**Literature Review Outline**

* **Is it possible to distinguish capsules of different membrane properties irrespective of their size?**

First, we will explore the ways in which capsule properties can be determined in Section [2](#page1) and then consider the current state of knowledge on the behavior of capsules in different flow situations in Section 3.

* **Characterizing Capsule properties**

There appear to be three main ways in which capsule properties are determined, detailed in the following three sections. All methods are generally validated using the compression method, detailed in section [2.1.](#page1)

**2.1 Compression between two plates**

A capsule is compressed between two plates at a fixed rate and the force exerted is recorded along with images to determine the shape of the capsule. A mathematical model is then used to extract the membrane shear modulus. The simpler approach is to use the result from thin-shell theory developed by Feng and Yang [[1]](#page2) and later Lardner and Pujara [[2].](#page2) This is the approach taken by e.g. Carin et al [[3,](#page3) 4]. The alternative is to solve the problem using a finite-element simulation and hence extract the shear modulus such as done by Rachnik et al [[5].](#page3)

**2.2 Osmotic Pressure changes**

A method developed by Sherwood et al [[6]](#page3) allows the determination of the diffusivity of the membrane of alginate capsules. With this information, an approximation for the elastic modulus can be made. While simple to carry out, the large number of parameters that have to be estimated mean the accuracy of this method is limited.

**2.3 Flow deformation**

A inverse numerical method has been developed to determine membrane properties of capsules flowing in cylindrical tubes [[7,](#page3) 8, 9]. This has been extended to square channels in the approx-imations made have been validated using a full 3D model [[10, 11].](#page3) The method is robust for determining the elastic moduli of capsules but the source code is not publicly available.

* **Flow Behavior**

**3.1 Unbounded Flows**

There are several numerical investigations of the properties of capsules in unbound shear flow [[12, 13]](#page3) which are consistent with the results for capsules in confined flows.

**3.2 Cylindrical Tubes**

The behavior of capsules in cylindrical tubes, both micrometric and millimetric, is well studied. The shape of capsules has been investigated numerically, [[14, 15]](#page3) as well as experimentally for human serum albumin [[16]](#page3) and ovalbumin capsule [[7,](#page3) 9] respectively. The effect of prestress

1. and lateral migration [[17]](#page3) is also well-documented, although not sufficiently experimentally confirmed.

Millimetric capsules generally are under pre-stress from osmotic inflation after production. This prestress suppressed buckling instabilities that can otherwise be observed at low flow rates. As the flow rate increases, the shape of the capsule changes from spherical to elongated. The curvature of the front remains approximately constant while the back becomes flat and eventually concave.

**3.2.1 Square channels**

In recent years, the focus of capsule flow has shifted from cylindrical to square cross-section. While independent numerical investigations have been conducted [[7, 10, 11],](#page3) there are few exper-imental investigations [[18,](#page3) 7].

In general, the behaviour of capsules in square channels is similar to that in cylindrical tubes with the exception that larger flow rates are required to attain equivalent deformations. At small capillary numbers or large capsule radii, the capsules extend into the corner, breaking the axisym-metry.

**3.2.2 Rectangular channels**

Only few investigation of rectangular cross-section exist [[19].](#page3) The capsule shape is different to square and cylindrical cross-sections in that the capsule extend in the lateral direction to attain a pebble-like shape.

* **Capsule flow in junctions and obstacles**

There appears to be only one investigation of the effect of a constriction on a capsule by Park and Dimitrakopoulos [[20]](#page3) and the effect of junctions by Wolfenden and Blyth [[21]](#page3) , both numerical.

Park and Dimitrankopoulos found capsules to adopt two distinct shapes when entering and leaving the constriction. Initially the front elongates as it enters the constriction. When it leaves the constriction, the back travels faster than the front leading to an increase in the size perpendicular to the direction of motion and a parachute like shape.

 Its notable that increasing the size of the capsules is equivalent in effect to decreasing Ca. The deformation of the capsule decreases with the viscosity ratio of internal to external fluid. A high viscosity ratio also increases the time the capsules take to return to its steady state in the channel once it left the constriction.

Wolfenden and Blyth investigate a junction where a daughter channel comes of at an angle from the main channel. The path of the capsule can be influenced by the relative width of the daughter channel and the relative flow rates. In cases where these conditions do not induce a bias toward one channel, the elasticity can be tunes such that the capsule goes into one or the other channel.

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