medium, as long as it is stagnant. For example, in the parallel-plate configuration droplets are squeezed into a disk-like shape. In this case, the droplet thickness is determined by the distance between the plates, and the area (S) of the liquid-fluid interface is $S \sim \pi dh$, where d is the droplet diameter. The parallel-plate configuration is perhaps the most common because confining the droplet facilitates key functions such as creation and division. Additionally, the distance between the plates (h) becomes the characteristic

dimension, which can be adjusted in order to scale the fluid mechanics. In this work, we explore liquid-gas systems because the reported chamber enables evaporation control and the use of gas-phase reagents; other capabilities may be more relevant to liquid-liquid systems.

Under normal atmospheric conditions, evaporation can be problematic for EWOD because sub-microliter droplets of common solvents (e.g., water, methanol, acetonitrile) vaporize in minutes or less. This problem grows rapidly with rising operating temperatures.

Using the proposed high pressure EWOD system (Figure 1), we demonstrate how to significantly reduce droplet evaporation rates by increasing the pressure of an inert medium (N₂), thereby preserving droplets for longer processing times. Also, we demonstrate how droplet reaction rates in a gas-phase reagent can be controlled by adjusting its partial pressure. Specifically, it is shown that the rate of a platinum black-catalyzed hydrogenation of methyl orange varies directly with the partial pressure of hydrogen gas.

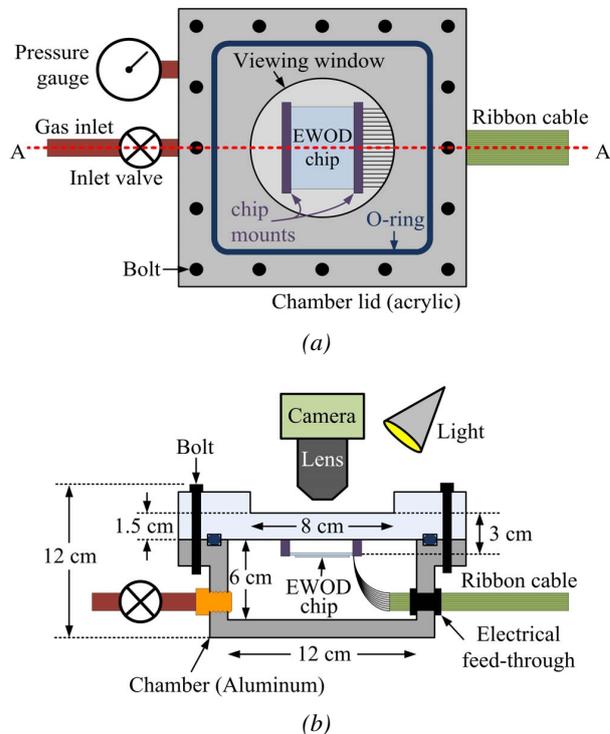


Figure 1: (a) Top view and (b) cross section A-A' of the EWOD pressure chamber. It has one gas input (left) and one electrical feed-through (right) for passing electrical signals into the pressurized environment.

METHODS

Pressure chamber

The pressure chamber is depicted in Figure 1. Our current design has ample space (6 x 12 x 12 cm) for a typical EWOD chip (1.5 x 3 x 3 cm used here), and easily fits under an optical microscope. The chamber body was fabricated by milling a cavity into a solid block of aluminum, and the lid is a 3 cm thick sheet of acrylic with a circular recess (8 cm diameter and 1.5 cm depth) milled and polished for the viewing window, which provides a short working distance for microscope lenses. The chamber was tested up to 200 psig (13.7 atm), at which point warping of the window caused unacceptable distortion of recorded images. At 100 psig N₂ the leak rate was approximately 0.1 psi/min. An electrical feed-through connects the EWOD device to the external control system via ribbon cables.

In every experiment, the procedure began with affixing the EWOD substrate (with patterned electrodes) to the chamber lid using double-sided tape. Then, reagents were pipetted onto the chip, and the top plate was attached to the EWOD substrate by adhesive spacers. Finally, the chamber lid was bolted to the chamber body prior to pressurization. For experiments with H₂, all steps were performed inside a glove box filled with N₂; the concentration of O₂ was kept below 1 ppm to eliminate the possibility of burning H₂.

EWOD chip and operation

The chip in this study, shown in Figure 2, has typical EWOD device dimensions and layout, and includes multifunctional electrodes for local heating, temperature sensing, and EWOD actuation [2]. EWOD substrates were fabricated as follows: (i) e-beam evaporation of 100/10 nm Au/Cr onto an ITO-coated (140 nm) glass wafer (TechGophers[®]), (ii) photolithographic patterning and wet etching of Au, Cr, and indium tin oxide (ITO) to form electrodes, (iii) photolithographic patterning and wet etching of Au and Cr to remove these metals from the actuation pads (leaving only transparent ITO electrodes), (iv) plasma-enhanced chemical vapor deposition (PECVD) of 1 μm Si_xN_y, and (v) spin-coating of 100 nm Cytop[®] hydrophobic coating. The top plates were fabricated by PECVD of 100 nm Si_xN_y onto ITO-coated glass wafers, followed by spin-coating of 100 nm Cytop[®].

The top plates and EWOD substrates were bonded together with spacers made of pieces of double-sided tape (3M[®]). For volatile liquid experiments, one piece of tape was used for each spacer, resulting in $h \sim 100 \mu\text{m}$. For testing with gas-phase reagents, five pieces of tape were stacked for each spacer, resulting in $h \sim 500 \mu\text{m}$. Thicker droplets were used in the latter experiments to increase color contrast for colorimetric measurements.

EWOD actuation was achieved using 40 to 60 V_{rms} at 10 kHz, routed to electrodes by a homemade multiplexer. Localized Joule heating and resistance temperature sensing was done by multifunctional elements operating under a custom PID algorithm written in LabView[®], as

previously reported [2].

Optical measurements

All experiments were recorded using a digital video camera (Pixelink[®]). Individual video frames were extracted using Phantom Cine Viewer 675 by Vision Research[®] and analyzed using ImageJ[®]. Images of dye hydrogenation experiments were analyzed using the split channels function to enhance contrast (B channel).

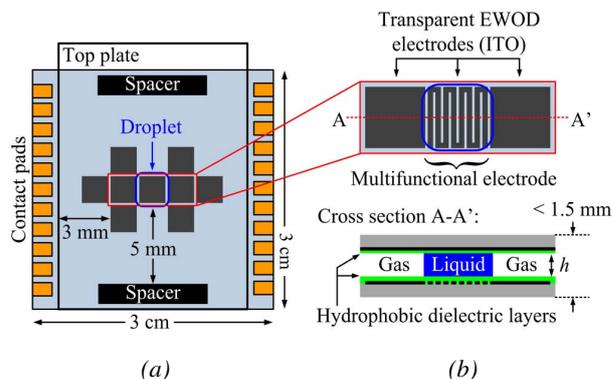


Figure 2: (a) Schematic top view of the EWOD chip used for testing inside the pressure chamber. Droplets on the electrodes outlined in red were 3 to 5 mm away from the edge of the chip during testing. (b) Close-up top view and cross section A-A' of the electrodes used for EWOD mixing and heating in the reported experiments.

THEORY

Evaporation control – vapor diffusion

Increasing the partial pressure of any component(s) of a gas mixture decreases the mean free path (and thus the diffusion coefficients) of the molecules therein. By this mechanism, high-pressure inert gas (N₂) can effectively lower the evaporation rate of liquid solvents including methanol, acetonitrile, and water in EWOD chips. To illustrate this concept, we examine Fick's First Law of diffusion in one dimension, x :

$$J = -D \frac{dc}{dx}, \quad (1)$$

where J is mass flux, D is the diffusion coefficient of vapor diffusing into a uniformly distributed gas, and dc/dx is the concentration gradient of vapor molecules in the x direction. Assuming the concentration gradient is constant at a given temperature, observed dependencies of J on the pressure (P) of the inert gaseous medium will be incorporated into D . Treating the binary system of vapor and gas as ideal at constant temperature, we have from kinetic theory [3] that $D \propto \lambda$ and $\lambda \propto P^{-1}$, where λ is the mean free path. Therefore, for this simplified system we expect to observe the following variation with $n = -1$:

$$\frac{J}{J_0} = \left(\frac{P}{P_0} \right)^n, \quad (2)$$

where J_0 is the mass flux at atmospheric pressure P_0 .

While Equation 2 represents perhaps the most basic physical model of our experimental system, it will be useful in analyzing our data. For example, upon fitting the data to Equation 2 with n as a variable parameter we will see to what extent our assumptions are valid by how closely n matches the ideal case, $n = -1$.

Gas-phase reagent delivery – Henry’s Law

In considering the situation of solutes diffusing within a liquid droplet (H_2 in water), let us again examine Equation 1. In contrast to the previous case of ideal gas diffusion, we expect the concentration gradient rather than the diffusion coefficient to be affected by chamber pressure. D now represents the diffusion coefficient of solutes in a liquid medium, which is assumed to be incompressible, and the associated kinetics are expected to be insensitive to chamber pressure. With respect to the concentration of dissolved H_2 , Henry’s Law states that, for a given temperature, the equilibrium concentration of solute in a liquid is proportional to the partial pressure of the solute in the surrounding gas phase. By this reasoning, we expect that the concentration of H_2 molecules dissolved in the droplet near the liquid-solid interface will be proportional to the H_2 partial pressure in the gas phase in the chamber. Further, in a mass transport limited regime (i.e., limited by diffusion of H_2 from the interface to the inside of the droplet), the partial pressure of H_2 is directly related to the processing time of the droplets on the EWOD chip.

RESULTS AND DISCUSSION

Volatile liquids

We investigated the effect of N_2 gas pressure on the evaporation of water, methanol, and acetonitrile droplets. These solvents are relevant to a broad spectrum of bio-analytical and chemical protocols, but they can pose problems in open digital microfluidic platforms due to rapid evaporation, especially when elevated temperatures are used. For example, excessive volume loss of liquid droplets can lead to undesired variations in solute concentrations throughout the course of an experiment. Also, if a droplet shrinks such that its diameter is smaller than the actuation electrode, it will be stranded, i.e., inaccessible to neighboring electrodes, and in need of rescue by another droplet.

Figure 3a has a striking result, comparing the evaporation of heated methanol droplets ($\sim 1 \mu\text{L}$ each on a $3 \times 3 \text{ mm}$ square EWOD electrode) under atmospheric and elevated pressures. For the former case, the chamber gas inlet valve was left open during the test, so the ambient medium was laboratory air. For the latter case, the chamber pressure was elevated by filling it with N_2 , without removing the laboratory air that was already in the chamber. Droplets were positioned and heated by a multifunctional EWOD electrode, which simultaneously measured the temperature (red lines). To calculate droplet volumes, video frames were analyzed for droplet liquid-solid area, which was then multiplied by the plate

gap h . Volume ratios V/V_0 (V_0 is at $t = 0$) show that at 0 psig (b.p. = 64.7°C) the droplet evaporated away from the heater in about 25 s, when the heater reached about 100°C (dashed line). In contrast, at 100 psig (b.p. = 130°C) the droplet evaporates much slower, withstanding 100°C (solid line) for ~ 2 minutes. No bubbling (i.e., boiling) was observed in either case.

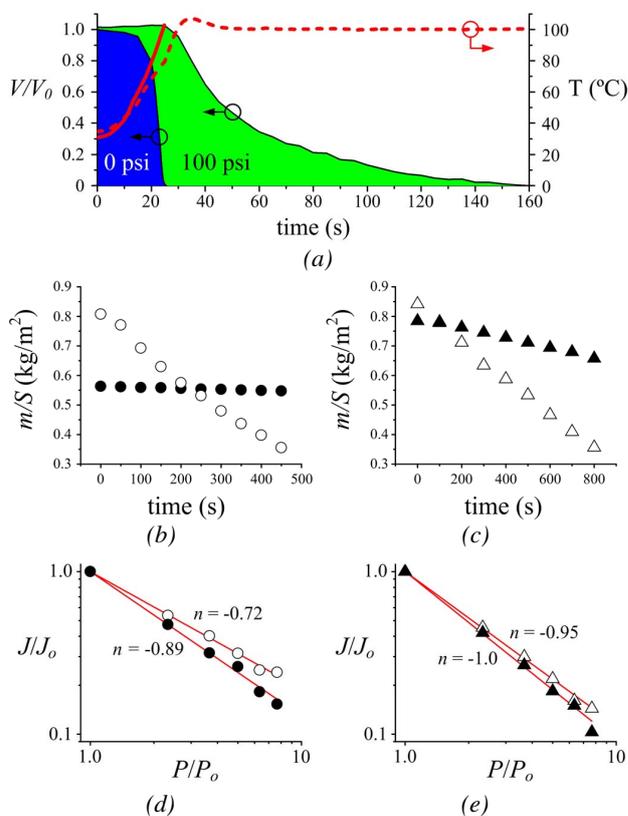


Figure 3: (a) Methanol droplet volume ratios V/V_0 (left axis) and heater temperature (right axis) versus time for 0 and 100 psig. (b&c) Droplet mass (m) divided by free surface area (S) versus time for water (b) and acetonitrile (c) at 60 psig. Black- and white-filled symbols correspond to unheated and heated droplets, respectively. Heaters were held at 80°C and 60°C for water and acetonitrile droplets, respectively. (d&e) Dimensionless mass flux versus dimensionless pressure for water (d) and acetonitrile (e) droplets. Red lines have the form: $J/J_0 = (P/P_0)^n$.

Figures 3b and 3c compare data for unheated (black-filled) and heated (white-filled) water and acetonitrile droplets, respectively. For the convenience of calculating mass flux (described below), the data are plotted in terms of droplet mass divided by liquid-vapor surface area: m/S . The plots in Figures 3b and 3c are representative of all data (i.e., in showing linear trends), indicating that the mass fluxes ($J = d(m/S)/dt$) were time-invariant. One value of J was calculated for each experiment by a linear fit of the corresponding m/S plot.

Figures 3d and 3e are log-log plots showing the variation of mass flux with N_2 pressure for water and acetonitrile droplets, respectively. Normalizing by 1 atm P_0 and flux at 1 atm J_0 , we fit the data using Equation 2

(red lines), and the resultant n values are shown on the plots. Acetonitrile data match very well with Chapman-Enskog theory, predicting $n = -1$, and deviations of water data are consistent with published results [4]. Further deviations from the theory at elevated temperatures are unsurprising given that we observed condensation around the droplet during heating. This is expected because multifunctional electrodes are designed for localized heating and therefore generate a hot spot beneath the droplet, not a uniform temperature over the entire chip.

Reactive gas

Chemical transformations involving reactive gases are generally difficult to perform in the macroscale due to the hazardous nature of the gases. Multi-phase reactions have been reported in continuous flow chips [5], but this is the first investigation using EWOD.

As a proof of principle study, we demonstrated multi-phase catalytic hydrogenations of methyl orange in the pressurized EWOD chamber. In this model reaction, 2 μL droplets of diazo dye solution (methyl orange in water) and solid catalyst suspension (Pt black in water) were transported to the reaction site and mixed by EWOD. The progress of each reaction was tracked by the color of the mixed droplet, which turned from orange to clear. Filling and pressurizing with H_2 effectively drove the reactions at pressure-dependent rates. Figure 4 has video frames of reactions over a range of H_2 partial pressures up to 50 psi.

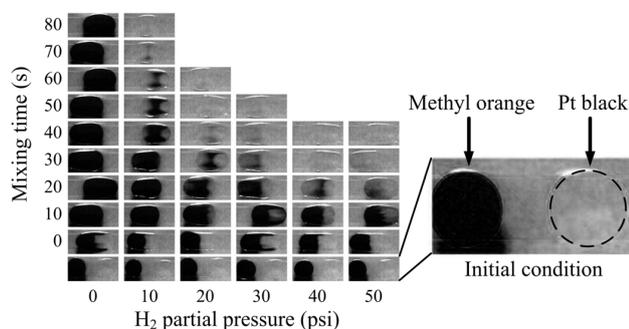


Figure 4: Video frames of hydrogenations at H_2 pressures (color contrast enhanced by ImageJ[®]). Initially, there are two 2 μL droplets composed of 1.5 mM methyl orange and 0.25 g/L Pt black (avg. diam. = 5 nm), both in DI water. Reaction progress is monitored by colorimetric change from orange to colorless, which occurs upon cleavage of the diazo bonds.

At 0 psi H_2 (leftmost column), there was no apparent color change after 10 minutes. In the other cases, we observed that the change was faster at higher H_2 pressures. This trend is attributable to the increased amount of dissolved gas-phase reagent at higher H_2 partial pressures. Additionally, the colorimetric data give a sense of the role of mixing in the process. Without mixing, the amount of gas-phase reagent within the droplet is diffusion-limited, depending on the concentration of dissolved H_2 at the liquid-vapor interface (Henry's Law) and the rate at

which H_2 is consumed inside the liquid. EWOD movement (i.e., mixing) generated recirculating flows (evident in Figure 4) that pushed H_2 -rich liquid from the liquid-vapor interface to the inside of the droplet and H_2 -lean liquid to the interface; this process hastened the color change to the same extent for each experiment.

CONCLUSIONS

The ability to operate in a pressurized environment opens the door to many processes previously incompatible with EWOD. As well as addressing the common problem of evaporation in EWOD chips, it enables new applications such as radiochemical tracer synthesis (which takes place in volatile organic solvents) [6] and hazardous material screening. The reported pressure chamber represents a first step towards future low-profile systems.

ACKNOWLEDGEMENTS

This work was supported by the NIH (R01 RR020070), DOE (DE-SC0005056), and the UCLA Foundation from a donation made by Ralph & Marjorie Crump to the UCLA Crump Institute for Molecular Imaging. WN acknowledges further support from the NSF Graduate Research Fellowship Program and a NSF Integrative Graduate Education and Research Traineeship (IGERT) through the UCLA Materials Creation Training Program.

REFERENCES

- [1] S.K. Cho, H. Moon, and C.-J. Kim, "Creating, Transporting, Cutting, and Merging Liquid Droplets by Electrowetting-Based Actuation for Digital Microfluidic Circuits," *J. Microelectromech. Syst.*, vol. 12, 2003, pp. 70-80.
- [2] W.C. Nelson, I. Peng, G. Lee, J.A. Loo, R.L. Garrell, and C. Kim, "Incubated Protein Reduction and Digestion on an Electrowetting-on-Dielectric Digital Microfluidic Chip for MALDI-MS," *Anal. Chem.*, vol. 82, 2010, pp. 9932-9937.
- [3] A.L. Hines and R.N. Maddox, *Mass Transfer: Fundamentals and Applications*, Prentice Hall, 1984.
- [4] C.V. Paganelli and F.K. Kurata, "Diffusion of water vapor in binary and ternary gas mixtures at increased pressures," *Respir. Physiol.*, vol. 30, 1977, pp. 15-26.
- [5] P.D.I. Fletcher, S.J. Haswell, E. Pombo-Villar, B.H. Warrington, P. Watts, S.Y.F. Wong, and X. Zhang, "Micro reactors: principles and applications in organic synthesis," *Tetrahedron*, vol. 58, 2002, pp. 4735-4757.
- [6] S. Chen, P.Y. Keng, R.M. van Dam, and C.-J. Kim, "Synthesis of ^{18}F -Labeled Probes on EWOD Platform for Positron Emission Tomography (PET) Preclinical Imaging," *Proc. IEEE Int. Conf. MEMS*, Cancun, Mexico, Jan. 2011, pp. 980-983.

CONTACT

* W.C. Nelson, tel: 310.825.3977;
wyattnelson@ucla.edu