INVESTIGATION OF BURSTING OF HEATED DROPLETS FOR CHEMISTRY APPLICATIONS IN DIGITAL MICROFLUIDICS

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ABSTRACT
This report investigates the phenomenon of uncontrolled droplet bursting observed when droplets in a digital microfluidic device are heated to temperatures close to or above the solvent boiling points. High-temperature steps are often required to perform chemical reactions, such as radiochemical synthesis of tracers for positron emission tomography (PET). Bursting poses a major challenge to this otherwise promising digital microfluidic platform for radiochemistry, and must be prevented to avoid catastrophic failure of the synthesis reaction. We experimentally study the effect of parameters like droplet size, geometry and surface temperature, in order to enable faster, burst-free, high-temperature chemistry in digital microfluidics.

KEYWORDS: Digital microfluidics, EWOD, radiochemistry on chip, heated droplet bursting

INTRODUCTION

Digital microfluidics presents a promising platform for chemical synthesis, e.g. for radiotracers used in positron emission tomography [1]. The syntheses require heating steps where surface temperatures (typically 85-120°C) are well above solvent boiling points (b.p.) (e.g. 81.6°C for acetonitrile, MeCN), which can lead to uncontrolled droplet behavior including bursting or splattering. Splattering is a challenge even for macroscale radiosynthesis [2], leading to product loss and potential chemical/radiation hazards; the confined geometry and microfluidic volumes in EWOD exacerbates the tendency. In previous reports, we found that slow temperature ramping (~0.2-0.3°C/s) minimized droplet bursting, presumably because most of the solvent evaporated before the high temperature was actually reached. But this undesirably prolongs the synthesis time, especially considering the short half-life of the radioisotope and the multiple (typically 3-6) high-temperature steps per synthesis. To understand droplet bursting and enable faster ramping to higher temperatures, we studied the influence of various parameters (droplet volume, gap height and surface temperature) on bursting frequency.

THEORY

Splattering caused by the formation and bursting of bubbles inside a superheated liquid, also known as “bumping”, is a commonly observed phenomenon in chemistry during high temperature reactions [3]. Bumping is often seen when the liquid is heated too quickly above the solvent boiling point, causing the vapor pressure inside the liquid to rise above the atmospheric pressure and eventually leading to a violent burst. Superheating is commonly required during radiochemical synthesis, for instance during the azeotropic drying step [4], where a mixture of acetonitrile and water is heated above the boiling points of the individual solvents as well as their azeotropic mixture in order to remove the water. High-temperature reaction steps (often 120°C or higher) also commonly require temperatures above the boiling points of one or more solvents present in the reaction mixture. Bursting is sometimes observed while performing these steps on our digital microfluidics platform, where the droplet is held in a flat geometry (typical height:width < 1:10) between two substrates of the EWOD device, and one substrate is heated above the solvent boiling point (Fig. 1).

Fig. 1: Droplet bursting in EWOD digital microfluidics during high temperature reactions: Droplet (dotted blue line) being heating by on-chip resistive heaters (concentric rings inside dashed black line) on an EWOD chip. During high temperature reaction steps, where the surface temperature needs to be above the solvent boiling point, the droplet can burst or splatter, causing loss of product and possible chemical/radiation hazards.

EXPERIMENTAL

Fig. 2(a) shows the experimental setup. To ensure a uniform surface temperature, the on-chip resistive heaters were replaced by a PID-controlled thermoelectric module, heating a metal sheet at the center through an aluminum block.
(15mm x 20mm x 15mm). In each run, droplets of acetonitrile, a commonly used solvent in radiochemistry, were placed on the pre-heated metal substrate and immediately covered with a Teflon-coated glass cover chip as used for EWOD. Different thicknesses of spacers were used. For each combination of surface temperature, gap height and droplet volume, we observed whether burst occurred or not (Fig. 3). Each combination is repeated 10 times, and the burst frequency was calculated.

Fig. 2: (a) Experimental setup (schematic (top) and image (bottom)) for droplet bursting experiments. The metal surface is heated by the thermoelectric module through an Al block below it. The droplet and the Teflon-coated glass cover are then placed on it. Droplet volume, gap height (between glass cover and metal surface) and the surface temperature on the bottom substrate are varied, while noting the droplet bursting frequency. (b) Vapor pressure of acetonitrile (blue) vs. temperature [5]. Temperatures used in the experiments range from 71 to 101 °C, corresponding to vapor pressures below and above the atmospheric pressure (red).

Fig. 3: Sample image sequences showing the cases of (a-c) bursting and (d-f) no bursting. Droplets were placed on the preheated surface, and immediately covered with the glass cover. Bursting frequency is influenced by several factors, including droplet volume, geometry and surface temperature. e.g. sudden violent bursting occurs in (a-c), at 91 °C, 0.34 mm gap in this case, causing the 20uL droplet to undesirably splatter and/or deform uncontrollably. On the other hand, at 91 °C, 0.51mm gap (d-f), the 20uL droplet evaporates without bursting. Small droplets around the central droplet are condensed solvent vapor.

RESULTS AND DISCUSSION

Fig. 4 summarizes the results. Droplet volumes were varied from 5 µL to 20 µL, as these are the typical volumes used in EWOD radiochemistry. Temperatures setpoints were chosen at 5°C temperature-intervals, from well below (71±1°C)
to well above (101±1°C) the b.p. (81.6°C). No bursts were observed below the boiling point but complete droplet evaporation took a long time (e.g. >2.5min at 76±1°C for a 5µL volume and 170µm gap). To avoid such long times, drying and evaporation steps are usually performed at much higher surface temperatures to reduce the evaporation time, but presumably due to the high vapor pressure at these temperatures (Fig. 2(b) [5]), there is greater tendency for droplet bursting (Fig. 4, y-axis).

Interestingly, bursting likelihood was found to decrease with decreasing volume (Fig.5, x-axis), which can inform how to safely operate at higher temperatures. For the same surface temperature, we also found that bursting tendency can be reduced by increasing the gap height. e.g., at 91±1°C, bursting was observed at all tested volumes (5-20µL) for gap heights of 0.17mm and 0.34mm (Fig.4(a-c)), but bursting was suppressed at 0.51mm (Fig.4(d-f)). Evaporating 20µL with 510µm gap at 91°C took < 40s (vs. the results above for 5 µL at 76°C).

CONCLUSION
These results suggest that while droplet bursting is a complex and dynamic phenomenon, processes can be performed in a controlled manner above the solvent boiling point even in digital microfluidics by choosing appropriate droplet geometry and/or ramp time to the required temperature. Future steps include studying the effect of surface hydrophobicity, droplet composition and gas-flow, and utilizing the understanding for faster on-chip radiosyntheses.

ACKNOWLEDGEMENTS
This work was supported in part by the Department of Energy Office of Biological and Environmental Research (DESC0001249, DE-SC0005056).

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