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The Formation of Hydroxyl Radicals during Hydrodynamic Cavitation in Microfluidic Reactors Using Salicylic Acid Dosimetry

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Abstract

Cavitation is a phase change phenomenon that generates highly energized bubbles due to low local pressures. The collapse of these bubbles releases this energy to the surrounding area in different forms upon the pressure recovery. Free radical production, which is considered as chemical effect of the bubble collapse, plays a major role in many applications, from wastewater treatment to material exfoliation. Although some studies underscore the importance of chemical effects for acoustic cavitation (AC), their investigations in hydrodynamic cavitation (HC) are challenging due to the difficulty in controlling cavitating flows. One of the approaches that could shed light on this challenging aspect is to shrink the reactor scale to micro-scale size ("HC on a chip"). In this regard, we investigated the chemical effects of HC using Salicylic Acid (SA) dosimetry in three different micro-scale designs (long diaphragm, micro-orifice, and micro-venturi configurations) and compared the results to those of a macro-scale HC reactor. High-speed visualization revealed important links between flow patterns and the formation of hydroxyl radicals ('OH), which contributed to the SA products. This study thus focused on comparing the effectiveness of the three micro-scale reactors in terms of 'OH formation. According to the results, the "HC on a chip" concept demonstrated significantly higher efficiency in generating SA products compared to the macro-scale HC reactor. For instance, the micro-scale HC reactors achieved an SA concentration

of approximately 0.6 μ g/mL in just 5 cycles, while the macro-scale HC reactor required 164 cycles to reach a similar concentration (0.45 μ g/mL). This substantial reduction in the number of cycles highlights the potential of micro-scale HC reactors for efficient and rapid generation of SA products.

Keywords: Hydrodynamic cavitation; HC on a chip; Microfluidic reactors; Chemical effects; Hydroxyl radical ('OH); Salicylic acid (SA)

1. Introduction

During recent decades, cavitation has become an important tool in the field of environmental science, has attracted considerable research interest, and has been investigated for its efficacy in organic chemical synthesis [1], the degradation of recalcitrant environmental pollutants [2], the production of nanomaterials [3] and catalytic processes [4]. Its applications include wastewater treatment (WWT) [5–7], microbial disinfection [8,9], biodiesel synthesis [10] and graphene exfoliation [11,12]. These diverse applications underline the potential of cavitation for tackling various environmental challenges.

Hydrodynamic cavitation (HC) results from the growth and collapse of small vapor bubbles because of a sudden pressure drop in the liquid inside a flow restrictive element or a turbomachine. As the bubbles collapse, they concentrate their energy in a very small spatio-temporal area and trigger conditions that can be divided into mechanical and chemical effects. The former include shockwaves, micro-jets, shear forces, and extreme temperatures [13,14], known as hot spots. These lead to the chemical effects, namely the homolysis of water molecules into hydroxyl ('OH) and hydrogen ('H) radicals [15–17], which makes cavitation an advanced oxidation process (AOP). While mechanical effects of cavitation can be detected by material wear-cavitation erosion, chemical effects require a dosimetry technique to trap highly reactive 'OH. Various dosimetry reactions, such as Fricke, iodide and hydroxylation of aromatic compounds, can be used. In Fricke dosimetry, Fe^{2+} is oxidized by 'OH, H atom, 'OOH and hydrogen peroxide (H₂O₂) under acidic conditions, and the resulting Fe³⁺ is then determined photometrically [18]. In iodide dosimetry, 'OH oxidizes iodide ions and triggers a cascade of chemical reactions. The end product, the triiodide (I₃⁻), is then measured by UV-Vis spectroscopy [19]. When aromatic compounds are selected to trap 'OH which is formed during cavitation, salicylic acid (SA) is often used [20]. SA selectively traps 'OH, and the hydroxylation products can be easily quantified with high sensitivity using liquid chromatography. In addition, its physico-chemical properties can be easily manipulated by adjusting the pH of its solution [21]. By lowering the pH below its pKa value and by thus influencing the hydrophobicity of the molecule, its trapping effect at the bubble interface, where the short-lived 'OH are formed, could be increased [22]. It is important to realize that the addition of different dosimetry compounds can affect the surface tension of the solution, reducing the violence of bubble collapse, as already shown by Zupanc et al. [20]. Therefore, the concentration of the scavenger needs to be low enough in order not to interfere with 'OH production or should be chosen based on the purpose of the investigation.

Although there are numerous studies demonstrating the effectiveness of the cavitation approach [20,23,24], reported cavitation reactors still lack the energy efficiency to outperform other AOP techniques [24]. This hurdle can be overcome by exploring the area of microfluidics, where related advanced technologies enable the design and manufacture of micro-scale HC reactors, opening new lanes of research and providing a great opportunity to enhance cavitation process intensification. At the small scale, the potential of controlling and manipulating cavitation effects

to achieve the desired chemical effects is much greater as the three-dimensional (3D) cavitation flow is transformed into a more controlled two-dimensional (2D) flow [25]. In addition, the confined space leads to a higher density of microbubbles and a larger surface area at the small scale to achieve different bubble collapse behavior, which can lead to a higher efficiency of the "microbubble reactors" in terms of physical and chemical effects [19].

Recent advancements in microfluidic HC reactors ("HC on a chip") have demonstrated unique advantages over macro-scale systems, including precise control over cavitation parameters, reduced reagent consumption, and enhanced optical accessibility for mechanistic studies [19,26,27]. For instance, Podbevšek et al. [26] developed a novel chemiluminescence mapping technique to pinpoint radical production in HC reactors using luminol. This method spatially resolves radical generation, correlating it with cavitation cloud collapse and enabling quantification of radical yield in both micro and macro-scale reactors. The study highlights the capability of characterizing even weak emissions from microfluidic HC systems, demonstrating its potential for applications in WWT and other AOPs. In another study, Podbevšek et al. [27] investigated radical production in venturi micro-scale reactors across the micro-to-milli scale transition using luminol chemiluminescence. While chemical yield generally increased with hydraulic diameter and driving pressure, an optimal geometry was identified for maximizing yield per treated volume. Analysis of bubble dynamics revealed that individual bubble collapse within the cavitation stream, rather than cloud collapse, is the primary radical generation mechanism, suggesting this may be the dominant mechanism across scales. Similarly, Talabazar et al. [19] highlighted the role of cavitating flow patterns in chemical yield, showing that micro-scale reactors operating at lower pressures (with rapid bubble implosions) achieve higher efficiency than highpressure systems prone to vapor coalescence. These studies underscore the potential of micro-scale HC reactors for energy-efficient applications like WWT.

These advancements offer a more detailed understanding of the fundamental mechanisms at play. Nonetheless, key aspects of HC in micro-scale need more investigation. These include geometric optimization. While studies such as [28] demonstrate that nozzle geometry and hydraulic diameter significantly impact radical yield, the interplay between micro-scale channel design and bubble dynamics remains poorly understood. For example, smaller channels exhibit reduced radical yields due to nucleation limitations, necessitating surface modifications or hybrid excitation methods [27]. The effect of bubble size and bubble dynamics on chemical production efficiency is another open research question. Even though some studies have pointed out that micro-scale bubbles can produce more efficient collapse [19,27], there is no detailed study to prove this claim and explain the underlying reasons. In addition, there are challenges when scaling down. Scalability and clogging: micro-scale reactors often require pre-filtered fluids to prevent clogging, limiting practical applicability [29]. Additionally, the transition from lab-scale "chip" systems to industrially relevant throughputs introduce complexities in maintaining cavitation efficiency [30]. The "HC on a chip" concept (microchannels with various length-height ratios of constrictions) has attracted considerable interest because of its potential for implementation in new applications and its fundamentally different underlying HC physics from HC on the conventional scale [31-34]. Reducing the flow constrictive channel size is desirable in HC because it can shorten the pressure recovery time and increase the intensity of cavitation bubble collapse, leading to higher temperatures and influencing radical formation rates [35]. Most of the existing studies focus on the cavitation dynamics in terms of cavitating flow patterns [36–38] and instabilities [39], while only a few studies have investigated the chemical effects of HC at the micro-scale [19,27,35,40].

In this study, to address this lack of information, the chemical effects of HC bubble collapse at the micro-scale were investigated using SA dosimetry. For this, cavitating flow patterns were characterized in three microfluidic reactors (micro-scale HC reactors) with different configurations, namely long diaphragm, micro-orifice and micro-venturi configurations. The amount of 'OH formed inside the reactors was scrutinized at various upstream pressures using SA dosimetry. To explain the observed radical yields in the investigated micro-scale HC reactors, the cavitation characteristics and developed flow patterns in deionized water were compared and linked to the yield. Furthermore, this study also provides a comparison in the formation of the SA product between the most effective micro-scale HC reactor and a macro-scale reactor [20].

2. Methods and Materials

2.1. Materials

High-purity salicylic acid (SA \geq 99 %), 2,3-dihydroxybenzoic acid (2,3-DHBA, 99 %), and 2,5-dihydroxybenzoic acid (2,5-DHBA, \geq 97.5 %) were obtained from Sigma-Aldrich. 1 M HCl was purchased from Honeywell Fluka, while trifluoroacetic acid (TFA, 99.5 %) came from Acros Organics. Methanol for liquid chromatography (LiChrosolv®) was acquired from Merck.

2.2. Salicylic acid dosimetry

The generation of 'OH was effectively monitored using the SA dosimetry technique. This method is based on the reaction of SA with 'OH leading to the formation of two products, 2,3-DHBA and, to a lesser extent, 2,5-DHBA. The detailed analytical procedure, including chromatographic conditions and method validation protocol, was described in the literature [20], where relative standard deviation for both measured SA products ranged from 0.2 to 2.5 % (the samples of each SA product were measured 6 times for three concentrations along the calibration curve). Accordingly, the analysis was performed using an Agilent Infinity 1260 High Performance Liquid Chromatography (HPLC) system with diode array detector. Separation was performed on a LiChrospher® 60 RP-Select B column (4 mm × 125 mm, 5 μ m) using isocratic elution with a mobile phase of methanol and water with 0.1 % TFA (20:80, v/v). Data were processed using the Agilent OpenLAB software. Stock solutions (20.0 mg/mL) of 2,3-DHBA and 2,5-DHBA were prepared in methanol and diluted with 0.1 % TFA solution for analysis to achieve concentrations of 0.016–4 μ g/mL. The stock solutions were stored at -20 °C.

2.3. Micro-scale HC rector design and fabrication

Three different micro-scale HC reactors, namely *Long diaphragm* (Reactor 1), *Micro-orifice* (Reactor 2) and *Micro-venturi* (Reactor 3), which have a footprint of $14 \times 6 \text{ mm}^2$, were designed and fabricated. All reactors (Fig. 1) had an inlet (1), a nozzle (2), and an extension (3) channel as the main sections with a uniform depth of 60 µm. Inlet (4) and outlet (5) ports with a diameter Φ = 900 µm have a distance d = 8900 µm and were connected to the sandwich holder for fluid delivery and discharge. The reactors had two layers of Silicon (Si) and glass, and the channels and ports were created in a Si layer.

The initial phase of the reactor fabrication involved RCA (Radio Corporation of America) cleaning followed by the deposition of a 500 nm silicon dioxide (SiO₂) layer on both sides of the substrate using a Süss ACS200 GEN3 coater. Photolithography was performed with an ECI 3007–2 μ m photoresist using the MLA 150 developer. A meticulous dry etching process using the SPTS APS apparatus was then applied to achieve the desired 500 nm depth in the SiO₂ layer. The photoresist

was stripped using Tepla machine and remover, targeting specifically the ECI 3007–2 μ m residue. Subsequent fabrication stages included a dual-layer sputtering process where a 10 nm layer of Titanium (Ti) followed by a 1 μ m layer of Aluminum (Al) which was deposited using the DP650. This was complemented by Electron Beam Lithography (EBL) using ZEP 520A – 500 nm, leading to further SiO₂ dry etching and resist stripping processes. The final photolithography phase utilized AZ 10XT-60 – 8 μ m photoresist, processed in rapid mode on the MLA 150, and targeted a critical dimension (CD) of 1800 μ m. Wet etching was subsequently applied to the removal of Al, Ti, and SiO₂ layers. The final cleaning of the Borofloat wafer was performed using a Piranha solution, followed by anodic bonding of the Si-Glass materials and an annealing process using the SB6 machine [28].



Fig. 1. Schematic of micro-scale HC reactors with main sections (A) Reactor 1: long diaphragm, (B) Reactor 2: micro-orifice and (C) Reactor 3: micro-venturi. Marked dimensions: step height (h), nozzle length (x), nozzle width (y) and Venturi convergent / divergent angle (δ).

2.4. Experimental setup and procedure

The experimental setup (Fig. 2) houses fittings interconnecting the tubing and flow elements. The working fluid stored within the 1 L container was driven by a nitrogen tank and delivered to the sandwich package that encloses the micro-scale HC reactor. The control valve and pressure gauge regulated the flow and pressure within the system. The upstream pressure was monitored using an absolute pressure transducer through the measurement card cDAQ NI-9219 and customized LabView software. The flow of deionized water within the micro-scale HC reactor was recorded using a high-speed camera, the Photron Fastcam SA-Z, at a frame rate of 87500 frames per second (fps), 84000 fps and 80000 fps for Reactor 1, Reactor 2 and Reactor 3, respectively. The utilization

of high-speed imaging played a crucial role in observing and comprehending the motion and behavior of cavitation bubbles and their interactions within the reactors. The sample temperatures were monitored prior and after the experiments with a mobile temperature probe (Thermocouple K-type) and never exceeded 25 °C.

The integration of rapid imaging and accurate data collection allowed for a thorough comprehension of the HC phenomenon inside the micro-scale reactors under different operating conditions presented in Table 1. For brevity, different cases are represented by a short code indicating the reactor type (R) and flow conditions (L/H for low/high upstream pressure). The upstream pressures were chosen based on visual perception of distinct selected cavitating flow patterns. The upstream pressures for each reactor were selected based on preliminary tests to achieve two distinct cavitation regimes. Downstream pressure was maintained at atmospheric pressure. The lower upstream pressure was chosen for the flow pattern corresponding to incipient cavitation (minor cavitation shedding), while the higher upstream pressure was set to have the fully developed cavitating flow (intense cavitation shedding). The hydraulic resistance in reactors varies due to the differences in channel geometry. Specifically, longer channels with constrictions (like Reactor 1) require larger pressure differences to achieve the same Reynolds number compared to shorter channels (like Reactor 2). This necessitates adopting different upstream pressures for reactors of different lengths to maintain equivalent flow conditions. The experiments were conducted by operating each reactor (R1, R2, and R3) separately. This was done to ensure controlled conditions for each test. The flow rate for each individual reactor was then estimated by calculating the mean flow rate observed over five operational cycles. Due to the design of our experimental setup, the flow rate within the channel is directly coupled to the upstream pressure. This interdependence restricts our ability to independently control both flow rate and pressure drop, and therefore, the cavitation number is primarily adjusted by changing the upstream pressure. We recognize that independent control of these parameters would be advantageous. One potential modification would be to maintain a fixed pressure drop across the reactor while independently adjusting both upstream and downstream pressures. This would enable us to achieve a broader range of cavitation numbers while keeping the flow rate relatively constant.

The SA stock solution for HC experiments was prepared in deionized water and diluted accordingly to achieve working concentrations of 300 mg/L on the day of the experiment. The main purpose for having this concentration was to be able to compare radical yields among the investigated micro-scale HC reactors [20]. Before the HC experiments, SA solution was acidified with HCl, to a pH of around 2.5 (below the SA's pKa = 2.97). For HPLC analysis, 1 mL of the sample was withdrawn after 0, 1, 3 and 5 HC cycles.



Fig. 2. Experimental setup with the microfluidic reactor and package reactor.

Table 1. Operating conditions

	Reactor 1		Reactor 2		Reactor 3	
Case	R1L	R1H	R2L	R2H	R3L	R3H
Upstream pressure (bar)	11.5	13.5	9	13	11	12
Flow rate (ml/s)	0.88	0.97	0.73	0.92	0.46	0.52
Flow velocity (m/s)	29.44	32.22	30.56	38.2	51.85	57.41
Cavitation number (-)	2.61	2.51	1.92	1.71	0.82	0.73

2.5. Post-Processing of the cavitating flow patterns

To quantify void fraction in this study, we employed a technique used in previous studies [41,42]. This method assumes a direct proportionality between the gray level value obtained from 2D highspeed camera images and the void fraction. Accordingly, given the channel's shallow depth, minimal variation is expected in the vapor distribution across its depth. This allows for the estimation of the mean and variance of the void fraction using the following equations (Eqs. 1 and 2):

$$\bar{\alpha}(x,y) = \frac{1}{Nt} \sum_{t=0}^{Nt} I(t,x,y) \tag{1}$$

$$var(\alpha(x,y)) = \frac{1}{Nt} \sum_{t=0}^{Nt} \left(I(t,x,y) - \bar{\alpha}(x,y) \right)^2$$
(2)

where I(t, x, y) represents the gray level intensity of a pixel located at (x, y) within the image captured at time step t. This value was obtained by first subtracting the background intensity and then normalizing it by the maximum possible pixel value (typically 255 for 8-bit grayscale images). A total number of 8000-time snapshots were used for the analysis of void fraction in the micro-scale HC reactor.

The frequency characteristics of cavitation regimes were evaluated using the power spectral density (PSD) at the region of maximum void fraction fluctuation (α'_{rms}) pathway. Sampling

intervals and rates were chosen as follows: $T \approx 0.091 s$ with $f_s = 8.75e4 Hz$ for Reactor 1, $T \approx 0.095 s$ with $f_s = 8.4e4 Hz$ for Reactor 2, $T \approx 0.1 s$ with $f_s = 8.0e4 Hz$ for Reactor 3.

The Welch method with Hanning window was utilized to compute PSD for a total of 31 equallength segments in time with 50% overlap [43,44]. Each segment comprised 512 samples, and the following frequency range was obtained for each reactor: $f = 0.22e2 \sim 5e4$ Hz for Reactor 1, $f = 0.2e2 \sim 4.2e4$ Hz for Reactor 2, $f = 0.2e2 \sim 4e4$ Hz for Reactor 3.

3. Results and Discussion

3.1. Cavitating flow patterns inside the Reactors 1, 2 and 3

This section presents the cavitating flow behavior within three micro-scale HC reactors with distinct constriction geometries and varying HC physics. Fig. 3 presents high-speed camera images illustrating different flow regimes in deionized water at lower and higher upstream pressures. The focus is on two primary flow regimes: minor (Figs. 3(a)-(c)-(e)) and intense cavitation shedding (Figs. 3(b)-(d)-(f)), resulting from varying upstream pressures and reactor configurations. At the micro-scale, surface characteristics and forces significantly influence nucleation and cavitation development, potentially enhancing the cavitation intensity [45]. Figs. 3(a) and (b) depict flow regimes in Reactor 1 at low and high upstream pressures, respectively. Cavitation initiates within the shear layer downstream of the leading edge (Twin shear cavities in Fig. 3(a)), analogous to flows over a forward-facing step [46,47]. Depending on Reynolds and cavitation numbers, three cavitation regimes—incipient, transition, and periodic—can emerge in general within all three reactors. Cavitation progression through these regimes involves distinct mechanisms. Incipient cavitation occurs within the separated shear layers, typically located in the low-pressure cores of coherent vortices [48]. As the cavitation number decreases, transition occurs, leading to sheet cavity formation over wedges, characterized by intermittent cloud-like shedding due to re-entrant jets [49,50]. The zoom-in image in Fig. 3(a) reveals that the flow regime within Reactor 1 nozzle is near the transitory regime at low upstream pressure. Generally, further decrease in the cavitation number is expected to transition this regime into a periodic regime, where a large sheet cavity forms near the wall and is periodically shed due to shockwaves generated by collapsing downstream cloud cavities. In Reactor 1 at higher upstream pressure, the cavity develops along the wall (marked as the 2nd separation bubble), which covers a significant portion of the nozzle. However, the shedding regime (seen in the extension part of the channel) remains similar to the transitory regime, with intermittent shedding creating small pressure waves from collapsing bubbles. The length of the 2nd separation bubble within the nozzle (Reactor 1) is influenced by factors such as Reynolds number, step height-to-boundary layer thickness ratio, and freestream turbulence level⁴⁵. Flow separation over the leading edge is linked to hydrodynamic instability and shear layer formation⁴⁶. Within this shear layer, hydrodynamic instabilities give rise to spanwise and streamwise vortices. A shorter separation bubble forms at lower upstream pressure (Fig. 3(a)) compared to higher pressure (Fig. 3(b)). An adverse pressure gradient near the contraction induces flow separation, leading to a stagnation point and the formation of a primary separation bubble. This happens in Reactor 1 and Reactor 2. The pronounced curvature at the constriction's leading edge triggers secondary separation, forming a 2nd separation bubble (Fig. 3(a)). Thus, two 2nd separation bubbles develop on the channel top and bottom sides (marked in Fig. 3(a)), while a sudden expansion induces a 3rd separation bubble downstream of the nozzle (marked only in Fig. 3(a)). In Reactor 1, most cavitation bubbles condense within the nozzle at low upstream pressure. On the other hand, at high upstream pressure (Fig. 3(b)), shed cavities are transferred to the shear

layer of the 3rd separation bubble as sparse cavitation clouds, while some recirculate within the recirculation zone and re-enter the flow.

Figs. 3(c) and (d) illustrate the flow patterns in Reactor 2 at low and high upstream pressures, respectively. Similar to Reactor 1, three shear layers and separation bubbles form before, over, and after the nozzle, driven by similar mechanisms. However, a key difference lies in the nozzle length. Reactor 2's shorter nozzle prevents reattachment of the separated flow, leading to the merging of shear layers over and downstream of the nozzle (Fig. 3(d)). Additionally, the shorter nozzle results in lower hydraulic resistance, higher flow rates, and larger pressure gradients across the shear layers, promoting the formation of stronger vortices within the shear layers. These vortices maintain low-pressure cores, sustaining vapor phase beyond the nozzle exit, even at low upstream pressure. In Reactor 2, cavitation initiates near the nozzle's leading edge at low upstream pressure (Fig. 3(c)). Insufficient pressure recovery prevents vapor condensation, leading to vapor transfer to the downstream shear layer. Within this shear layer, cavities are carried, intensified, and new ones form within vortices (spanwise vortices are evident from the vapor cloud shape in Fig. 3(c)). An adverse pressure gradient induces reverse flow near the wall, where reattachment occurs. Strong pressure recovery during reattachment condenses vapor downstream, while some bubbles re-enter the shear layer. At high upstream pressure (Fig. 3(d)), a similar cavitation pattern is observed, but stronger pressure drops within the shear layers lead to a more intense cavitation extent. Shed vortices maintain low-pressure cores and vapor within these cores well beyond the reattachment point.

In both low and high upstream pressure cases, Reactor 2 exhibits a transitory regime of cavitation shedding in the nozzle channel. A key distinction between Reactor 1 and Reactor 2 lies in pressure recovery. Reactor 1's longer nozzle allows for pressure recovery within the nozzle, leading to vapor condensation before the expansion region. The turbulent boundary layer has sufficient time to recover, making the downstream flow resemble a backstep configuration. In contrast, Reactor 2's shorter nozzle and higher flow rate result in stronger shear layer vortices, which can sustain cavitation downstream of the step.

Reactor 3's geometry differs from Reactors 1 and 2 so that the cavitation phenomenon in this reactor includes attached cavitation at the diverging region's leading edge as well as localized cavitation on the channel's bottom surface near the constriction (Figs. 3(e) and (f)). Cavitation within diverging regions typically occurs on only one side, with the location varying depending on pressure. According to our tests, cavitation occurs usually on one side of the nozzle and rarely occurs on both sides [25, 47]. At lower pressures, cavitation tends to initiate in the upper part of the diverging section, while it shifts to the lower part at higher pressures. This can be attributed to a similar phenomenon that is typically observed in micro-orifice channels in the presence of a jet flow downstream of the expansion. For the large expansion, any flow disturbance can make the flow deviate towards one side of the channel wall in the extension region. This deflection creates a confined region between the flow and wall. The suction induced by the flow leads to a significant pressure drop within this confined area. This pressure drop further pushes the jet towards the wall, hindering its ability to switch sides within the channel. Similar observations of flow behavior in Reactor 3 have also been reported in both experimental and numerical studies [38,51]. Vapor generation occurs due to pressure drops within the shear layer, with vapor development extending over a longer distance due to smoother pressure recovery. This phenomenon aligns with previous studies on attached cavitation inception [49].

Cavitation formation on the bottom surface has a distinct mechanism. Inception occurs due to local pressure drops exposing gas nuclei trapped on the surface. Gas bubbles originate from either

the free stream or remnants shed from attached cavities. This mechanism resembles the findings reported by Gluzman and Thomas [52]. The separated cavitation clouds originating from the sheet cavitation along the side wall can interact and merge with the cavities arising from the bottom surface. A significant observation lies in the presence of wavy structures within the cavitation zone developed on the bottom surface, originating from the formation of Kelvin-Helmholtz instabilities [39]. This suggests a strong correlation between the surface cavitation and local low-pressure zones within the core of vortices generated downstream of the sheet cavity.

In this shallow micro-venturi channel, the mechanism likely involves the exposure of surface nuclei trapped on the bottom surface to these shedding vortices downstream of the constriction. The low-pressure regions within the vortex cores create favorable conditions for the growth and expansion of these nuclei, leading to the formation of a cavitation zone on this surface. The only observable difference between low and high upstream pressure in Reactor 3 is more intense cavity formation on the surface at higher pressure.



Fig. 3. High-speed camera snapshots of various cavitating flow regimes within the reactors under different operating conditions: (a) R1L, (b) R2L, (c) R3L, (d) R1H, (e) R2H and, (f) R3H. To keep the figure clearer, all specific parts of the cavitating flow are marked in the snapshots. Flow is from left to right in all cases.

Fig. 4 provides schematic representations of cavitating flow patterns for different configurations and upstream pressures, offering a clearer visualization of cavitation development, while Fig. 5 presents time series for sequential snapshots inside the reactors at higher upstream pressures. In Reactors 1 and 2 (Fig. 4(a), (b), (c) and (d)), flow separation downstream of the expansion zone

generates a new shear layer. Under sufficiently large velocity gradients (as in Reactor 2 due to high mean velocity), this shear layer can act as an additional source of cavitation (the corresponding region is marked as "shear cavitation" in Figs. 4(c) and (d)). In Reactor 1 (Fig. 4(a), (b)), the shear layer in the third separation bubble is not strong enough to induce cavitation.

The dynamics within this shear layer closely resembles that observed in backward-facing step configurations (Figs. 4(c) and (d)), with a strong dependence on the incoming turbulent boundary layer characteristics [49-51]. Pressure fluctuations within this downstream shear layer create favorable conditions for cavitation inception. In addition to free nuclei carried by the flow, two other sources significantly contribute to cavitation within these shear layers. Fragmentation of twin cavities forming within the contraction nozzle region (2nd separation bubble) introduces cloud cavities into the downstream shear layer (represented by sparse and large dense clouds in Figs. 4(b), (c), and (d)). This is the primary source of sparse clouds and bubbles observed downstream of the nozzle in Fig. 4(b). Cavitation bubbles shed from the downstream shear layer in the 3rd separation bubble (more pronounced in Reactor 2, Figs. 4(c) and (d)) can re-enter into the shear layer due to reversed flow patterns.

In both Reactors 1 and 2, increasing upstream pressure and mean velocity intensifies cavitation within the nozzle while the 2^{nd} separation bubble in Reactor 1 (Fig. 2(b)) is extended (Reactor 2's 2^{nd} separation bubble reaches its maximum size at both low and high upstream pressures). Additionally, this increase strengthens shear layers both over and downstream of the nozzle. In Reactor 2 at high upstream pressure, the downstream shear layer is strong enough to sustain vapor phase within shed vortices, even after reattachment.

In Reactor 3, as discussed previously and shown in Figs. 4(e) and (f), increasing upstream pressure primarily intensifies cavitation on the surface. As it was discussed earlier, it can be detected from the patterns that the locations of surface cavitation should coincide with shed vortices downstream of the constriction region. An increase in the upstream pressure leads to an increase in the velocity and strength of shed vortices, which subsequently intensifies surface cavities. Collapse of these cavities is usually accompanied by the formation of dispersed bubbles moving upstream through the re-entrant jet, helping in the formation of new cavitation.



Fig. 4. Schematic presentation of cavitating flow patterns in micro-scale HC reactors: (a) R1L, (b) R1H, (c) R2L, (d) R2H, (e) R3L and, (f) R3H.

Fig. 5 presents time-series visualizations of cavitating flows in all reactors at high upstream pressure. In Reactor 1 (Fig. 5(a)), a small portion of the shed cavity over the nozzle joins the downstream shear layer as a sparse cloud of bubbles. The energy released from the collapse of these sparse bubbles induces weak pressure waves, initiating subsequent shedding. In Reactor 2 (Fig. 5(b)), condensation primarily occurs downstream of reattachment. While the energy released from this condensation significantly affects a portion of the downstream shear cavity, its influence on the nozzle shear cavitation is minimal. In this case, the higher mean velocity leads to a significantly higher shedding rate compared to Reactor 1, with more substantial condensation. In Reactor 3 (Fig. 5(c)), the attached cavity expands gradually, filling the near-wall region. Additionally, cavity packets emerge on the bottom surface due to localized low-pressure zones. Growth and collapse of these surface cavities are primarily synchronized with downstream vortices from the constriction region, which induce localized pressure drops. Collapse of surface cavities generates strong pressure waves, leading to the condensation of the attached cavitation (Fig. 5(c)). Comparing Figs. 5(a), (b), and (c), it can be observed that Reactor 2 exhibits the fastest shedding rate, while Reactor 1 displays the slowest and weakest shedding.



Fig. 5. Time sequence of cavitation development and dynamics for the (a) R1H, (b) R2H, and (c) R3H.

3.2. Mean characteristics of void fraction and spectral analysis

In this section, following the data processing techniques outlined in Section 2.5, the statistical characteristics of the void fraction were calculated and are presented in Figs. 6 and 7. In addition, Fig. 8 presents the power spectral density (PSD) of the void fraction for all investigated cases.

In Reactor 1, several notable observations can be made regarding the behavior of void fractions and cavitating flow patterns. Firstly, the intensity of the mean void fraction is found to be significantly higher within the nozzle compared to the extension region, as evident from Figs. 6(a) and 7(a). Furthermore, an increase in upstream pressure leads to an enhancement in the mean normalized (by nozzle width) void fraction length. Interestingly, higher void fraction fluctuations are observed in the extension region compared to the nozzle region in case R1H (Fig. 7(a)). As the upstream pressure increases (and cavitation number decreases), attached cavitation over the constriction grows along the wall, covering a substantial portion of its surface. Under these conditions, only a small portion of the attached cavity is shed from the end, merging with the shear cavity within the shear layer. The collapse of small bubbles in the extension region generates intermittent pressure waves, which subsequently initiate another shedding process in the attached cavity. Consequently, case R1H exhibits very small perturbations in the attached cavity, contrasting with the behavior of bubbles in the extension region (Fig. 7(a)). For the Reactor 2 configuration, mean void fraction and standard deviation of void fraction are presented in Figs. 6(b) and 7(b). Standard deviation void fraction reveals that large fluctuations occur primarily in the initial section of the shear layer for the low upstream pressure (case R2L), while they concentrate towards the end of the shear layer for the high upstream pressure (case R2H). This suggests continuous cavity shedding along the shear layer in the former and intermittent shedding at the shear layer end in the latter one (Figs. 6(b) and 7(b)). In Reactor 3, similar to Reactor 2, the regions with remarkable mean and standard deviations coincide with the shear layer (Figs. 6(c) and 7(c)). To further investigate the spectral content of the void fraction, a rectangular probe

(specified in yellow colors in Figs. 6 and 7) with constant size was used to analyze regions with the highest fluctuation levels.



Fig. 6. Mean value for void fraction (left) and standard deviation of void fraction (right) for cases (a) R1L, (b) R2L, and (c) R3L. Yellow rectangles show the probes used for spectral analysis.



Fig. 7. Mean value for void fraction (left) and standard deviation of void fraction (right) for cases (a) R1H, (b) R2H and (c) R3H. Yellow rectangles show the probes used for spectral analysis.

The PSD plots shown in Fig. 8 consistently demonstrate two or three peaks in both the low- and high-frequency regions. The low-frequency peaks range from 1.7×10^2 Hz to 1.5×10^3 Hz, while the high-frequency peaks fall between 0.25×10^4 Hz and 1.7×10^4 Hz. Based on previous studies [52, 53] the high-frequency peaks in the PSD could be associated with vortex shedding within the

shear layer behind the expansion, while the low-frequency peaks likely correspond to the shear layer flapping motion. The analysis reveals a relationship between upstream pressure and dominant frequency fluctuations in the contraction region of Reactor 1. An increase in the upstream pressure (from 11.5 bar to 13.5 bar, Figs. 8(a) and (b)) triggers a rise in the low-frequency peak and a decrease in the high-frequency peak, which implies a potential shift in the dominant shedding mechanism at higher pressures. In the case of Reactor 1, two dominant frequencies can be identified at 2×10^2 Hz and 2×10^3 Hz for the low upstream pressure value, with a pronounced high-frequency component. Conversely, the high upstream pressure case leads to a significantly larger PSD level at lower frequencies (around 2×10^2 Hz), indicating the dominance of low-frequency separation bubble motions. The spectral content of Reactor 1. This suggests an approximately order-of-magnitude increase in frequency in Reactor 2, likely due to the higher Reynolds number.

A key observation from the comparison between PDS levels of Reactor 3 and Reactors 1 and 2 lies in the significantly sharper distribution PSD levels in Reactor 3 (Figs. 8(e) and (f)), indicating a higher concentration of vapor shedding at specific frequencies. This suggests a more regular shedding pattern in Reactor 3 compared to the more uniform distribution observed in Reactors 1 and 2. As previously discussed, this difference in shedding behavior can be attributed to the differences in shedding mechanisms. In Reactor 3, periodic cavitation shedding within the channel leads to small variations in shedding frequencies. Conversely, the intermittent shedding in the transition regime in Reactors 1 and 2 (Figs. 5 (a) and (b)) leads to a wider range of shedding frequencies. The PSDs of the shear layer downstream of the nozzle follow the trends in the cavitation regimes within the nozzles in each configuration since cavitation shedding in this region is modulated by the upstream shedding within the nozzle. This influence is particularly evident in the low-frequency range, potentially linked to the flapping motions of the separation bubbles.



Fig. 8. PSD value of void fraction in the probes specified in Figs. 6 and 7 for cases (a) R1L, (b) R1H, (c) R2L, (d) R2H, (e) R3L and (f) R3H.

3.3. Chemical Effects of cavitation determined in Reactors 1, 2 and 3

The results given in Fig. 9 show the formation of the two measured SA products 2,3-DHBA and 2,5-DHBA in all three micro-scale HC reactors investigated after 1, 3 and 5 HC cycles. For Reactor 2, three experimental repetitions were performed, with error bars presenting their standard deviation. The concentrations of both SA products increase with the HC cycles, and the sum of the concentrations of the SA products tends to be higher at lower upstream pressures in all three cases. In addition, 2,3-DHBA products form to a greater extent than 2,5-DHBA. Although it was shown that 'OH interact with compounds like SA, however, the studies demonstrating higher concentrations for 2,5-DHBA compared to 2,3-DHBA in AC and HC, while Jen et al. [54] showed higher concentrations of 2,3-DHBA over 2,5-DHBA in a reaction with hydrogen peroxide. This indicates the influence of oxidation process and experimental conditions, i.e., temperature, pressure and flow pattern, on the production rate of the products which necessitates the importance of further investigating the cavitation-induced oxidation processes.

The highest amount of SA products after 5 HC cycles is obtained from the micro-orifice reactor (Reactor 2) at both upstream pressures, followed by Reactor 3 and Reactor 1. In addition, a more linear trend in the formation of products with increasing cavitation cycles can be observed in the micro-orifice reactor (Reactor 2) compared to other reactors. The difference in the sum of SA products between the upstream pressures seems most pronounced in Reactors 1 and 2, where the highest values are reached at the low upstream pressure. In Reactor 3, on the other hand, the differences in the results are not so tangible. Furthermore, in Reactors 1 and 3, the product 2,5-DHBA is less at higher upstream pressure at all HC cycles. In the case of Reactor 2, the lower extent of 2,3-DHBA formation at higher upstream pressures leads to a lower sum of SA products. To explain this trend in detail, further experiments and analyses are required as the future research perspective.



Fig. 9. Concentrations $[\mu g/mL]$ of the two main SA products formed in a long diaphragm (Reactor 1), micro-orifice (Reactor 2) and micro-venturi (Reactor 3) reactors at low and high upstream pressures using 300 mg/L SA. Error bars for Reactor 2 present standard deviation of three experimental repetitions.

When comparing chemical effects based on SA products, it can be recognized that the number, size and distance between individual cavitation bubbles are important for 'OH formation. Although it is expected that cavitating flows at higher upstream pressures would lead to increased chemical effects as shown in the literature [16], our results present the opposite trends as already shown by [19]. The higher upstream pressures directly affect the number of the generated cavitation bubbles and their collapse, which should consequently increase the amount of local hot spots as well. The results, however, suggest that cavitation conditions achieved at lower upstream pressures lead to more continuous generation of chemical effects. In the tested reactors, the intensity (Fig. 6) and periodicity (Fig. 7) of the formation and collapse of cavitation bubbles and flow patterns vary depending on the reactor configurations and pressure conditions upstream of the reactor's nozzle. The observation of cavitating flow patterns in all three reactors (Fig. 3) reveals that cavitating flow structures have more spatiotemporal nature at high upstream pressures than at lower upstream pressures. This indicates that it is likely for bubbles to merge into larger bubbles under these conditions (due to lower static pressure in the extension channel region), which consequently results in fewer or less intense cavitation events due to cushioning effects leading to lower 'OH formation at higher upstream pressure. As a result, chemical effects favor cavitation conditions with less cavitation intensity.

Reactor 2 exhibits more turbulent flow conditions and more intense and periodic cavitation at higher pressure conditions compared to Reactor 1 (at both pressures) (Figs. 3 and 4). These conditions could lead to enhanced mass transfer, exposing a larger amount of SA to the generated 'OH, which promotes the formation of 2,3-DHBA and 2,5-DHBA. Furthermore, the results related to Reactor 2, showing the highest chemical yield (Fig. 9), distinctively support the importance of the number, size, and distance between the individual cavitation bubbles. As previously mentioned, sufficiently large velocity gradients in Reactor 2 create an additional shear layer (Figs. 4(c) and (d)), causing more cavitation events and better dispersion of individual cavitation bubbles, which cause more chemical effects. In addition, the cavitating flow in micro-scale HC reactors can exhibit the Kelvin-Helmholtz instability at the interfaces between the liquid and vapor phases [39]. This instability could also enhance mixing at the micro-scale and could thus facilitate chemical reactions [54]. Giving the configuration difference between the Reactor 3 and Reactors 1 and 2, the slower pressure recouperation downstream of the constriction nozzle could be the reason for the observed lower chemical yield of Reactor 3 in comparison to Reactor 2. By considering cavitating flow morphology conditions in Reactor 3 (Figs. 3 and 8(e) and (f)), it can be observed that shedding of cavitation structures from the attached cavitation bubble occurs at different frequencies. At low upstream pressure, the shedding frequency is approximately two times higher than at high upstream pressure.

As can be seen from Fig. 10, there is a clear difference in the formation of SA products between micro- and macro-scale reactors. A detailed description of the macro-scale reactor, including dimensions, flow rates, fluid velocity, and the operating conditions (a pressure difference of 7 bar, resulting in a processing time of 5.5 s/pass for 1 L of sample), is provided in [20]. A higher yield of SA products is attained in the micro-scale reactor (Reactor 2) than in the macro-scale reactor from the study of Zupanc et al.[55]. Similar amount of SA products can be achieved after 5 HC cycles (0.510 μ g/mL) in the micro-scale reactor compared to 164 cycles required in the macro-scale reactor (0.481 μ g/mL). Furthermore, for the macro-scale reactor, it can be seen that after 655 cavitation cycles, the increase in SA product formation does not follow a linear trend, which was included in detail (Zupanc et al. [55]). One of the reasons for the observed difference in the oxidation of SA could be the larger surface area to volume ratio in the micro-scale reactor and the

resulting higher mass transport rates and reaction kinetics. Another possible explanation could be linked to better mixing, which is achieved in the micro-scale reactor and could contribute to the transport of the reactive species formed at the bubble-liquid interface into the bulk solution, facilitating their reaction with SA. The same mechanism was also observed when cavitation was combined with external oxidants to generate higher amounts of radical species, leading to their better dispersion [55].



Fig. 10. Comparison of the sum of the two main SA products formed during micro-scale cavitation (Reactor 2 in the current study) compared to macro-scale cavitation investigated in a previous study [55], by number of cavitation cycles.

As detailed in our previous work [19], we have analyzed the energy requirements of the reactors. To account for the inherently lower flow rates of micro-scale devices, we considered a parallel array of 100 micro-scale reactors, a configuration achievable through various design and packaging strategies. Based on mean values from our experiments, we compared five cycles in the micro-scale reactors (R1, R2, and R3) with 164 cycles in the macro-scale reactor, as these conditions yielded comparable SA production. Our analysis indicates the potential for significant time and energy savings with the parallel micro-scale reactor approach. For instance, 100 parallel R2 reactors require only 0.06 of the time and 0.054 of the energy compared to the macro-scale reactor to produce 1 liter of solution. While micro-scale reactors offer these advantages, challenges such as clogging and low flow rates exist. As discussed in [36] clogging can be mitigated with appropriate filters, and parallelization addresses low flow rates. We also acknowledge the potentially higher fabrication costs and complexity associated with micro-scale devices, requiring specialized infrastructure and equipment.

	100×R1	100×R2	100×R3	RMac
	(5 cycles)	(5 cycles)	(5 cycles)	(164 cycles)
Flowrate [ml/s]	92.5	82.5	49	181.8
Time per Liter [s/L]	54	60.6	174.8	902
Pressure[bar]	12.5	11	11.5	7
Head[m]	127.5	112.2	117.3	71.4
Input Energy [kJ/L]	6.375	5.610	5.865	117.1

Table 2. Time energy evaluation for parallel micro-scale HC reactors vs a macro-scale HC reactor.

4. Conclusions

This study investigated the chemical effects of micro-scale hydrodynamic cavitation (HC) bubble collapse using salicylic acid (SA) dosimetry. We characterized cavitating flow patterns in three microfluidic reactor configurations: long diaphragm, micro-orifice, and micro-venturi.

The micro-orifice reactor demonstrated superior cavitation performance compared to other reactors, attributed to intensified flow dynamics and shedding mechanisms. Power spectral density (PSD) analysis revealed a strong correlation between dominant frequencies and Reynolds number. Notably, at comparable upstream pressures, the micro-orifice reactor exhibited dominant frequencies approximately an order of magnitude higher than those observed in other reactors.

Upstream pressure had a significant impact on cavitation regimes. Lower upstream pressures resulted in minor cavitation, while higher pressures led to intensified cavitation shedding. With 2,3-DHBA, increasing the upstream pressure correlated with its decreased SA production across all three reactors. This aligns with our previous work [19], which demonstrated higher cavitation yields in the minor cavitation shedding regime compared to the intense shedding regime.

A striking difference in efficiency was observed between micro- and macro-scale reactors. The micro-scale HC reactors achieved comparable concentrations of SA products in just 5 cycles, whereas the macro-scale HC reactor required 164 cycles. This demonstrates significantly reduced processing time and energy requirements at the micro-scale, highlighting the potential of microfluidic systems for rapid and efficient production of SA products. The superior performance of micro-scale reactors can be attributed to several factors. These include the higher surface-to-volume ratio and localized concentrations of reactive species inherent in microfluidic systems. Furthermore, the increased bubble density and collapse events per unit volume in micro-scale cavitation likely enhance reactant interaction at the vapor interfaces. We hypothesize that the increased number of smaller bubbles in micro-scale cavitation leads to a larger total water vapor interface area, enhancing the interaction between reactants and the products of cavitation collapse.

Several avenues for future research emerge from this work. Further investigation of geometric optimization is crucial to understanding the interplay between microchannel design (nozzle

geometry, hydraulic diameter) and bubble dynamics, ultimately influencing radical yields. Exploring surface modifications or hybrid excitation methods is necessary to overcome nucleation limitations in smaller channels. Critically, further investigations using time-resolved diagnostic tools is required to validate the hypothesis that the collapse of clusters of micro-scale bubbles, rather than large bubbles, is more efficient. These studies are essential to confirm the claim of enhanced micro-scale bubble collapse efficiency and fully elucidate the underlying mechanisms. Finally, expanding the range of target compounds and integrating cavitation with other advanced oxidation or catalytic methods holds promise for scalable chemical synthesis.

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