NUMERICAL INVESTIGATION OF THE COUPLING EFFECT OF HEAT AND VIBRATION ON TRIGGERING THE RELEASE KINETICS OF DOUBLE EMULSION FOR DRUG DELIVERY

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1. INTRODUCTION

The core-shell structured microcapsule formed from double emulsions has been attracting growing attention, given its capability of effectively encapsulating, transporting, and releasing functional materials. In addition to its wide applications in the food and beverage industry [1], cosmetic components [2], chemical catalyst reactions [3] et al., and its ability to provide an enclosed stable microscale environment also makes it a promising candidate for drug delivery [4]. Also, a large body of literature can be found illustrating different methods triggering the release of functional compounds from such core-shell microcapsules, including pH change [5], acoustical stimulus [6], and infrared laser [7].

A recent study by Ren et al. [8] investigated the release kinetics of such microcapsules fabricated of thermally triggered phase-changing material. The study provided a novel approach for the use of core-shell structured microcapsules in drug delivery, yet several questions arose. It was showed that microcapsules with small thickness require less time to change phase, yet the mechanical property of the shell may compromise due to the small thickness, which could lead to unintended shell break. Moreover, due to the relatively low thermal conductivity of human tissue [9], such methods might be limited to the superficial body parts of lesion.

2. AIMS AND GOALS OF THIS WORK

This work aims to explore a heat-vibration coupled way of triggering the phase-change of the core-shell structured microcapsules for the potential drug delivery application to overcome the aforementioned limitations. The study will focus on several core-shell structured microcapsules flowing inside a portion of the arbitrarily curved tube-shaped flow field (resembling a portion of the blood vessel). These scenarios of interest will be investigated numerically:

- The possible mechanisms of shell failure due to the small thickness in the flow field with various flow rates.
- The effects of applying pressure fluctuations on the tube wall on the deformations & break of the microcapsule under various flow rates.
- The combined effects of heat and applied pressure fluctuations with different thermal conditions and pressure level & frequencies under various flow rates.
- The above cases would be carried out with different shell materials.
- The coupling effect of the blood vessel wall & the flow field under applied fluctuations will also be investigated.

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3. NUMERICAL MODEL

To achieve the above-mentioned goals, a 2D numerical model was developed to investigate the fluid-solid interaction between the flow field and the microcapsule. At the current stage, the heat and external vibration coupling is not yet taken into consideration.

3.1 Governing Equations and Materials

To better illustrate the dramatic difference between the two setup, an aggressive flow speed of 0.2 m/s was adopted in this work. Due to the miniature scale of the flow field and the relatively small flow velocity (take for instance, 0.2 m/s, liquid water), the Reynolds number of the flow is calculated as follows:

$$Re = \frac{\rho VL}{\mu} = \frac{998.29kg/m^3 \times 0.2m/s \times 1mm}{1.002 \times 10^{-3} N \cdot s/m^3} \approx 200$$

And considering the scale of the inlet flow velocity from 0.03-0.2 m/s, the Reynolds number for this configuration would fit into the range of 30 to 200, thus it is safe to consider the flow to be laminar under all operating conditions. The basic equations governing the fluid motion are mass and momentum conservation:

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (p\vec{v}) = 0$$

$$\frac{\partial}{\partial t}(\rho\vec{v}) + \nabla(\rho\vec{v}\vec{v}) = -\nabla \mathrm{p} + \nabla \cdot (\bar{\bar{\tau}}) + \vec{F}$$

Where ρ stands for the density of the fluid, p is the static pressure, $\bar{\bar{\tau}}$ is the stress tensor, and $\vec{F}$ is the external body forces (for instance from the interaction with the solid structure), respectively.

The Solid material was assumed to be linear elastic. This work considers the mechanical properties of polydimethylsiloxane (PDMS), and the density, Young's modulus and Poisson's ratio adopted in this work are 970 kg/m^3, 750 kPa, and 0.49, respectively. The Bond number of the capsule in the current setup was calculated as:

$$Bo = \frac{\Delta\rho g l^2}{\sigma} \approx 0.00001 \ll 1$$

Where g stands for the gravitational acceleration, l stands for characteristic length of the capsule (diameter), $\Delta\rho$ stands for the density difference between the PDMS and liquid water, and σ for the surface tension of the capsule.

3.2 Geometry Setup and Meshing

The microchannel with 10 mm in length, and 1 mm in width was applied in the numerical study. A microcapsule with an outer diameter of 0.25 mm and a shell thickness of 0.1 mm was adopted in the model. The microcapsule was initially located with the distance between the centre of the capsule and the channel inlet to be 1.5 mm, as shown in Figure 1. The encapsulated fluid is set to be liquid water as well. The density and dynamic viscosity of liquid water adopted in this work was $998.29kg/m^3$ and $1.002 \times 10^{-3} kg/m \cdot s$, respectively, at temperature of 293.15K (20°C). The mesh was generated within Comsol, with element sizes ranging from 0.003 mm to 0.67 mm. Inflation was applied near boundaries with a maximum growth rate of 1.3. The curved microchannel with arbitrary value of radius of curvature was adopted to mimic a more realistic environment of blood flow inside a section of blood vessel, and the results will be compared with those in the straight microchannel which serves as a

baseline. A time dependent study of Fluid-Structure Interaction was conducted, with a time range of 0 to 0.03 second, at a time step of 0.005s. The microcapsule's initial position was set to 1.5mm from the inlet (location of the centre of the capsule), and would move downstream along the microchannel. FSI

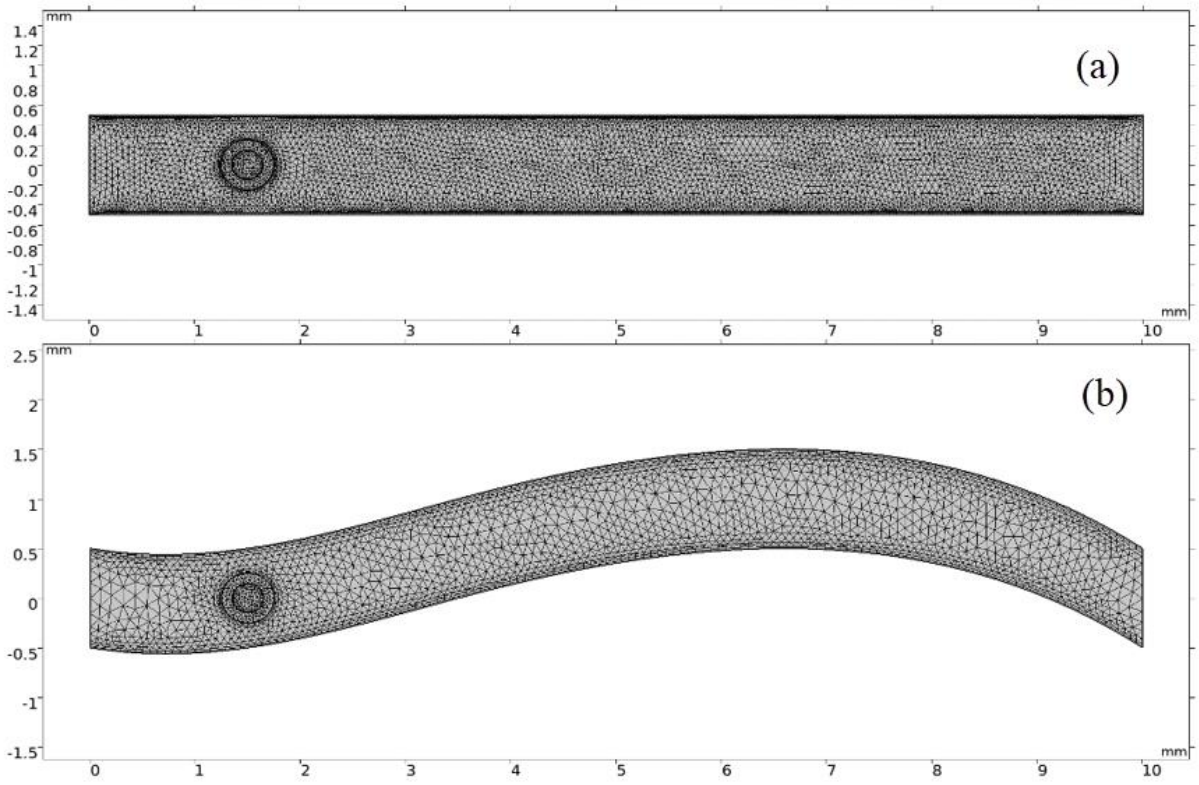

Figure 1 Geometry and mesh of the model of (a) straight microchannel and (b) curved microchannel

couplings appear on the boundaries between the fluid and the solid. The Comsol Fluid-Structure Interaction interface uses an arbitrary Lagrangian-Eulerian (ALE) method to combine the fluid flow formulated using an Eulerian description and a spatial frame with solid mechanics formulated using a Lagrangian description and a material (reference) frame. In the straight and curved microchannel configurations, at the end of the time range (0.03s), both microcapsule had travelled for about 7 mm away from their initial locations along the axial direction.

4. RESULTS AND DISCUSSION

The von Mises Stress on the capsule shell was observed. To achieve consistent initial values when conducting the Fluid-Structure Interaction analysis, Backward Euler method was implemented for initialization, and consequently unphysical stress spikes were observed in both configurations. To circumvent this problem, results from 0 to 0.004s were discarded. According to an analytical solution for fully developed laminar pipe flow from White et al. [10]:

$$u_{max} = \left(-\frac{dp}{dx}\right)\frac{R^2}{4\mu}$$

Where for a fully developed pipe flow, the u_{max} equals to twice of the unified inlet velocity, and R stands for the radius of the flow field and μ for the viscosity of the fluid; $\frac{dp}{dx}$ indicates how static pressure of the flow field changes along the axial direction. From the outlet zero gauge pressure boundary

condition it can be calculated that the static pressure inside the channel near the middle section of the channel is

$$p_0 = 3.209\ Pa.$$

An equation for the calculation of the hoop stress for a thin shell sphere proposed by Ozturk, Y. et al [11] was adopted for the current configuration:

$$\sigma_H = \frac{p_0 r}{2t} \approx 4$$

Which corresponds to a von Mises stress of the same amount, is in the same scale of the numerical outcome. The simulated results is thus considered acceptable.

Three key time frames were chosen to show the stress distribution over the microcapsule shell, namely around 0.006s, around 0.015s and 0.02s. It can be observed that in both configurations, the microcapsule stays relatively near the centreline of the flow field, and the horizontal displacement of the microcapsule was considerably close, as indicated by the X-axis of each individual plot.

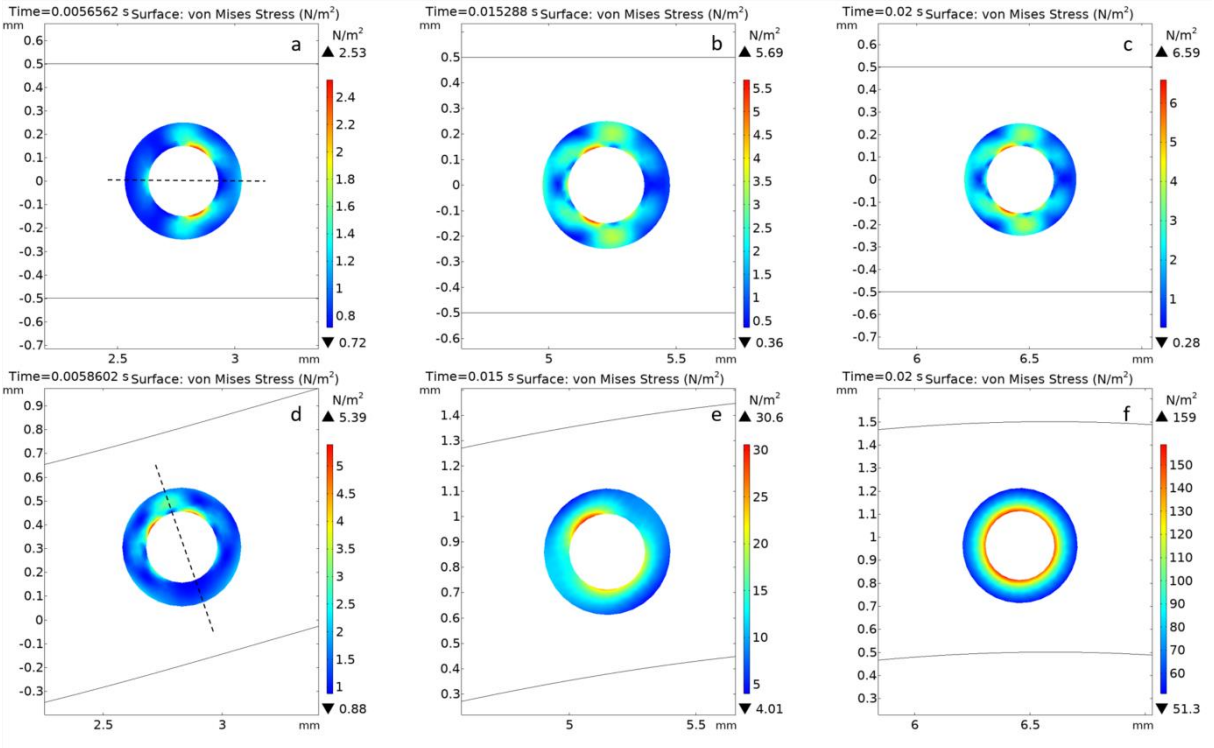

Figure 2 Time lapse images of von Mises Stress distribution over microcapsule shell at flow velocity of 0.2 m/s, in the straight microchannel (a-c), and the curved microchannel (d-f), lines were drawn in each plot to indicate the channel walls

The stress distribution over the capsule shell at different time in a straight microchannel and a curved microchannel are shown in Fig.2a-c, and Fig.2d-f, respectively. It was observed that at similar time frame, the stress information were quite different. At the first time frame, a symmetrical stress distribution can be observed in the straight channel configuration (Fig.2a) about the capsule moving direction. Yet possibly due to the curvature of the channel, in the curved channel configuration, the stress on the capsule shell tends to be distributed towards one side, demonstrating a symmetrical distribution perpendicular to the capsule moving direction (Fig2.d). As the microcapsule continue to move downstream, it was observed that in the straight microchannel setup, the concentration location of the stress oscillate once from near the moving direction side of the capsule to the opposite side (Fig.2a,

Fig.2b), and at around the time frame of 0.015s, a stable condition was achieved, and the stress distribution was consistent afterwards, with a slight accumulation of maximum stress. Yet for the curved channel configuration, the observed stress accumulation process was in a much more dramatic manner, with a maximum stress of over 30 N/m^2 (Fig.2e), which was 4 times larger than that of the corresponding straight channel configuration, and this trend continues as the microcapsule moves farther downstream. Moreover, unlike the baseline setup, the stress distribution was eventually nearly centrosymmetric for the capsule in the curved channel. The reason causing this difference is not yet understood, and further investigations are required. The same simulation under a more realistic flow speed of 0.08 m/s, resembling the flow rate of human blood vessel of similar size is to be conducted in the future.

5. CONCLUSION

A 2D numerical investigation regarding the stress distribution of the shell of a microcapsule was conducted in both straight and curved microchannels at the same flow speed of 0.2m/s. It was observed that:

- In both configurations, symmetrical patterns of the stress distribution were observed prior to the 0.015s time frame;
- The symmetrical stress pattern is affected by the curvature of the microchannel, and the stress accumulation effect observed would vary subject to the geometrical curvature of the microchannel;
- The stress in the shell would tend to distribute evenly when the capsule is in a reciprocally curved channel under the current settings.

It is worth noting that this work is still at a very early stage, and many interesting topics are yet to be discussed. For one instance, the explanation of the difference in previously discussed stress distributions is to be addressed. Energy and heat transfer is not yet taken into account. The present investigation focuses on the interaction between the fluid and a microcapsule inside the flow field constrained by a rigid channel, it is also of importance to model the deformation of the blood vessel wall and its effects on the flow field as well as the deformation of the capsule in the future work.

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