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Numerical design of a T-shaped microfluidic device for deformability-based separation of elastic capsules and soft beads

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We propose a square cross section microfluidic channel with an orthogonal side branch (asymmetric T-shaped bifurcation) for the separation of elastic capsules and soft beads suspended in a Newtonian liquid on the basis of their mechanical properties. The design is performed through 3D direct numerical simulations.

When suspended objects start near the inflow channel centerline and the carrier fluid is equally partitioned between the two outflow branches, particle separation can be achieved based on their deformability, with the stiffer ones going ‘straight’ and the softer ones being deviated to the ‘side’ branch. The effects of the geometrical and physical parameters of the system on the phenomenon are investigated.

Since cell deformability can be significantly modified by pathology, we give a proof of concept on the possibility of separating diseased cells from healthy ones, thus leading to illness diagnosis.

I. INTRODUCTION

Flow of suspensions carrying deformable inclusions has many important applications. Suspensions of elastic capsules, i.e., liquid droplets wrapped in thin elastic membranes, can be found in several fields, both of scientific and industrial interest, such as blood circu-

lation, cosmetic and food processing [1, 2]. Deformable beads, i.e., solid particles made of (visco)elastic materials, are of interest in the biomedical and process fields (see, for example, microgel suspensions, biological cells, filled polymers, etc.) [3].

Elastic capsules and soft beads are also good models for biological cells [4, 5], and several works deal with the dynamics of such

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systems in microfluidic devices with characteristic dimensions and flow conditions suitable for their manipulation. It is indeed of great practical interest the efficient separation of such suspended inclusions based on their mechanical properties, either for design or analytical purposes [6].

Bifurcating channels seem to be a viable tool to promote separation of suspended particles. Numerous papers available in the open literature demonstrate that rigid particles can be effectively sorted when a channel bifurcates into two branches, with particle distribution in the downstream branches different from the partitioning of the fluid stream [7–9]. The distribution of the particles in the downstream branches depends on the bifurcation geometry (especially the angle formed by the branches), the volume fraction of the suspended particles, and the flow rate ratio in the outlet branches.

It has been shown that in Y-shaped bifurcations, particles tend to enrich the stream at higher flow rate, and this enrichment is enhanced as confinement increases. A similar phenomenon, known as the ‘Zweifach-Fung effect’ [10, 11], has been observed for RBCs, and finds a natural occurrence in the peripheral circulatory system, where the partitioning of blood constituents (RBCs, WCs, and platelets) at vessel junctions has relevant physiological consequences [12, 13]. In non-symmetric bifurcations such as T-shaped or

oblique channels, where one outlet branch is the straight prosecution of the inlet branch and the other is at an angle with it, rigid particles preferentially ‘choose’ the main outlet, this effect being enhanced at increasing the branching angle from 90° to 135° [8].

Interparticle interactions become dominant in concentrated suspensions, and, at low confinement, particles are almost equally divided between the downstream branches regardless of flow rate ratios [14].

The nature of the suspending fluid also has an effect on particle separation. In non-Newtonian viscoelastic liquids, indeed, particle dynamics through the bifurcation is affected by the development of normal stresses in the suspending liquid that induce particle cross-streamline migration [15, 16].

Beside the above mentioned partitioning mechanisms, basically relying on a flow rate unbalance, several studies have investigated the possibility of exploiting particle deformability for their separation in bifurcations [17–19]. The capability of sorting particles based on their mechanical properties is of primary importance in medicine, since cell deformability is a clinical indicator of a wide range of diseases, e.g., malaria [20] and leukemia [21]. Blood is, then, a preferential sample, because it is composed by a heterogeneous mixture of cells that continuously respond to the physiological and pathological changes

of human body. In this regard, another interesting target for selective separation are circulating tumor cells (CTCs), which are responsible for blood-borne metastasis and most cancer-related deaths [22]. It is known from the literature that diseased cells can soften 3 to 10 times with respect to healthy ones (see [5] and the references therein), thus the difference in cell stiffness might be used to discriminate neoplastic transformations in cell samples, leading to possible applications in the diagnosis and treatment of cancer diseases.

In the last decade, Secomb et al. [17, 18] used the finite element method to compute the motion of a red blood cell (modeled as a viscoelastic drop) in both Y- and T-shaped bifurcations. Despite being two dimensional, their calculations qualitatively reproduce some experimentally observed RBC behaviors, such as tank-treading and cell elongation. Woolfenden et al. [19] investigated with the Boundary Integral Method (BIM) the behavior of a two-dimensional elastic capsule moving through a channel with a side branch, and found that, when the inlet flow rate is equally divided between the outlet channels (of equal width), capsules with different elastic properties follow different routes out of the bifurcation. They also found that capsule deformation in the splitting region depends on the bifurcation angle. Koolivand and Dim-

itrakopoulos [23] employed the boundary element method to simulate the deformation of elastic capsules at the stagnation point of a T-junction, showing how to extract a measure of the membrane elastic modulus from deformation information.

With a combination of BIM and spectral element method, Zhu et al. [24] simulated in 3D the behavior of a microfluidic device made of a rectangular cross section duct with a semi-cylindrical obstacle followed by a cross section expansion. They succeeded in driving capsules of different membrane compliances to different streamlines in the downstream channel. Wang et al. [25] performed, with the immersed boundary lattice Boltzmann method, 3D simulations of the motion of an initially spherical capsule in a cylindrical tube with an orthogonal side branch at finite inertia ($0.25 \leq Re \leq 40$), showing that inertial effects can direct the capsule to flow into the downstream tube aligned with the inlet one even when this receives a much lower flow rate than the orthogonal side branch.

Elastic beads were studied with finite element approach by Trofa et al. [26], hinting at the possibility of their sorting based on their elastic moduli in a T-shaped microchannel.

In this work, we develop 3D direct numerical simulations to prove the validity of a microfluidic device for the mechanical-property-based separation of elastic capsules and soft

beads suspended in a Newtonian liquid. We consider a T-shaped channel with a square cross-section (to meet the typical microfluidic fabrication procedures). A systematic analysis is carried out by varying the operating conditions, and investigating the effects of geometrical confinement and capsule/bead deformability on separation.

II. GOVERNING EQUATIONS

We consider a 3D square cross section T-shaped channel with one inlet and two outlets, schematically represented in Fig. 1. The device is composed of a ‘main’ straight channel and an orthogonal ‘side’ branch. The portion of the channel upstream to the bifurcation, i.e., the inflow branch, has length L_0 , the main outflow branch has length L_1 , and the side outflow branch has length $L_2 = L_1$. Everywhere in the device, the square cross section has side H . As illustrated in inset (b) of Fig. 1, the corners between the main channel and the side branch are rounded and have a curvature radius $R_f = 0.1H$.

In the case of a spherical elastic capsule, its initial outer radius is R_e and its membrane thickness is δ . In this work, δ is always 5% of R_e , which lets us classify the capsule membrane as ‘thin’ [27]. We remark that the membrane is considered of finite thickness and its elasticity is modeled as a bulk property,

thus we do not use the thin film approach with a two-dimensional constitutive law [28] (see below).

We denote by Ω_e the external liquid domain, by Ω_m the capsule elastic solid membrane, and by Ω_i the liquid internal to the capsule. We denote by Σ_0 the device inflow section, by Σ_1 and Σ_2 the main and side outflow sections, by Σ_w the channel walls, and by Σ_e and Σ_i the capsule external and internal liquid-solid interfaces, respectively (see the main Fig. 1 and inset (a)). A Cartesian system of coordinates is set with its origin in the middle of the inlet section Σ_0 and the x -axis orthogonal to it and oriented in the direction of the fluid flow.

In microfluidic devices, the Reynolds number is generally very small due to the characteristic flow velocities and length scales involved [29], thus inertia can be neglected. Assuming also incompressibility of both the suspending and the suspended phases, the continuity and momentum balance equations governing the dynamics of the ambient liquid and the elastic capsule read

$$\nabla \cdot \mathbf{u} = 0 \quad (1)$$

$$\nabla \cdot \boldsymbol{\sigma} = \mathbf{0} \quad (2)$$

with $\mathbf{u}$ the velocity vector and $\boldsymbol{\sigma}$ the total

FIG. 1: Schematic representation of the T-shaped channel with a capsule suspended on its centerline. (a) Zoom of the section of the capsule in the xy -plane at $z = 0$. (b) Zoom of the smoothed corners with curvature radius $R_f = 0.1H$ between the main and the side channel.

stress tensor. For $\boldsymbol{\sigma}$ we can write

$$\boldsymbol{\sigma} = -p\mathbf{I} + 2\eta\mathbf{D} \quad \text{in } \Omega_e, \Omega_i \quad (3)$$

$$\boldsymbol{\sigma} = -p\mathbf{I} + \boldsymbol{\tau} \quad \text{in } \Omega_m \quad (4)$$

e.g., protein-reticulated membranes [30, 31].

Such equation reads

$$\overset{\nabla}{\boldsymbol{\tau}} = 2G\mathbf{D} \quad (5)$$

where p is a pressure, $\mathbf{I}$ is the identity tensor, η is the viscosity of the external and internal liquids (assumed to be the same), $\mathbf{D} = (\nabla\mathbf{u} + (\nabla\mathbf{u})^T)/2$ is the symmetric part of the velocity gradient tensor, and $\boldsymbol{\tau}$ is the extra-stress in the elastic solid. To model this contribution, we use the neo-Hookean constitutive equation, which conjugates implementation simplicity (it has only one parameter) with a good capability of describing the behavior of capsule membranes of practical interest,

with G the shear modulus of the elastic material. As usual, the symbol $(\overset{\nabla}{\boldsymbol{\tau}})$ denotes the upper-convected time derivative, defined as

$$\overset{\nabla}{\boldsymbol{\tau}} \equiv \frac{\partial \boldsymbol{\tau}}{\partial t} + \mathbf{u} \cdot \nabla \boldsymbol{\tau} - (\nabla \mathbf{u})^T \cdot \boldsymbol{\tau} - \boldsymbol{\tau} \cdot \nabla \mathbf{u} \quad (6)$$

The continuity and momentum balance equations for the suspending medium and the suspended particle are solved with the following boundary conditions on the channel

walls, inlet and outlets

$$\mathbf{u} = \mathbf{0} \quad \text{on } \Sigma_w \quad (7)$$

$$\mathbf{u} = [u_{0,x}(y, z), 0, 0] \quad \text{on } \Sigma_0 \quad (8)$$

$$\boldsymbol{\sigma} \cdot \mathbf{m} = -p_1 \mathbf{m} \quad \text{on } \Sigma_1 \quad (9)$$

$$\boldsymbol{\sigma} \cdot \mathbf{m} = -p_2 \mathbf{m} \quad \text{on } \Sigma_2 \quad (10)$$

Equation (7) is the no-slip condition for the suspending fluid on the channel walls. Equation (8) imposes the parabolic velocity profile for a Newtonian fluid in a straight channel with a square cross section, given by [32]

$$u_{0,x}(y, z) \simeq 3.67\bar{u}_0 \sum_{n,\text{odd}} \frac{1}{n^3} \sin\left(n\pi\left(\frac{1}{2} + \frac{y}{H}\right)\right) \left(1 - \frac{\cosh \frac{n\pi z}{H}}{\cosh \frac{n\pi}{2}}\right) \quad (11)$$

where $\bar{u}_0$ is the mean inflow velocity. In the numerical implementation, Eq. (11) is truncated at $n = 5$. Finally, Eqs. (9) and (10) express the outflow conditions for the matrix fluid in the main and the side branch, with $\mathbf{m}$ the outwardly directed unit vector normal to sections Σ_1 , Σ_2 , and p_1 , p_2 the corresponding outflow pressures. The pressure difference $\Delta p = p_1 - p_2$ sets the relative weight of the two outlet flow rates.

The boundary conditions on both the liquid-solid interfaces Σ_e and Σ_i read

$$\mathbf{u}|_l = \mathbf{u}|_s \quad (12)$$

$$(\boldsymbol{\sigma} \cdot \mathbf{n})|_l = (\boldsymbol{\sigma} \cdot \mathbf{n})|_s \quad (13)$$

where l and s identify the liquid and the solid phase, respectively, and $\mathbf{n}$ is the unit vector

normal to the liquid-solid interface and directed toward the liquid phase. Equations (12) and (13) express the continuity of velocity and traction across the above mentioned interfaces.

Since both the capsule and the suspending medium are inertialess, no initial conditions on the velocities are required. Only an initial condition for the extra stress in the capsule membrane needs to be specified, and we assume that the membrane is initially stress-free, i.e.,

$$\boldsymbol{\tau}|_{t=0} = \mathbf{0} \quad (14)$$

The motion equations and the boundary conditions are made dimensionless by choosing H as the characteristic length, $\bar{u}_0$ as the characteristic velocity, $H/\bar{u}_0$ as the characteristic time, and $\eta\bar{u}_0/H$ as the characteristic stress. Therefore, the following dimensionless parameters appear in the equations: the confinement ratio $\beta = 2R_e/H$, a capillary number $\text{Ca} = \eta\bar{u}_0 R_e/(HG\delta)$, and the dimensionless pressure difference $\Delta P = \Delta p/(\eta\bar{u}_0/H)$.

When a homogeneous elastic bead is considered instead of a capsule, balance and constitutive equations analogous to Eqs. (1)-(5) can be written on the suspending liquid and the solid domains. The boundary and initial conditions expressed by Eqs. (7)-(14) are the same, but, of course, only one solid-liquid interface exists in this case. The other difference with the capsule case is that in the

dimensionless form the ‘elastic’ capillary number is $\text{Ca}_e = \eta \bar{u}_0 / (HG)$.

All the results presented in the following are given in terms of dimensionless quantities, the usual superscript * being omitted for the sake of simplicity.

III. NUMERICAL METHOD AND CODE VALIDATION

The model equations presented in Sec. II are solved through the arbitrary Lagrangian Eulerian (ALE) finite element method (FEM) using well-known stabilization techniques such as SUPG and log-conformation. A detailed description of our numerical approach to the simulation of the behavior of suspensions with deformable inclusions is given in [33].

Both the matrix fluid and the suspended capsule domains are discretized by a mesh of quadratic tetrahedra. Both the external and the internal interfaces align with element faces (sharp interfaces made of quadratic triangles). During the simulations, the elements of the volume mesh progressively warp because of the capsule deformation and displacement along the flow direction. In particular, the elements ‘upstream’ of the particle are stretched, whereas the elements ‘downstream’ of the particle are compressed by its advancement in the x -direction. Any time the ‘quality’ of the volume elements in the domain

becomes unacceptable in terms of a threshold, a remeshing is performed, and the solution is projected from the old mesh to the new one, as technically detailed in [34, 35]. Moreover, since the capsule undergoes a great deformation as it approaches the bifurcation corner, when necessary, the remeshing is conjugated with a mesh refinement, where the resolution of the elements on the bifurcation corner is adapted to ensure the presence of a minimum number of tetrahedra in the gap between the capsule and the corner.

Given the model proposed above, we have verified that the distance between the device entrance Σ_0 and the capsule initial position on the channel axis is such that the presence of the particle does not perturb the suspending liquid velocity profile close to Σ_0 . In other words, our geometry is suitable to simulate devices whose inlet branch is arbitrarily long upstream of the particle. Moreover, the length of the inflow branch has been chosen sufficiently larger than the capsule dimension to allow the capsule attain its equilibrium deformed shape in a square cross section straight channel before ‘feeling’ the effect of the bifurcation. We have verified that a length of the inflow branch $L_0 = 2.5H$ satisfies such condition for every R_e considered. In addition, the length of the outflow branches is chosen sufficiently larger than the particle to avoid any spurious effects on its dynamics in the bifurcation

region due to the imposed outflow boundary conditions. A length of the outflow branches $L_1 = L_2 = 2H$ fulfills this requirement.

It is worth specifying once for all that, wherever in the text we mention the particle position and velocity, we refer to the position and velocity of its center of volume.

Before running simulations, convergence tests have been performed in space and time, namely, mesh resolution and time-step for the numerical solution of the equations proposed in Sec. II have been chosen so as to ensure invariance of the results upon further refinements. For the simulations presented in this paper, we have found that meshes with 50 - 60 line elements on the capsule equator, a total initial number of tetrahedra around 3×10^4 (that grows up to $O(10^5)$ due to the above mentioned refinements), and time-steps in the order of $10^{-3} \times H/\bar{u}_0$ are adequate. A detailed description of the procedures adopted to run convergence tests for a 2D problem analogous to the one considered here is given in [26].

We validate our code reproducing the case of an initially spherical capsule suspended on the centerline of a straight channel with a square cross section at $\beta = 0.9$ and $Ca = 0.02$ as in Hu et al. [30]. The capsule deformed shape is used in the comparison reported in Fig. 2, where the solid line denotes the intersection between the steady-state deformed external surface of the capsule and the chan-

FIG. 2: Steady-state deformed shape of the external surface of a capsule at the centerline of a square section straight channel for $\beta = 0.9$ and $Ca = 0.02$. Solid line: our numerical simulations; symbols: results from Hu et al. [30].

nel midplane obtained from our simulations, while the symbols report the corresponding results from Hu et al. [30]. For both the profiles, the capsule center of volume is located at (0,0); due to symmetry, only the upper half of the profiles is displayed. It is apparent that the two shapes almost overlap. The capsule dimensionless translational velocity is predicted to be 1.322, within 2.5% of Hu et al. value.

IV. RESULTS AND DISCUSSION

All the simulations are run with an initially spherical capsule/bead placed with its center of volume on the centerline of the inlet channel. This initial position is chosen since, in pressure-driven flows, deformable objects,

e.g., elastic beads, capsules, and cells, naturally migrate toward the channel centerline of axisymmetric channels [36–41]. Therefore, the inlet channel can be considered as the final part of a sufficiently long straight channel. For the sake of completeness, the effects of small offsets with respect to the channel axis will be also analyzed.

All the simulations are carried out by choosing the outlet pressure difference ΔP such that the flow rates in the two outlet sections are the same. This implies that, in the absence of particles, the streamline corresponding to the inlet channel centerline would end up at a stagnation point on the bifurcation corner, neither entering the main branch nor the side branch. Particles starting on the inlet channel centerline are then convected close to the bifurcation corner. One aim of this work is to investigate how particle deformability may determine the particle ‘choice’ in favor of an outlet rather than the other. We compare the predictions for an elastic capsule with those for an initially spherical elastic bead under the same operating conditions.

A. Elastic capsules

We present simulation results for the capillary number Ca ranging between 10^{-3} and 10^{-1} and the confinement ratio β in the range 0.2 - 0.8. Such β -range was selected because,

when the particle is very small as compared to the channel ($\beta \lesssim 0.2$), it almost follows the suspending fluid streamline and its deformability plays no role.

Figure 3 shows the trajectories and shapes of a capsule with $\beta = 0.4$ for capillary numbers ranging from 0.01 to 0.05. The dashed lines track the position of the particle center of volume in the device. On each of such lines, four symbols of the same color are present, referring to four different ‘significant’ time values during capsule evolution, namely, $t = 0.3, 0.8, 1.4, 2.4$. In addition, at $t = 0.3, 0.8, 2.4$ and every Ca , solid lines report the trace of the intersection between the capsule external surface and the xy -plane at $z = 0$. Capsule shapes at $t = 1.4$ are not displayed in order to avoid superposition with shapes at $t = 2.4$, which would make the figure unclear.

We observe that, in the inlet channel, the capsule trajectories almost superimpose, then, as the capsule approaches the bifurcation, at increasing Ca it feels an increasing migration force toward the side branch. This force makes the particle move increasingly below the streamline that ends up on the bifurcation corner and separates the fluid flowing to the main branch from the one flowing to the side branch (not shown in Fig. 3 for the sake of clarity). As the capsule comes close to the bifurcation corner, complex hydrody-

FIG. 3: (Color online) Dashed lines: trajectories of a capsule in the T-shaped device. Symbols: positions of the capsule center of volume at $t = 0.3, 0.8, 1.4, 2.4$. Solid lines: capsule shapes at $t = 0.3, 0.8, 2.4$. $\beta = 0.4$, Ca ranging from 0.01 to 0.05.

dynamic interactions arise. The overall effect of such complex interactions is of inducing the particle to ‘choose’ to enter the main or the side branch depending on the capillary number. Specifically, lower Ca -values (given by lower membrane deformability and/or lower matrix fluid flow rate) drive the capsule to take the main branch, thus reproducing the behavior of a rigid particle [9], while greater capillary numbers (higher membrane deformability and/or higher suspending liquid flow rate) make the capsule deviate to the side branch. Hence, a critical value of the capillary number Ca_c exists that makes the particle ‘switch’ from one outlet to the other.

When the particle is still in the inlet chan-

nel, its shape is slightly affected by the Ca -value, but, when the capsule approaches the corner, the effect of the capillary number becomes progressively substantial. This is apparent in Fig. 4, where deformed shapes are shown in four different panels, each corresponding to a selected time value (see caption for details). It should be noticed that the shapes are shifted such that the centers of volume coincide. While very slight deviations are visible in Fig. 4a (capsule still in the inlet branch), the shapes increasingly differentiate at varying Ca as the particle approaches the corner. In Figs. 4b-c, the capsule deformed shapes appear progressively more elongated with Ca . Finally, in Fig. 4d, the proximity of

FIG. 4: (Color online) Deformed shapes of a capsule with $\beta = 0.4$ and Ca between 0.01 and 0.05 at $t = 0.3, 0.8, 1.4, 2.4$. For the legend, refer to Fig. 3.

the particle to the channel bifurcation makes it attain a bean-like shape, the more bended the higher Ca .

Figure 5 reports the temporal trends of the x - and y -components of the capsule velocity $u_{p,x}$ and $u_{p,y}$ for $\beta = 0.4$ and Ca ranging from 0.01 to 0.05. (The z -component is always null due to symmetry.) For all Ca -values, after

a very brief transient, the particle attains almost the same translational x -velocity, given by the nearly horizontal portion at the beginning of the curves (see Fig. 5a). Such velocity is slightly lower than the suspending liquid velocity at the centerline of the inlet channel (Eq. (11)), which means that the capsule lags the fluid. When the particle is still in the

FIG. 5: (Color online) Temporal trends of the x -component $u_{p,x}$ (a) and of the y -component $u_{p,y}$ (b) of a capsule velocity at $\beta = 0.4$ and Ca between 0.01 and 0.05. The symbols on each curve mark the time values $t = 0.3, 0.8, 1.4, 2.4$.

inlet branch, its y -velocity is nil (Fig. 5b). As the capsule approaches the bifurcation corner, it slows down in the x -direction, whereas $u_{p,y}$ first increases in magnitude (its value being negative because the bifurcation corner has a lower y -coordinate than the inlet channel centerline), it attains a maximum, then it slows down as well; both the velocity components tend to zero in the proximity of the bifurcation corner. At this stage, the differ-

ences in particle deformation at varying Ca shown above reverberate on its velocity. At $Ca \leq 0.02$, $u_{p,x}$ stays positive, whereas $u_{p,y}$ crosses zero and becomes positive, meaning that, in the vicinity of the bifurcation corner, the capsule moves ‘up’ and takes the main outlet branch. If the latter is sufficiently long, the capsule would eventually migrate toward its centerline. On the other hand, at $Ca \geq 0.03$, $u_{p,x}$ becomes slightly negative and $u_{p,y}$ keeps negative and has a new increase in magnitude due to the fact that the capsule ‘slides’ down to the side branch. Analogously to the case at $Ca \leq 0.02$, if the side branch is sufficiently long, the particle would eventually migrate toward its centerline.

We now analyze the influence of the capillary number on the capsule deformation and stress state. In the top row of Fig. 6 we report a 3D perspective view of the capsule deformed shape at $t = 0.3, 0.8, 2.4$ for the two extreme Ca -values considered above, i.e., $Ca = 0.01$ (panel a) and $Ca = 0.05$ (panel b). At $Ca = 0.01$, it is apparent that the particle almost keeps its undeformed spherical shape until reaching the channel bifurcation corner, where it attains a bean-like shape. It is interesting to observe that, in addition to the concavity in the xy -plane already shown in Figs. 3-4, the portion of the capsule external surface ‘facing’ the corner has also a concavity in the orthogonal direction (namely, in the plane identified

FIG. 6: (Color online) Upper row: von Mises stress σ_{VM} on the external surface of a capsule with $\beta = 0.4$ at $t = 0.3, 0.8, 2.4$ for $Ca = 0.01$ (a), 0.05 (b). Lower row: σ_{VM} in the intersection between the capsule membrane and the xy -plane at $z = 0$ for $\beta = 0.4$, $t = 2.4$, $Ca = 0.01$ (c), 0.05 (d).

by the direction $x = y$). On the other hand, at $Ca = 0.05$, the deformations are visibly more pronounced, even when the capsule is still ‘far’ from the T-shaped bifurcation. In particular, at $t = 2.4$, the capsule appears much stretched, with its shape almost ‘conforming’ to the bifurcation rounded corner, and the concavities in the surface portion facing the corner are patently enhanced. The bottom row of Fig. 6 displays the intersections between the capsule membrane and the xy -plane at $z = 0$ for $t = 2.4$ and $Ca = 0.01$ (panel c) and 0.05 (panel d). In both cases, it can be noticed that, even when the capsule attains its maximum deformation, the elastic membrane essentially maintains a uniform thickness.

The color maps in Fig. 6 show the fields of

the von Mises stress σ_{VM} on the capsule external surface (top row) and in the membrane xy -section (bottom row), defined as [42]

$$\sigma_{VM} = \sqrt{\frac{3}{2} \boldsymbol{\tau} : \boldsymbol{\tau}} = \sqrt{3II_{\boldsymbol{\tau}}} \quad (15)$$

Such indicator gives an overall scalar measure of the stress state in the capsule. It is worth remarking that the full-scale of the color map, equal to 600, means that the stress level in the membrane is very high as compared to the characteristic stress $\eta \bar{u}_0 / H$ that refers to the fluid. It is apparent from Figs. 6a-b that, at each given Ca , during its motion in the T-shaped channel, the capsule is the most stressed when it is close to the bifurcation corner. In particular, from the 3D views, it emerges that, for both $Ca = 0.01$ and 0.05 , the stress is maximum in a band almost parallel to the corner smoothed boundary, which can be put in relation with the fact that the particle is squeezing ‘against’ the corner, thus it elongates orthogonally to it. From the quantitative point of view, the σ_{VM} -level at $Ca = 0.01$ is quite higher than the one at $Ca = 0.05$, since a greater value of the capillary number corresponds to a more compliant elastic membrane that is, then, less prone to accumulate stress than the stiffer membrane at $Ca = 0.01$. By looking at the σ_{VM} -maps in the membrane cross section in Figs. 6c-d, two comments can be made. Firstly, as already noticeable from the 3D images reported in

the top row, one can see that, for both the Ca -values considered, the maximum stress values are not attained in the system symmetry plane; secondly, the color gradients show that the stress variations in the direction orthogonal to the membrane are much smoother than the ones in the direction parallel to it.

FIG. 7: (Color online) Critical capillary number for an elastic capsule Ca_c as a function of the confinement ratio β . Inset: Ca_c as a function of the particle initial position y_{p0} at $\beta = 0.6$.

We mentioned above that, at $\beta = 0.4$, a critical capillary number Ca_c exists such that, for $Ca > Ca_c$, the particle deviates to the side outflow branch, otherwise it ends in the main branch. We carried out an analogous investigation, aimed at detecting Ca_c , at varying the confinement ratio β .

In Fig. 7, we report the $Ca_c(\beta)$ trend for $0.2 \leq \beta \leq 0.8$. Notice that there is not a ‘sharp interface’ between the side branch and main branch attraction basins (denoted in

the figure by the red and blue areas, respectively), yet the two are separated by a gray band of thickness 0.01. This is due to the fact that, for each β -valued considered, we varied Ca with a step of 0.01. The upper boundary of the gray band is, then, given by the minimum Ca -values making the particle take the side branch, whereas the lower boundary of the gray band is given by the maximum Ca -values making the capsule exit through the main branch. Therefore, Ca_c falls within the gray band. It is apparent in Fig. 7 that a quite high capillary number is ‘needed’ to drive the particle to the side branch at low confinement ratios, then Ca_c -value decreases of almost an order of magnitude as confinement grows. Moreover, a non-monotonic dependence of Ca_c on β is found, with a minimum achieved at $\beta \approx 0.6$. The slight increase of Ca_c at high β might be due to the stronger influence of interactions of bigger particles with the channel walls.

We recall that the diagram in Fig. 7 is obtained with a pressure difference between the device outlets yielding the same suspending liquid flow rate in the two branches. In principle, different choices of the ΔP -value could be taken, so determining different outlet flow rate distributions. However, if this is the case, the streamline at the centerline of the inlet branch (where particles start) would not end up on the bifurcation corner, but it

would move towards the outlet branch with the greatest flow rate. Hence, an additional ‘driving force’ to particle displacement toward the main or the side branch would be provided. If the flow rate unbalance is small, its effect on the $Ca_c - vs. - \beta$ line is weak, a slightly higher flow rate in the main branch would make the gray band move upwards (i.e., a greater membrane deformability would be needed to make the capsule take the side branch), whereas a slightly higher flow rate in the side branch would make the gray band move downwards (namely, even stiffer capsules would exit through the side branch). On the contrary, substantial flow rate unbalances would make the separation impossible, as all the particles would take the outlet branch with the higher flow rate regardless of their mechanical properties.

The critical capillary number values reported in Fig. 7 are obtained in the hypothesis that the capsule initially lies on the inlet channel centerline (as stated in Sec. II). As it can happen that the particle focusing in the straight channel preceding the bifurcation is not perfect, it might be of value to consider such an offset. The inset of Fig. 7 shows the effect of a capsule out-of-centerline initial position on Ca_c at $\beta = 0.6$. A relative deviation of 2.5% with respect to the capsule maximum available initial position (dictated by the confinement ratio β) is considered in

both the positive and negative y -direction (the z -coordinate always being equal to 0, for the sake of simplicity): at increasing y_{p0} , Ca_c correspondingly increases. In other words, a particle starting below the inlet channel centerline exits through the side branch even at values of Ca for which a particle starting on the centerline goes straight, whereas a particle starting above the centerline takes the main branch also at values of Ca for which a particle starting on the centerline takes the side branch. Such result is actually expected: starting below the centerline gives the particle an additional ‘thrust’ toward the side branch, which has to be ‘contrasted’ by a greater membrane rigidity if one wants the capsule to go straight; on the contrary, a capsule starting above the centerline is initially on a streamline ending in the main outlet, thus a greater membrane deformability is needed to take the side branch.

To summarize, for a given confinement, all the capsules with $Ca < Ca_c$ take the main branch. For given suspending fluid, flow rate, membrane thickness, and geometrical confinement, such condition is equivalent to say that capsules with membrane elastic modulus G higher than a critical value G_c end up in the main outlet. In contrast, particles with $Ca > Ca_c$ (namely, with membrane elastic modulus $G < G_c$) deviate to the side branch. This phenomenon could be exploited to sep-

arate softer from stiffer capsules, or even to select a sample of capsules with membrane elastic moduli in a desired range $[G_1, G_2]$. Indeed, in a first step, a flow rate could be selected such that particles with $G < G_2$ deviate to the side branch; in a second step, these particles could be reflowed with a lower flow rate (thus, lowering G_c , Ca_c being fixed), so making the particles with $G < G_1 < G_2$ move to the side branch. Hence, capsules with membrane elasticities in the range of interest could be collected from the main branch. Of course, the inverse procedure would be possible too, ‘cutting’ first the softer particles and then the stiffer ones, the optimal procedure depending on the elastic moduli distribution of the suspension to treat. From a different point of view, this procedure can be regarded as an interval measure of the membrane elastic properties of a capsule sample.

As reported above, fixed all the other parameters, the quantitative value of Ca_c has a dependence on the particle position prior to the bifurcation. By the way, it is worth remarking that, in the range of y_{p0} considered (see the inset in Fig. 7), the variations in Ca_c stay within a factor of about three, thus the separation of elastic capsules based on their membrane deformability is not dramatically affected by a moderate uncertainty on the particle starting position, namely, by a slightly imperfect focusing in the inlet channel.

However, it is also apparent from the inset of Fig. 7 that, in the process conditions considered here, for particles starting below the inlet channel centerline, the main branch attraction basin shrinks until almost disappearing. To enlarge the interval of Ca -values for which a particle is attracted toward the main branch (i.e., translating the $Ca_c(y_{p,0})$ band upwards) a ΔP might be chosen such that the flow rates in the outlet branches are slightly unbalanced in favor of the main branch (see above).

B. Elastic beads

We now consider the case of an initially spherical elastic bead.

At given β , the qualitative behavior of elastic beads at varying Ca_e is the same as the one of capsules, i.e., lower Ca_e -values make the particle continue straight, whereas higher values of the parameter promote particle deviation toward the side branch.

The top row of Fig. 8 shows 3D perspective views of the bead deformed shape at $t = 0.3, 0.8, 2.0$ for $Ca = 0.01$ (panel a) and $Ca = 0.05$ (panel b), corresponding to a particle exiting through the main and the side branch, respectively. At $Ca = 0.01$, the particle almost holds its undeformed spherical shape until coming very close to the channel bifurcation corner, and even there it is only moderately deformed into a bean-like

shape. On the contrary, at $Ca = 0.05$, the deformation is more pronounced: at $t = 2.0$, the capsule shape almost ‘conforms’ to the bifurcation rounded corner. The bottom row of Fig. 8 displays the intersection between the elastic particle and the xy -plane at $z = 0$ for $t = 2.0$ and $Ca = 0.01$ (panel c), 0.05 (panel d).

The color maps in Fig. 8 show the fields of the von Mises stress on the bead external surface (top row) and in its xy -section (bottom row). At both the Ca_e -values considered, largest stresses are observed when the bead reaches the bifurcation corner, and the stress attains its maximum in the portion of the particle surface area with the largest curvature. From the quantitative point of view, at $Ca = 0.01$ the σ_{VM} -level is quite higher than at $Ca_e = 0.05$. Like for capsules, a greater value of the elastic capillary number corresponds to a more compliant elastic material that is, then, less prone to accumulate stress than the stiffer material at $Ca_e = 0.01$. By looking at the σ_{VM} -maps in the particle cross section in Figs. 8c-d, it can be noticed that for both the Ca_e -values considered, at variance with what happens for capsules (see Fig. 6), the maximum stress values lie in the system symmetry plane.

The comparison of the von Mises stress maps for a capsule (Fig. 6) and an elastic bead (Fig. 8) at the same β and Ca - (or Ca_e -)

FIG. 8: (Color online) Upper row: von Mises stress σ_{VM} on the external surface of an elastic bead with $\beta = 0.4$ at $t = 0.3, 0.8, 2.0$ for $Ca = 0.01$ (a), 0.05 (b). Lower row: σ_{VM} in the intersection between the particle and the xy -plane at $z = 0$ for $\beta = 0.4, t = 2.0, Ca_e = 0.01$ (c), 0.05 (d).

values yields that the maximum stress level in the capsule membrane is almost five times the stress level in the elastic particle. In other words, fixed all the dimensionless parameters, the elastic membrane of a capsule stores a much higher stress than a ‘bulk’ elastic particle. This can be related to the different definitions of the capsule capillary number Ca and the elastic bead capillary number Ca_e , from which it follows that (given the same device

geometry and the same suspending medium viscosity and average velocity) a bead has an elastic modulus 20-times lower than the membrane of a capsule with $\delta/R_e = 0.05$, thus it is less prone to accumulate stress.

Given a confinement ratio β , similarly to the case of capsules, a critical elastic capillary number $Ca_{e,c}$ can be identified for an elastic bead such that, for $Ca_e > Ca_{e,c}$, the particle deviates to the side branch, otherwise it takes

FIG. 9: (color online) Critical elastic capillary number for an elastic bead $Ca_{e,c}$ as a function of the confinement ratio β .

the main branch. In Fig. 9, we report $Ca_{e,c}$ vs. β for $\beta \in [0.2, 0.8]$. It is apparent that a quantitatively similar $Ca_{e,c}(\beta)$ -trend is found to the one shown for capsules in Fig. 7. Therefore, the same considerations made above on the deformability-based separation of capsules hold for elastic beads as well.

Finally, by comparing the $Ca_{e,c}(\beta)$ -trend shown in Fig. 9 with the one identified by Trofa et al. in their 2D preliminary study [26], a major qualitative difference can be identified: indeed, here $Ca_{e,c}$ decreases with β , whereas in 2D the opposite trend arises, with $Ca_{e,c}$ increasing at growing β . This could be ascribed to the fact that in 2D the finite confinement measured by the β -parameter has a meaning only in the y -direction (the dimensions of both the particle and the channel being infinite in the z -direction), while in 3D β expresses the ratio of the particle initial

dimension (finite and equal in every space direction due to sphericity) and the channel dimensions in both the y - and the z -direction orthogonal to the flow (both equal to H given the square cross section of the device). Hence, the fully 3D simulations are crucial to get quantitative information of application interest.

C. Feasibility analysis

In Secs. IV A-IV B, we have presented results concerning the separation of capsules and elastic beads in terms of the dimensionless parameters Ca (or Ca_e) and β governing the phenomenon. Here, we make some considerations about the actual feasibility of this operation under typical microfluidic process conditions.

First of all, let us justify the assumption of negligibility of inertial effects, i.e., $Re \ll 1$, on the basis of which we have written the mass and momentum balance equations (1)-(2) in the Stokes formulation. We recall that the Reynolds number can be written as

$$Re = \frac{\rho \bar{u}_0 H}{\eta} \quad (16)$$

where ρ is the carrier medium density and the other symbols have been defined above.

For a capsule, by means of the definitions of the capillary number Ca and of the confinement ratio β given in Sec. II, the Reynolds

number can be also written as

$$\text{Re} = \frac{\rho H^2}{\eta^2} \frac{G\delta}{R_e} \text{Ca} = \frac{4\rho R_e G\delta}{\beta^2 \eta^2} \text{Ca} \quad (17)$$

We have shown in Sec. IV A that, for $0.3 \lesssim \beta \lesssim 0.8$, Ca_e is in the range between 0.01 and 0.04, thus let us consider the conservative values $\beta = 0.4$ and $\text{Ca} = 0.05$. If we deal with capsules of biological interest, e.g., cells, $G\delta$ is in the order of 10^{-5} N/m [43, 44], whereas R_e is in the order of a ten of microns, i.e., 10^{-5} m.

If a ‘water-like’ suspending liquid is employed, the density is about 10^3 kg/m³, while the viscosity is about 10^{-3} Pa s. The estimate of the Reynolds number corresponding to these parameter values is around 0.06, thus the above mentioned assumption would hold true. This leads to an average flow velocity in the order of mm/s and a flow rate in the order of 0.1 $\mu\text{L}/\text{min}$. On the other hand, if artificial microcapsules are considered, typical R_e -values are in the order of hundreds of microns (10^{-4} m) [45] and $G\delta$ is in the order of 10^{-1} N/m [46, 47]. By keeping the confinement ratio fixed at 0.4, this means that a matrix fluid with a viscosity some hundreds times larger than that of water is needed to maintain Re in the same order of magnitude as above, which, for instance, could be achieved by employing a glycerol aqueous solution. In this case, the average flow velocity is in the order of cm/s, while the flow rate is in the order of mL/min. We remark that, in our device, cap-

sule deformation is not such that bursting can occur, since neither the characteristic shapes preparatory to bursting [47] nor membrane thinning [48] are observed.

For an elastic bead, the definition of the elastic capillary number Ca_e given in Sec. IV B yields the following expression for the Reynolds number:

$$\text{Re} = \frac{4\rho R_e^2 G}{\beta^2 \eta^2} \text{Ca}_e \quad (18)$$

Again, for $0.4 \lesssim \beta \lesssim 0.8$, $\text{Ca}_{e,c}$ is in the range 0.01 - 0.04, so we consider $\beta = 0.4$ and $\text{Ca}_e = 0.05$. Both for soft microgel beads and biological cells (when regarded as ‘bulk’ particles), G is in the order of $10^3 - 10^4$ Pa, whereas R_e is in the order of tens of microns [5, 49, 50], from which it emerges that, depending on the particle stiffness, an ambient liquid 100 to 1000 times more viscous than water (see above) guarantees negligible inertial effects. This leads to an average flow velocity in the order of cm/s and a flow rate in the order of 10 $\mu\text{L}/\text{min}$.

Let us now consider another practical issue, namely, capsule/bead focusing in the proximity of the inlet channel centerline, assumed as the initial condition for our simulations. In order to estimate the focusing length, i.e., the channel length in the flow direction traveled by a particle while cross-stream migrating from the vicinity of a wall toward the centerline, we make use of the expression given in

[37] for elastic beads in Poiseuille flow, which can be written as

$$L_{\text{focus}} = \frac{2.6R_e}{\beta^3\text{Ca}_e} \quad (19)$$

For an elastic bead with $R_e = 30 \mu\text{m}$, $\beta = 0.4$, $\text{Ca}_e = 0.05$, Eq. (19) gives a focusing length of about 2.5 cm, reasonably feasible in the microfluidic practice. If greater objects are taken into account, the focusing length can be kept under control by compensating the R_e -increase with a β -increase: for example, if R_e becomes equal to $300 \mu\text{m}$, increasing β to 0.6 allows to contain the focusing length within about 7 cm.

Notice that, at varying β , the maximum uncertainty on Ca_c (or $\text{Ca}_{e,c}$) is of a factor two (see Figs. 7-9). Therefore, since, many cancer cells are three to ten times softer than the corresponding healthy ones [5], a separation of diseased cells based on their mechanical properties is in principle possible through our device.

Finally, since our simulations show that the deformation dynamics in the proximity of the bifurcation corner prior to ‘choosing’ an outlet branch takes a certain time, we remark that the particle suspension to be processed in the device proposed here needs to be sufficiently diluted to avoid particle reciprocal disturbances at the bifurcation corner.

V. CONCLUSIONS

In this work, we perform a numerical-assisted feasibility study on a square cross section T-shaped microfluidic device for the separation of elastic capsules and soft beads suspended in a Newtonian liquid depending on their mechanical properties.

We find that, when the pressure difference between the two outlet branches of the device is such that the exit flow rates are equal, and the capsule starts on the inlet channel centerline, at every confinement ratio, higher capsule membrane deformability promotes particle deviation toward the side branch (orthogonal to the inlet), whereas stiffer capsules are more prone to end up in the main outflow channel (aligned with the inlet). Therefore, for every confinement ratio, a critical deformability can be identified, below which capsules take the main branch and above which they take the side branch. Such critical value decreases with the confinement ratio. The effect of an imperfect capsule alignment on the inlet channel centerline is also investigated, yielding moderate variations in the critical deformability. However, these variations do not hinder the possibility of performing a deformability-based separation of capsules with sufficiently different membrane elasticities.

The above mentioned results for elastic cap-

sules are compared with the ones for initially spherical elastic beads in the same device, highlighting a quantitative correspondence between the behaviors of the two systems.

Elastic capsules and soft beads are good models for biological cells [4, 5]. Since many

pathologies can significantly modify cell deformability, e.g., softening cells from three to ten times [5], our numerical results give a proof of concept on the possibility of separating diseased cells from healthy ones, thus leading to illness diagnosis.

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