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Procedia IUTAM 16 (2015) 106 – 114
Procedia IUTAM
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IUTAM Symposium on Dynamics of Capsules, Vesicles and Cells in Flow

Characterization of capsule membrane properties using a microfluidic photolithographied channel: consequences of tube non-squareness.

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Abstract

An inverse analysis of the flow of capsules in a square section microfluidic channel has been proposed to evaluate the elastic modulus of the membrane of microcapsules. It is based on the comparison of the capsule deformed profiles measured experimentally with the ones computed numerically in the same flow situation. Experimentally, the microchannel is never exactly square. The objective of this paper is to evaluate the intrinsic error, which is made by analyzing the flow of a capsule in a slightly rectangular channel by means of the numerical results obtained in a perfectly square channel. This is done by computing exactly the flow of a capsule in slightly rectangular channels and comparing the results with those obtained in square channels. It is found that, within a rectangular channel with an appropriately defined deviation from squareness of 5%, the capsule deformed profiles are close to those in a square channel, and that the inverse analysis procedure can be used.

Peer-review under the responsibility of the organizing committee of DYNACAPS 2014 (Dynamics of Capsules, Vesicles and Cells in Flow).

Keywords: Inverse Analysis method, Capsule deformation, Robustness to uncertainty

1. Introduction

Microcapsules consist of liquid drops surrounded by a thin elastic membrane that separates the inner fluid from the outside medium. In addition to being a simple model of red blood cells, such particles can be artificially produced for diverse applications in pharmaceutics, cosmetics or the food industry. The mechanical properties of the membrane play an essential role in the control of deformation and breakup. However, capsules are usually fragile and small with diameters of order of a few micrometers, so that specific measurement techniques must be devised to evaluate the membrane mechanical properties.

Recently, a new microfluidic method has been proposed to measure the mechanical properties of a population of initially spherical artificial microcapsules. A dilute suspension of such microcapsules is flowed into a cylindrical capillary tube with inner diameter of the same order as the capsule one. Under the combined effect of confinement and

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Peer-review under the responsibility of the organizing committee of DYNACAPS 2014 (Dynamics of Capsules, Vesicles and Cells in Flow).
doi:10.1016/j.piutam.2015.03.013

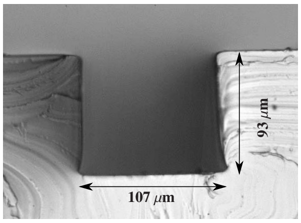

Fig. 1. Microphotograph of a channel cross-section with design specification $100 \times 100\,\mu\text{m}^2$ square section.

viscous stresses, the capsules deform. A high-speed camera mounted on a microscope is used to measure the velocity and deformation of the initially spherical capsules. A numerical model of a flowing capsule has been designed[1] and a database has been created which gives the capsule deformation as a function of the flow strength, the membrane mechanical properties and the confinement ratio. An inverse analysis technique then allows one to find the membrane elastic modulus from the capsule deformation under flow. This technique has been successfully applied to characterize capsules with a polymerized ovalbumin membrane[2].

With the growing amount of microfluidic applications, such as in-line fabrication of microcapsules[3,4,5], it is convenient to be able to perform in-line characterization. The measurement technique has thus been extended to square-section microfluidic channels. To analyze the data and proceed with the inverse analysis technique, a database was created[6] using the model of the flow of a capsule in a square-section channel[7].

The most common method used to make microfluidic channels is PDMS (polydimethylsiloxane) replica molding[8]. It consists of pouring and curing PDMS onto a silicon wafer with channel network etched on a resin layer. The PDMS is peeled off and the resulting inprint is bound to a glass plate to create a microfluidic channel, the geometry of which depends on that of the mold. The depth $2h$ of the channel is controlled by the thickness of the resin deposit, which is achieved by spin coating. The width $2w$ is determined by the precision of the photolithography mask used to make the resin mold. Altogether, the channel size specifications are often fulfilled within a few micrometers. For small channels (e.g. a square channel with a specified $100 \times 100\,\mu\text{m}^2$ section) the fabrication errors can lead to significant distortions of the section geometry as shown in Fig. 1. In the pioneering work of Hu *et al.*[6], the channel section was assumed to be a square with the same surface area as the actual section. The side of this square was then used as the reference length scale to normalize the experimental data and search the square channel database.

The question which arises then pertains to the precision of the inverse analysis in a slightly rectangular channel, knowing that the database corresponds to a perfectly square channel. In order to answer this question, we perform a numerical study of the flow of a capsule in slightly rectangular channels and compare the results to the ones that are obtained in a square channel with the same surface area. Finally, we perform an inverse analysis on the rectangular channel results and show how the channel geometry affects the precision of the parameter values that are thus obtained.

2. Problem statement and numerical method

2.1. Problem description

An initially spherical capsule (radius a) flows along the z-axis of a microfluidic channel of rectangular cross-section $2h \times 2w$ in the perpendicular xy-plane (Fig. 2). The deviation from squareness of the channel cross-section is defined as

$$\delta = \frac{w-h}{w+h}. \tag{1}$$

In this study we consider channels, which are either wider than deep ($h < w, \delta > 0$) or deeper than wide ($h > w, \delta < 0$) with $\delta = \pm 5, \pm 10$ and $\pm 15\%$.

The interior and exterior of the capsule are incompressible Newtonian fluids with the same density ρ and viscosity μ. The thin membrane of the capsule is an impermeable hyperelastic isotropic material with surface shear modulus G_s and area dilatation modulus K_s. As the membrane thickness is negligibly small compared to the capsule dimensions, the membrane is treated as a hyperelastic surface devoid of bending stiffness. The in-plane deformation is then mea-

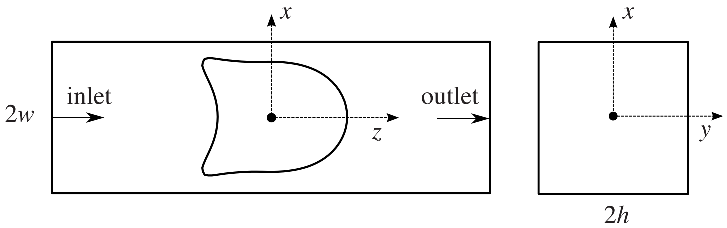

Fig. 2. Prismatic channel with axis Oz. The cross-section is rectangular with dimensions $2h \times 2w$.

sured by the principal extension ratios λ_1 and λ_2. Owing to the combined effects of hydrodynamic forces, boundary confinement and membrane deformability, the capsule can be highly deformed as shown in Fig. 3. Consequently the choice of the membrane constitutive law is important. In this study, we consider the widely used neo-Hookean law, which models the membrane as an infinitely thin sheet of a three-dimensional isotropic and incompressible material. The principal Cauchy in-plane tensions (forces per unit arc length of deformed surface curves) are expressed as[9]

$$\tau_1 = \frac{G_s}{\lambda_1 \lambda_2}\left[\lambda_1^2 - \frac{1}{(\lambda_1\lambda_2)^2}\right] \text{ (likewise for } \tau_2). \tag{2}$$

The membrane dilatation modulus K_s is then given by $K_s = 3G_s$. The flow Reynolds number is assumed to be very small, so that the internal and external liquid motions satisfy the Stokes equations. Far from the capsule, the flow field is undisturbed by the presence of the capsule. For each channel geometry, we implement the corresponding analytical solution[10] of the velocity profile with mean velocity V. Apart from the capsule membrane mechanical properties, the other main parameters of the problem are the size ratio a/h between the radius of the initially spherical capsule and the channel depth, the channel aspect ratio δ and the capillary number

$$Ca = \mu V/G_s, \tag{3}$$

which measures the ratio between viscous and elastic forces.

2.2. Numerical model

The motion and deformation of a capsule flowing in a rectangular channel under Stokes conditions is solved by means of the method developed by Hu *et al.*[7]. The numerical model has already been well documented and is just briefly explained here. The problem is solved by coupling a boundary integral method to compute the fluid flow and a finite element method to compute the membrane mechanics. The equations are solved in a reference frame moving with the capsule center of mass, so that the capsule remains centered in the tube domain. The advantage of the procedure is that only the boundaries of the flow domain are discretized. The capsule mesh is composed of 1280 P_2 elements and 2562 nodes. The mesh of the external tube walls is generated using P_1 elements with Modulef (INRIA Rocquencourt, France) and is refined in the central portion of the channel, where the capsule is located[7]. Three different channel geometries are considered corresponding to $\delta = 5\%$ (3020 nodes and 5998 elements), $\delta = 10$ and 15% (3340 nodes and 6634 elements). The results are obtained with a non-dimensional time step $\Delta t \times V/h = 1 \times 10^{-4}$.

All the following results pertain to the equilibrium state. At steady-state, the membrane and the internal fluid translate as a rigid body. This means that assuming the same value of viscosity for the internal and external liquids does not limit the validity of the results, as the viscosity ratio only influences the time the capsule needs to reach a steady state. For a given channel aspect ratio δ, the model inputs are the capillary number Ca, the size ratio a/h and the membrane law. The model outputs are the capsule centroid velocity v_o and the steady deformed capsule shape. In the experimental set-up, all we can observe is the projection of the deformed profile onto the xz-plane (Fig. 3a). Correspondingly, we plot the deformed capsule profile in the plane $y = 0$, as shown in Fig. 3b, where the overall capsule deformation is quantified by the maximum length L/h in the z-direction and the parachute depth L_p/h. An apparent capsule volume is defined as the volume of the cylinder with height $2h$ and basis the surface area S of the xz capsule profile. The apparent capsule radius is then $a_{app} = 3\sqrt[3]{2hS}/(4\pi)$. The relation between the apparent and actual radius of the capsule can be computed numerically and used to infer a from the measurement of a_{app}[6].

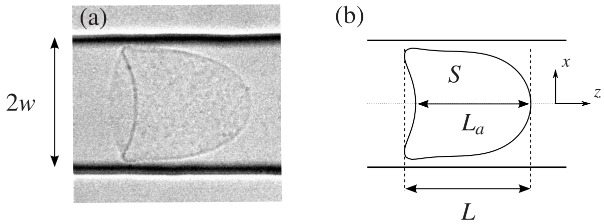

Fig. 3. (a) Experimental capsule profile in a specified $50 \times 50\,\mu\mathrm{m}^2$ channel. (b) Numerical deformed profile in the plane $y = 0$, $L_p = L - L_a$, S is the contour surface area.

2.3. Comparison between the rectangular and square channel results

The results obtained in the slightly rectangular channels are compared to the corresponding ones in a square channel following the method proposed by Hu et al.[6]. We first define the side 2ℓ of the equivalent square channel by

$$2\ell = \sqrt{4wh} = 2h\sqrt{\frac{1+\delta}{1-\delta}}, \tag{4}$$

which corresponds to the side of a square with the same area as the rectangular section. We then compare capsules with corresponding confinement ratios a/ℓ in the square channel and a/h in the rectangular one. The two ratios are related by

$$a/\ell = a/h\sqrt{\frac{1-\delta}{1+\delta}}. \tag{5}$$

3. Results

3.1. Effect of δ on capsule profiles for $a/\ell = 1$

We first investigate the effect of Ca and δ on the deformation of a capsule with confinement ratio $a/\ell = 1$. We focus on the profiles in the $y = 0$ plane, which are the ones that can be observed experimentally. In Fig. 4, the dotted lines correspond to a square channel and the full lines to the slightly rectangular channel with a given value of δ. We first consider a rectangular channel with $\delta > 0$ that is therefore wider and shallower than the square one (Fig. 4a,b,c). For a slight distortion of the channel ($\delta = 0.05$), the boundaries of the two channels are very close, and not surprisingly, the deformed profiles of the capsules are almost superimposed (Fig. 4a). For more distorted channels ($\delta = 0.1$ or 0.15), the profiles in the equivalent square channel and in the rectangular one are quite distinct (Fig. 4b,c). The capsule is less deformed in the rectangular channel than in the square one, because it is less constrained by the lateral walls. For $\delta = 0.15$, the parachute depth L_p, which is an important criterion in the inverse analysis, is greatly underestimated even for the fairly large value $Ca = 0.08$.

In Fig. 4d,e,f, we consider the complementary case, when the channels are narrower and deeper than the equivalent square channel ($\delta < 0$). For the slight distortion of the channel ($\delta = -0.05$), the square and rectangular profiles are again very close. For larger distortions ($\delta = -0.1$ or -0.15), the capsule is more deformed in the rectangular than in the square channel. For $\delta = -0.15$ and $Ca = 0.02$, the back of the capsule is undergoing the transition from a convex to concave (parachute) shape; it experiences buckling because it is under compression.

The relative difference in profile geometry between the square and rectangular channels may be measured by

$$\Delta L/\ell = |L_{square} - L_{rectangle}|/\ell \tag{6}$$

with a similar expression for $\Delta L_p/\ell$. These relative length differences are plotted as a function of δ for different values of Ca in Fig. 5. We note that, for $|\delta| \leq 5\%$, the differences in total length $\Delta L/\ell$ and in parachute depth $\Delta L_p/\ell$ remain less than 0.04, which is the typical experimental tolerance. For larger deviations from squareness ($|\delta| \geq 10\%$), the differences in characteristic lengths increase sharply.

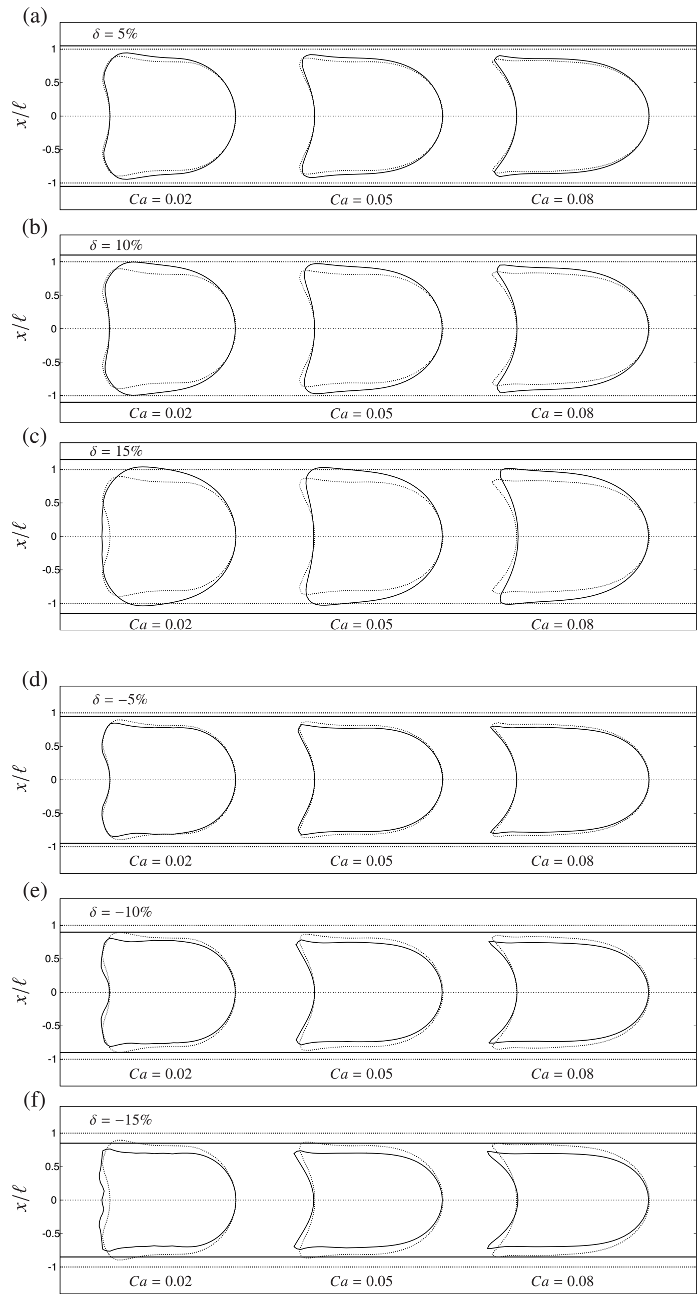

Fig. 4. Deformed profiles of a capsule in the plane $y = 0$ for a square (dotted line) or slightly rectangular channel (full line) with $a/\ell = 1$. The horizontal lines correspond to the channel walls. (a) $\delta = 0.05$, $a/h = 1.05$; (b) $\delta = 0.1, a/h = 1.1$; (c) $\delta = 0.15, a/h = 1.16$; (d) $\delta = -0.05$, $a/h = 0.95$; (e) $\delta = -0.1, a/h = 0.9$; (f) $\delta = -0.15, a/h = 0.86$.

3.2. Effect of confinement ratio for δ = 5%

We now focus on $\delta = 5\%$ for which we study the effect of confinement ratios a/ℓ varying from 0.95 to 1.1 (Fig. 6). For the smallest capsule ($a/\ell = 0.95$), the superposition of the two profiles is almost perfect and the section

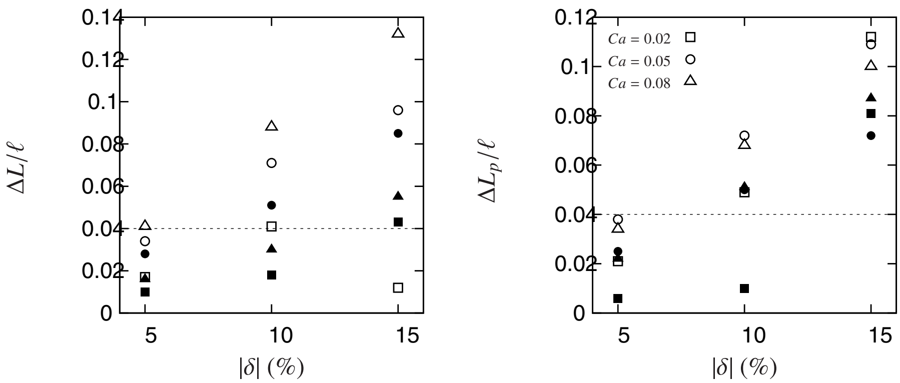

Fig. 5. Characteristic lengths differences as a function of δ, for different Ca and $a/\ell = 1$. Open symbols: $\delta > 0$, filled symbols: $\delta < 0$.

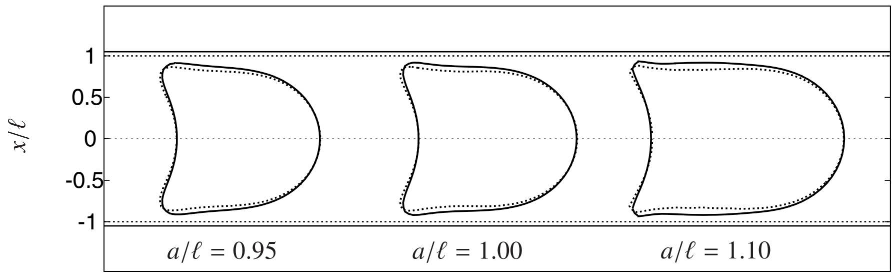

Fig. 6. Effect of a/ℓ on the deformed profile in the plane $y = 0$ for a capsule in a square (dotted line) or slightly rectangular channel (full line) with $\delta = 0.05$ and $Ca = 0.05$.

deviation from squareness has a negligible effect. The relative difference on the parachute depth is only 11%, which is considered as negligible experimentally. As the confinement increases, the capsule is getting closer to the walls, so that the profiles become more distinct. Still, the relative difference ΔL remains below 2%, while ΔL_p is below 20%.

3.3. Inverse analysis results

We have previously shown that it is possible to infer the membrane elastic shear modulus of capsules flowing in a square microchannel[6]. The principle of the inverse analysis is briefly outlined. A capsule profile is extracted from an experimental image such as Fig. 3a. The two characteristic lengths L, $L_p = L - L_a$ and the profile area S are measured (Fig. 3b) and the apparent radius a_{app} is computed. From the solution of the numerical model of a capsule flowing in a square-section channel of side 2ℓ, a numerical database has been created[7], which relates the values of L/ℓ, L_p/ℓ, a_{app}/ℓ and v_c/V to Ca and a/ℓ on an interpolated regular grid (10^{-3} and 5×10^{-3} intervals for Ca and a/ℓ, respectively). The algorithm then determines the ensemble of geometric and dynamic parameters $\{a/\ell, Ca\}$ on the database grid, for which the experimental and numerical values of $\{a_{app}/\ell, L/\ell, L_p/\ell\}$ correspond to one another within tolerances linked to the experimental uncertainties. For each value of $Ca \in \{a/\ell, Ca\}$, we calculate the mean fluid velocity V from the capsule velocity v_c and the velocity ratio v_c/V of the database. We then calculate the shear modulus that corresponds to each $Ca \in \{a/\ell, Ca\}$ by means of the relation $G_s = \mu V/Ca$. The mean value of the possible shear modulus ensemble is finally computed.

The present objective is not to characterize the surface shear modulus G_s of a capsule population, but to evaluate the intrinsic error that is made by analyzing the flow of a capsule in a slightly rectangular channel by means of the numerical results obtained in a perfectly square channel. We thus apply the inverse analysis to the numerical profiles calculated in a slightly rectangular channel as if they were experimental results. We consider the same tolerances that have been used to study experimental profiles: ±0.04 on L/ℓ and L_p/ℓ, ±0.02 for a_{app}/ℓ. If $L_p/\ell < 0.04$, we consider that $L_p \in [0, 0.04]$. We denote $\overline{a/\ell}$ and $\overline{Ca}$ the mean ensemble values of all possible inverse analysis fits $\{a/\ell, Ca\}$. We then compare the couple of parameters $\{a/\ell, Ca\}$ provided by the inverse analysis technique in the case of a perfectly square channel to the cases of slightly rectangular ones.

The results are gathered in Table 1 for $a/\ell = 1$ and different values of δ and Ca. The $\delta = 0$ results, which correspond to the application of the inverse analysis to the exactly square channel results, give an estimate of the precision of the method. We find that, for $\delta = 0$, the value of $\overline{Ca}$ differs from the actual value by 15% for $Ca = 0.02$ and is as low as 1% for $Ca = 0.08$. This is due to the fact that the inverse analysis method is based on the relation between the capsule deformation (measured by L/ℓ and L_p/ℓ) and the flow strength (measured by Ca). At low Ca, the capsule is not much deformed so that the tolerance on the deformed lengths is relatively large, particularly so for the parachute depth L_p.

Table 1. Results of the inverse analysis for various δ and Ca values for a confinement ratio $a/\ell = 1$.

δ (%)	Ca	$\overline{a/\ell}$	$\overline{Ca}$	$(\overline{Ca} - Ca)/Ca$ (%)
0	0.02	1.00	0.023	15
	0.05	1.00	0.051	2
	0.08	1.00	0.081	1
5	0.02	0.99	0.020	0
	0.05	1.00	0.042	-16
	0.08	1.00	0.073	-9
-5	0.02	1.00	0.024	20
	0.05	1.00	0.057	14
	0.08	0.99	0.087	9
10	0.02	0.98	0.016	-20
	0.05	1.01	0.032	-36
	0.08	1.00	0.066	-18
-10	0.02	1.00	0.025	25
	0.05	0.99	0.064	28
	0.08	0.98	0.091	14
15	0.02	1.00	0.007	-65
	0.05	1.01	0.025	-50
	0.08	1.00	0.060	-25
-15	0.02	1.01	0.006	70
	0.05	1.00	0.067	34
	0.08	0.98	0.095	19

Table 2. Results of the inverse analysis for $Ca = 0.05$ and different size ratios.

a/ℓ	δ (%)	$\overline{a/\ell}$	$\overline{Ca}$	$(\overline{Ca} - Ca)/Ca$ (%)
0.95	0	0.95	0.049	-2
	5	0.95	0.041	-18
	-5	0.94	0.058	16
1.00	0	1.00	0.051	2
	5	1.00	0.042	-16
	-5	1.00	0.057	14
1.10	0	1.10	0.050	0
	5	1.10	0.046	-8
	-5	1.09	0.053	6

From Table 1, one first notes that the size ratio $\overline{a/\ell}$ is well calculated with the inverse analysis algorithm whatever the value of δ or of Ca. This means that the estimation of the confinement ratio based on the apparent capsule radius a_{app} is quite insensitive to δ. We also note that the capsule deformation increases as Ca increases. For $\delta > 0$, the channel is slightly wider than the square one: the capsule has more space to expand and is thus less deformed (Fig. 4a,b,c). This leads to a value of $\overline{Ca}$ that is underestimated as compared to the true value Ca. For $\delta < 0$, the channel is narrower than the square one, so that the capsule is more constrained and has to deform more. It then follows that $\overline{Ca}$ is systematically overestimated compared to the true value Ca. For $\delta = 5\%$, the estimated capillary number $\overline{Ca}$ falls within 20% of the true value Ca at most. This is within what is considered an acceptable margin in actual experiments, where there are slight variations between the capsules of a population[2]. For $\delta \geq 10\%$, the deviation between $\overline{Ca}$ and Ca is too large to be acceptable except maybe for high flow strengths ($Ca \geq 0.08$), which are not always easy to attain.

We finally consider the effect of the confinement ratio for the small channel distortion ($\delta = 5\%$) and a mid-range value of flow strength $Ca = 0.05$ (Table 2). For the square channel, the error on the estimation $\overline{Ca}(0)$ decreases with the confinement ratio a/ℓ, since a larger confinement leads to a larger capsule deformation. We find excellent results for $a/\ell = 1.1$ with little error. The square tube results can thus be used to analyze the data obtained on channels with a small distortion from squareness, provided we can satisfy ourselves with a 20% precision for the method.

4. Discussion and conclusion

The present study was focused on the flow of capsules in slightly rectangular channels and on the possibility to deduce the capsule elastic resistance from its deformed shape. The objective was to find the effect that the channel distortion from squareness may have on the precision of an inverse analysis, if one analyzes the results using a numerical database computed in a perfectly square channel. The goal was also to assess the validity of the method used by Hu *et al.*[6], i.e. to approximate slightly rectangular channels with square channels and neglect the experimental uncertainty due to mould fabrication.

By comparing profiles of a capsule flowing into a square channel and a rectangular channel with $\delta = 5\%$, we show that this approximation can be made with a fair accuracy. The profile differences are of the order of the precision in the detection of the membrane contour on experimental images. The resulting uncertainty on the characteristic lengths is small, and within the tolerances admitted by the inverse analysis procedure. The latter then provides reliable results that are very close to results that would be obtained in a square channel. This means that we can validate the study of Hu *et al.*, in which $\delta \simeq 5\%$.

Larger δ values were also studied to determine when the square approximation can no longer be made with good precision. For $\delta = 10\%$, the profile difference is larger than the contour detection precision. It is only for high flow strengths ($Ca > 0.08$) that the inverse analysis becomes about 18% accurate. Another approach to render the measurement more accurate is to use a channel that is smaller than the capsule size to ensure a confinement ratio larger than at least 1.1. But, for $\delta \geq 15\%$, the deviated channel can no longer be treated as a square channel to perform the inverse analysis method whatever the values of capillary number and size ratio. One either needs to resort to using the numerical database corresponding to the rectangular channel at stake, or, preferably, make more accurate channels.

In conclusion, the squareness of the channel appears as a limit to the microfluidic method to determine the mechanical property of microcapsules, but it is a satisfying result that the method remains accurate in the case of rectangular channels that have up to a 5% deviation from squareness. We have shown that the capsule resistance can still be inferred by analyzing the capsule deformed shape by means of the numerical results obtained in a perfectly square channel.

Acknowledgements

This research was funded by the Conseil Régional de Picardie (MODCAP grant), the French Ministère de la Recherche (Pilcam2 grant) and the French Agence Nationale de la Recherche (CAPSHYDR grant ANR-11-BS09-013 and Labex MS2T ANR-11-IDEX-0004-02 within the program "Investment for the Future").

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