Bioencapsulation Research Group

Bioencapsulation Innovations

September 2011

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ÉDITORIAL

THE FUTURE OF ENCAPSULATION TECHNOLOGY: THE NEED FOR COLLABORATIVE RESEARCH TO BREAK FRESH BOUNDARIES

Ian Marison, Dublin City University and National Institute of Bioprocessing Research and Training, Dublin, Ireland

I have been involved in encapsulation technology for over 25 years; consequently this is a form of anniversary editorial for me! My own work began, by trying to develop high density yeast cell cultures for the production of alcohol from whey fermentations for use as a biofuel. The problem then, and to a considerable degree now, was the lack of systems to produce microcapsules of defined properties at a scale to enable them to be put into bioreactors, and even the fluidized-bed bioreactors necessary to carry out these cultures. Fortunately being in an engineering department in a Swiss university, we had no problem building both with the help of colleagues at the ETH-Zurich. The result was a prototype of a vibrating nozzle system which became the basis for the foundation of a start-up. There followed work on bioartificial organs, in particular xeno- and holo-transplants of pancreatic islets, which resulted in the development of a sterilisable system but still only a single nozzle and limited flow rates.

> THE PROBLEM ... WAS THE LACK OF SYSTEMS TO PRODUCE MICROCAPSULES OF DEFINED PROPERTIES

Many years of research followed and some excellent work was carried out by COST840 and 865 groups to define the methods to characterize capsules. However, while excellent equipment has been developed and presented at many of the BRG meetings, the majority are based on classic methods (some of which are described in the article within this news letter) and, although some might disagree, there are still major limitations in the production of microcapsules of defined size, certain size ranges, shape and properties at a scale suitable for commercial application and under controlled environmental conditions.

In addition, the polymer systems still represent a major limitation to many developments and applications, since they are often of natural origin and highly variable in composition and properties, which make them difficult to prepare using the encapsulation devices e.g. variable molecular weight distribution, wide range of viscosities, purity, degree of substitution etc. Indeed synthetic polymers frequently suffer from the same problems!

The applications of encapsulation are far to numerous to list, in an enormous range of areas covering food technology, biomedical, taste- masking, protection of active ingredients, water treatment and many more. In my view however, a lot of collaborative work has been hampered by the desire to commercialise the results which has limited true collaboration between researchers. It is my request that we define some of these areas, whether equipment design and development, polymer production or specific applications to attack these problems before another 25 years passes- I am certainly open to discussion!

Presently I am the Director of a new research centre in Dublin (NIBRT) and I welcome you all to look up the website (www.nibrt.ie) and visit the centre both virtually and by coming to Dublin for a visit and a Guinness. These industry-like facilities (GMP-compatible) are open for use by all of you, and I would be very keen to set-up an encapsulation laboratory with your support- sabbaticals, secondments and collaborations are welcome!

Ian Marison

CONFERENCES

CONFERENCES : 20TH ANNIVERSARY !

XIX INTERNATIONAL CONFERENCE ON BIOENCAPSULATION

Amboise, France - October 5-8, 2011

1991-2011 : Our association is already 20 years old, one generation so to say; it was therefore decided to organise an exceptional event on the occasion of the 20th anniversary.

Our annual internatioOur annual international conference will take place in one of the most beautiful touristic areas of France, the Loire Valley.

Conference and accommodation will both be located in a charming castle-like resort close to the beautiful town of Amboise For three days you can meet other experts in Bioencapsulation from all over the world in a friendly atmosphere, enjoy the French gastronomy and visit Leonardo da Vinci's last residence.

→ October 5th, 2011

- **Registration & buffet**

→ October 6th, 2011

- **Registration**
- **Welcome**
- Session 1 : **Missing Challenge**
  Chairperson : Dr. E. Perier, LVMH, Fr
- Session 2 : **Food and Nutrition**
  Chairperson : Prof J.P. Simon, Eurobiotech, Be
- Exhibitor special session
  Chairperson : Mr J.A. Meiners, MCC, Ch
-
- Session 3 : **Probiotic and enzyme-**
  Chairperson : Prof. C. Lacroix, ETHZ, Ch
- Session 4 : **Environment and Agriculture**
  Chairperson : Prof. B. Boh, Univ. Ljubljana, Sl.
- Conference banquet

→ October 7th, 2011

- Session 5 : **Cell immobilization Story**
  Chairperson : Prof. J.N. Barbottin, Univ. Amiens
- Session 6 : **Engineering from the lab to the manufacture**
  Chairperson : Prof. R.J. Neufeld, Queen's Univ. Ca
- Session 7 : **Biopolymers, first key of success**
  Chairperson : Prof. G. Skjak-Braek, NTNU, No
  Guided tour to Chateau le Clos de Lucé & French specialities buffet

→ October 8th, 2011

- Session 8 : **Deliver biopharmaceuticals**
  Chairperson : Prof. Thierry Vandamme, Strasbourg (Univ., Fr)
- Session 9 : **New therapies using microcapsules**
  Chairperson : Prof. E. Markvicheva, IBCH, Ru

More information at :

- http://bioencapsulation.net/2011_Amboise

By offering grants to students and researchers from all over the world to attend, we wish to increase the quality of the conference BUT we need the support from our industrial partners as sponsors or as exhibitors. For more information see the conference web site or do not hesitate to contact:
contact@bioencapsulation.net

UPCOMING EVENTS

XV INDUSTRIAL SYMPOSIUM AND VI TRADE FAIR ON MICROENCAPSULATION

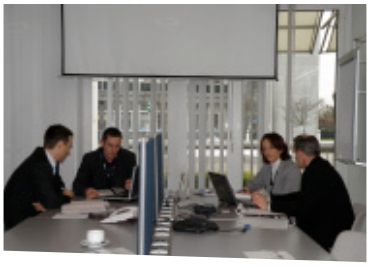
Archamps/Geneva, France - March 20-22, 2012

Why this symposium ?

Over the last 20 years, BRG organized more than 50 successful events on microencapsulation. BRG acquired a unique expertise in organising industrial events based onone of the largest address books in the domain. This event will bring together leaders in microencapsulation & nanoencapsulation from a variety of industries. We expect up to 150 industrials coming from all over the world and plan to organize more than 600 individual meetings.

Organization

- Conference Program : 14 lectures from leading experts in microencapsulation.



- Technology Trade Fair : based on your pre-selection among the list of participants, get up to 20 one-to-one 40 minute appointments.

- Exhibition : a broad state-of-the-art showcase presenting R & D, Equipment, Material & Chemicals.

MARCH 20TH, 2012

Session 1 : Overview

- Encapsulation: Overview on Technologies and Applications Ron Neufeld, Queen's Univ. Canada
- Opportunities and challenges in encapsulation for Home & Personal Care Products - Katherine Thompson (Unilever, UK)
- One-to-one meetings + exhibition

Session 2 : Technologies

- Spray drying technologies and applications - Stephan Druch (Beuth Hochschule fur Technik, Germany)
- Fluid Bed Coating: Theory and Practice - Chuck Frey (Coating Place, USA)
- Encapsulation ... a success story -Richard Dring (Kerry, Irlande)
- One-to-one meetings + exhibition

MARCH 20TH, 2012

Session 3 : Materials

- Microencapsulation by chemical methods - Vriezema (Encapson, Netherlands)
- Silicon sol gel encapsulation - Leon Marteaux (Dow Corning, Belgium)
- One-to-one meetings + exhibition

Session 4 : Innovations

- Colloidal Polyelectrolyte Complexes for the Delivery of Pharmaceuticals - Thierry Delair (Lyon University, France)
- Cosmetics and microencapsulation - Sven Gohla (La prairie, Switzerland)
- Performance of industrial enzyme formulations through the years, with respect to wear resistance - Gabrie Meester (DSM, Netherlands)
- One-to-one meetings + exhibition

MARCH 20TH, 2012

Session 5 : Applications

- Food and feed ingredient encapsulation - Jean-Antoine Meiners (MCC, Switzerlands)
- Flavour encapsulation - Jenny Weissbrodt (Symrise, Germany)
- One-to-one meetings + exhibition

MORE INFORMATION

http://bioencapsulation.net/2012_Archamps

EXHIBITORS DEAL

We would like to offer the exhibitors a deal. Each registered exhibitor will receive a promotion code, which can be shared along with symposium invitations to customers, suppliers and partners. Use the code for:

- **5 registrants: half-price registration for exhibitor**
- **10 registrants: FREE registration for exhibitor**

ARTICLE

MICROENCAPSULATION BY DRIPPING AND JET BREAK UP.

Dr. Micheal Whelehan (Dublin City University, Dublin, Rep. of Ireland) and Prof Ian W. Marison (Dublin City University and National Institute of Bioprocessing Research and Training, Dublin, Rep. of Ireland)

INTRODUCTION

Microencapsulation can be defined as a process, which involves the complete envelopment of pre-selected core material(s) within a defined porous or impermeable membrane (shell) using various techniques, to give miniature sized particles ranging in size from 1-1000 µm [1]. Microcapsules can take many structural forms (Figure 1) and have proven to have many exploitable characteristics for application in many different processes. They can be manufactured from a wide range of natural and/or synthetic materials, but are also commonly found in nature i.e. plant seeds, bacterial spores, egg shells etc [1].

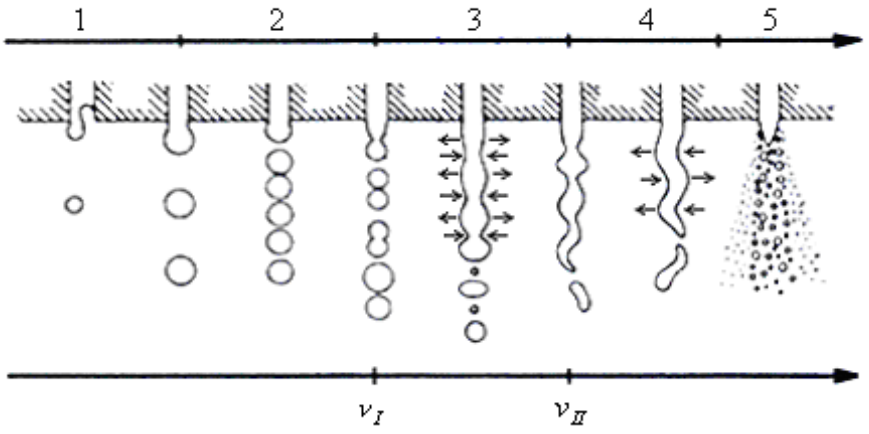


Figure 2: Different mechanisms of dropplet formation as a function of the jet velocities [1]

For over a half a century now, microencapsulation and encapsulated products have played a very important role in numerous industries like agriculture, chemical, pharmaceutical, cosmetic and the food industry. In recent decades these particles have been applied to numerous biotechnology and medical processes, including cell encapsulation for the generation of artificial implants [2-4], and the production of high density cell cultures [5, 6] and the encapsulation of recombinant therapeutic proteins [7, 8] as a means of delivery. This has opened up a whole new exciting field for the technology and resulted in the development of new production procedures to help manufacture the desired microcapsules [9].

Due to its many existing and potential applications in many diverse areas, microencapsulation has received much attention from both academic and commercial bodies and its further development is seen as a major interest both from an economic and scientific point of view. The growing interest is demonstrated by the exponential increase in the number of publications (non-scientific and scientific articles and patents) reporting on the subject over the decades since the 1950s [10].

In industries like agricultural, food and cosmetic, the prerequisite for the successful employment of the technology is usually only limited to high production rates at low cost, however for application in medical and biotechnological processes the criteria is somewhat more stringent and will be discussed later in this article. To-date no established or newly developed encapsulation technique can fully adhere to the criteria, and the limitations possessed by all have slowed down and/or prevented the use of encapsulation technology at an industrial level for biotechnological and medical applications.

Production of microcapsules by technologies based on dripping and jet break up have gained significant interest mainly due to their relatively simplistic approach to produce the microcapsules. These techniques include simple dripping, electrostatic extrusion, coaxial airflow, vibrating nozzle, jet cutting and spinning disk atomization.

The goal of this article is to compare and contrast some of the commonly used encapsulation techniques (based on dripping and jet break up phenomenon) on their ability to produce microcapsules for application in medical and biotechnological processes.

Requirements of an encapsulation technique for producing microcapsules for medical and biotechnological applications

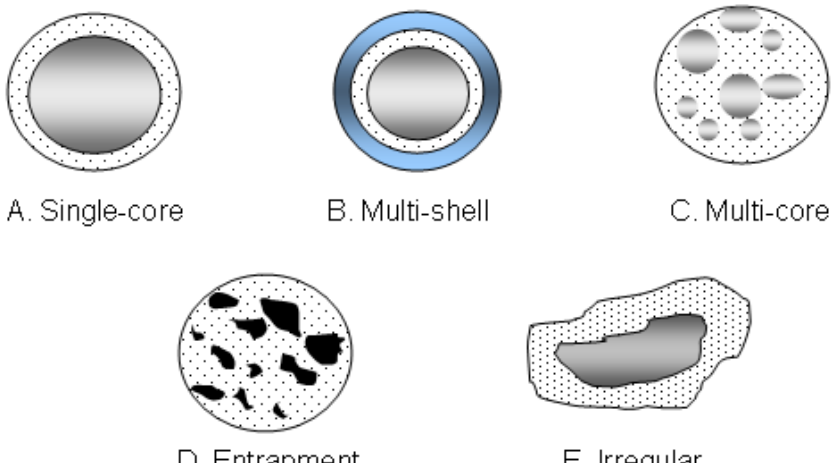


Figure 1. The five main structural forms of microcapsules

A methodology used to produce microcapsules for medical and biotechnological process must have the capability to produce mono-dispersed, homogenous and spherically shaped capsules, of a small size and with a narrow size distribution, which is performed under simple conditions with a short production time, obtaining a high efficiency and production rates, using many different materials, including highly viscous solutions. It should also enable different sizes to be produced and many different core materials to be encapsulated, and finally if required, can be performed under sterile conditions [1].

PRODUCTION OF MICROCAPSULES BY TECHNIQUES BASED ON DRIPPING AND LIQUID-JET BREAK UP

Many different techniques for the production of microcapsules have been described in literature [11, 12] and a description/comparison of all techniques is beyond the scope of this article. This review will describe the production of droplets (converted into microcapsules) by techniques based on dripping and liquid-jet break up principles. Obtainment of the droplets in both cases requires the extrusion of a liquid through a nozzle/orifice.

DROPLET FORMATION AT AN ORIFICE

The extrusion of a liquid through an orifice results in one of five different droplet formation processes occurring at the discharge point of the nozzle (Figure 2), with the mechanism dependent on the velocity of the extruded liquid [13]. The different mechanisms arise due to the interaction of gravitational, surface tension, impulse and frictional forces [14]. At very low velocities, the extruded liquid sticks to the edge of the nozzle until the gravitational force is high enough to overcome the surface tension, resulting in the release of a drop (mechanism 1). A small rise in the velocity increases the number of droplets formed, whilst further escalation amplifies droplet formation (mechanism 2), and can result in coalescence of the droplets occurring, reducing mono-dispersity.

Mechanism 1 and 2 are commonly used at lab scale where only small volumes of droplets are required and the process is commonly known as 'dripping'. Further increasing the velocity causes the formation of an uninterrupted laminar liquid-jet (continuous stream), which eventually breaks up into droplets by axial symmetrical vibrations and surface tension (mechanism 3). An additional escalation of the jet velocity leads to statistical distribution of the droplet size, which is caused by either spiral symmetrical vibrations (mechanism 4) or by the high frictional forces that are present, when the jet is sprayed (mechanism 5) and neither mechanism for droplet formation will be discussed further in this article.

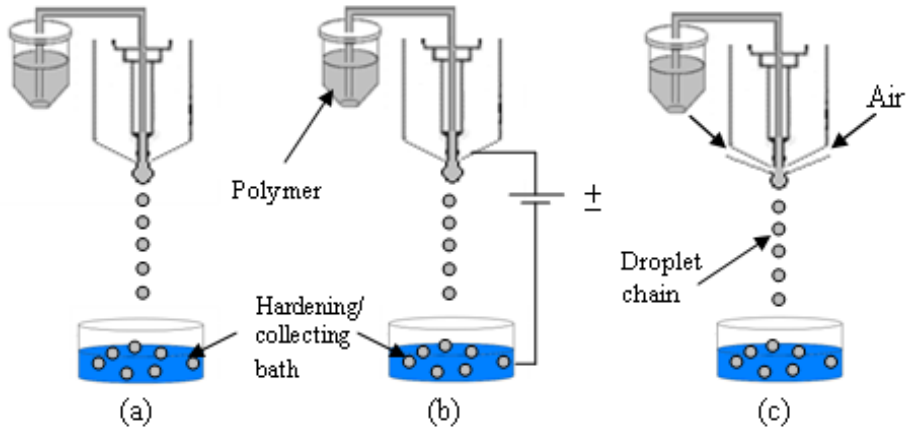


Figure 3: Different droplet/capsule production processes by techniques based on dripping. (a) simple dripping, (b) electrostatic extrusion and (c) coaxial airflow.

MICROCAPSULE PRODUCTION BASED ON DRIPPING

Simple dripping

Dripping is the oldest technology for the production of microcapsules. After formation (Figure 1, mechanism 1 and 2) the droplets are immediately solidified to capsules by either physical e.g. cooling or heating, or chemical means e.g. gelation (Figure 3a) and the size of the droplet is mainly dependent on the orifice diameter [15]. However the process is subjected to two main disadvantages: (1) Very low quantities of droplets are produced for pilot-scale or industrial application and (2) droplets formed have very larger diameters (usually → 2mm), which prevent the particles being applied to many medical and biotechnological processes.

Electrostatic dripping (extrusion)

The basis of electrostatic dripping for droplet generation (Figure 3b) is the acceleration of the normal droplet formation process using electrostatic forces to pull the droplets off the orifice (needle) at a considerably faster rate compared to the normal dripping process, whereby removal is based solely on gravitational force. The electrical potential, which can be static or pulsed [16] is applied to the extruded polymer solution by passing it through a charged nozzle, with the produced droplets subsequently falling into a collecting/hardening solution, which has being earthed or holds an opposite charge [17, 18]. If the electrodes are parallel plates, a uniform electric field is generated with respect to direction and strength, thus a uniform force is applied to the droplets at the tip of the nozzle [19]. It has been reported that the strong electric fields do not cause cells to lose viability and activity during the producing (encapsulation) process [20]. This technique is capable of producing smaller microbeads compared to normal dripping (↗ 50 µm in diameter), of uniform size and shape under reproducible conditions and can also be performed under sterile conditions [20].

Coaxial airflow

The coaxial air-flow technique (also known as the concentric air-jet technique), like the electrostatic extrusion method, is also based on the acceleration of the normal dripping process at an orifice (Figure 3c). The technique uses a stream of compressed air to pull the liquid droplets from the nozzle at a faster rate compared to the normal gravitational force [21, 22]. The coaxial concentric nozzle consists of an inner orifice, in which the polymer material is extruded and an outer orifice, through which the compressed air flows and strips the droplets formed at the tip of the internal nozzle [21]. The process is capable of producing capsules with diameters → 200 µm, of uniform size and shape, under reproducible and mild conditions and can be performed under sterile conditions [11, 22-24]. The main disadvantage of the system, like electrostatic extrusion, is the low production rates due to the low flow rate of the polymer solution through the nozzle. This can be overcome to some degree by increasing the air flow rate, but this can increase the trajectories of the produced drops resulting in a larger surface area being required, which could increase the complexity of the process. Even with these increases, significantly smaller throughputs are achieved in comparison to the other methods such as jet cutting and vibrating techniques [11].

Liquid-jet break up

As discussed previously, the extrusion of a liquid through an orifice at medium to high velocities will result in the formation of a continuous laminar liquid jet which can break up into droplets after a certain distance by natural vibrations (Figure 1, mechanism 3). Droplets can be formed at a higher rate by this method compared to dripping, however, jet break up is irregular and not fully controllable. This results in the formation of droplets which are not of equal size and shape [1].

Vibrating-jet (nozzle) technique

The method is based on the principle of controlled break up of the laminar jet by the application of a controlled vibrational frequency with defined amplitude to the extruded jet, as discovered by Lord Rayleigh. The exerted frequency causes the continuous liquid stream to break up freely into uniform droplets of equal size (Figure 4a).This highly regular and reproducible break-up occurs only at vibrational frequencies that are near the natural frequency for the break up of the jet itself.

The sinusoidal force can be applied by either vibrating the nozzle (vibrating nozzle technique), pulsating the polymer in a chamber before passing through the nozzle (vibrating chamber technique), or periodic changes of the nozzle/orifice diameter during extrusion [1]. Whilst no set agreement exists, the authors suggest that collectively these different methods of applying the sinusoidal force to the laminar jet be termed the "vibrating-jet break up techniques" [1]. The choice of method used to administer the vibrational force is dependent on the system which it is being applied too. The ability of this technique to produce microcapsules for medical and biotechnological applications will be discussed later in more detail.

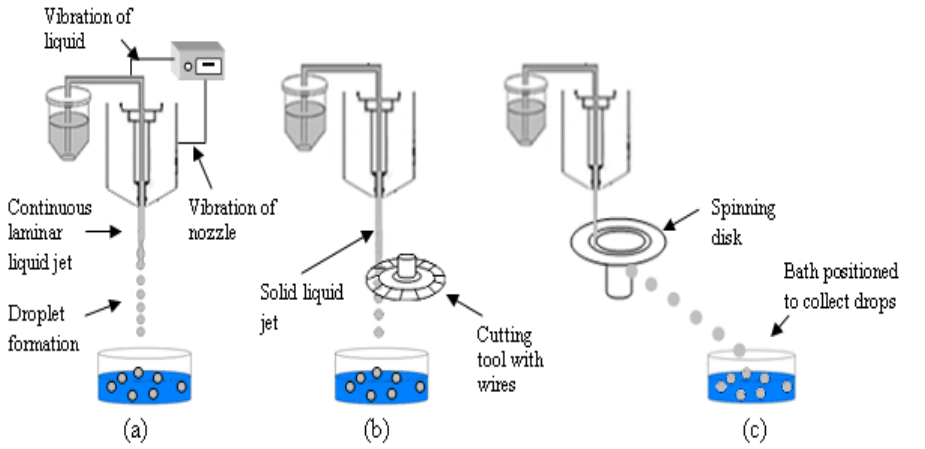


Figure 4: Production of microcapsules by techniques based on liquid-jet break up. (a) vibrating jet, (b) jet cutting and (c) spinning disk.

Jet cutting technique

The jet cutting technique was developed by Vorlop and Breford in 1994, and is based on the mechanical impact of a cutting wire on a solid liquid jet [25] (Figure 4b), the solid jet being formed by using special nozzles. When a polymer is forced through the nozzle at high velocity, a solid liquid jet is formed within a very short distance of the orifice (even with the use of the special nozzles, natural jet break will still occur after certain distances). This jet can then be broken-up into equal cylindrical segments when passed through a cutting tool, which consists of several wires fixed onto a holder [25] (Figure 4b). Due to surface tension, these cylindrical segments form spherical droplets/beads when passing through the air. The diameter of the resulting droplet is dependent on: (1) the number of cutting wires; (2) the number of rotations of the cutting tool; (3) the mass flow rate through the nozzle and (4) the mass flow depending both on the nozzle diameter and the velocity of the fluid [26]. This simple and effective method enables the production of small mono-dispersed homogenous shaped beads, → 200 µm to several millimeters in diameter, with a narrow standard size deviation using viscous fluids at high production rates [25, 27]. The main disadvantage of this method is the inability to produce microcapsules ← 200 µm, loss of material incurred during each cut of the liquid jet (known as the cutting loss) and to produce high quantities and these disadvantages will be discussed in more detail in the next section.

Rotating (spinning) disk atomization

Spinning disk atomization is a technique which is based on the disintegrating of a feed liquid performed on disc(s) to produce droplets [28] (Figure 4c). When a liquid is dropped onto the surface of a rotating disk it is centrifugally accelerated to a high velocity and distributes as a thin film on the disc. Depending on the flow rate of the feed, droplets are then released due to the centrifugal forces at the tip (teeth) of the rotating disk or from ligamentry streams released from the edge of the disk [29]. The size of the droplets

produced is determined mainly by the rotation speed of the disk. This simplistic technique has shown the capability to produce microspheres ↗ 200 µm in diameter [29], with a narrow size distribution and is easily scalable, with possible production capacities of tons/day using a multi-disk system [30] and will be discussed in more detail in the next section.

IMPLEMENTATION OF A CAPSULE PRODUCTION AT AN INDUSTRIAL LEVEL: CHALLENGES AND POSSIBLE SOLUTIONS

Table 1 displays the criteria which a capsule production methodology must adhere to in order for it to be employed in industry as a viable technique to produce microcapsules for medical and biotechnological applications. The ability of the six techniques discussed in this article to meet the criteria is also presented.

From Table 1 it can be seen that none of the production techniques can fully adhere to all the necessary criteria. For an industrial point of view the most important criterion is the ability to produce high quantities (tons/day) of the particles to meet product requirements. For the methodologies of simple dripping, electrostatic extrusion and co-axial air flow; the ability to produce large quantities is not viable, as even increasing the number of nozzles will not significantly increase the microcapsule output. This is highlighted by a study undertaken by Bugarski and coworkers using electrostatic extrusion, which showed that when scaled-up to a system of 20 needles, it was still only possible to obtain a low flow rate of 0.7 l/h (36 ml/h per needle) [18]. Furthermore, increasing cell and alginate concentrations hugely increase the size and size distribution of microcapsules produced by this system [20]. Due to their inability to be scaled-up adequately for industrial purpose, these three techniques will not be discussed further. The remainder of this section will focuses on the challenges facing the implementation of the vibrating jet, jetting cutting and spinning disk at an industrial level.

Challenge 1: Producing small sized particles

At present both the jet cutting technique and the spinning disk processes seem incapable of producing particles of less than 100 µm in size. For the jet cutting technique this could be overcome by using an inclined cutting plane, increasing the rotational speed of the cutting device, increasing the number of cutting wires and their diameter, whilst also decreasing the nozzle diameter and the viscosity (usually obtained using lower concentrations) of the extruded polymer. Reducing the latter can cause the production of fragile particles, or more importantly can result in the capsules losing their spherical shape during entry in the gelling solution. Loss of shape can be prevented by a pre-gelling step, performed before droplets

Table 1: Comparison of all six production techniques on their capabilities to meet the criteria outlined. The criteria is divide into (1) required characteristics of the produced capsules and (2) required features of the technique

CRITERIA	Simple dripping	Electrostatic extrusion	Coaxial air-flow	Vibrating jet	Jet cutting	Spinning disk
Capsules characteristics						
Mono-dispersed	✓	✓	✓	✓	✓	✓
Homogeneous and spherical shape	✓	✓	✓	✓	✓	✓
Small size[a]	X	✓	X	✓	X	X
Narrow-size distribution[b]	✓	✓	✓	✓	✓	✓
Characteristics of the technique						
Relatively easy set up and simple operation[c]	✓	✓	✓	✓	✓	✓
Short production time to produce droplets	✓	✓	✓	✓	✓	✓
High efficiency[d]	✓	✓	✓	✓	X	X
High production rates[e]	X	X	X	X	X	✓
Ability to extrude viscous solutions	X	X	X	X	✓	✓
Produce a range of different sized droplets	✓	✓	✓	✓	✓	✓
Operate under sterile conditions	✓	✓	✓	✓	✓	✓

✓ conforms to requirement, X Doesn't conform to criteria. [a]size smaller then 100 µm, [b]overall deviation of smaller than ± 5% from the mean size, [c]does not require experts to repeatedly set up, nor extensive training and supervision to operate the process, [d]no extensive loss of membrane and encapsulated material and [e]production capacity of tons/day

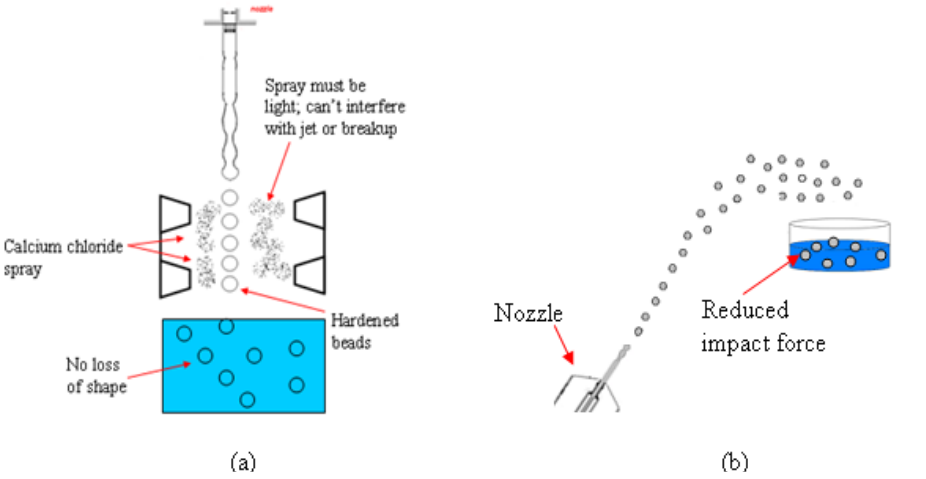


Figure 5: Methods to prevent droplets losing their shape before entry into the hardening solution. (a) Pre-gelling of alginate droplets and (b) soft landing method before entry of droplets into a gelling bath of calcium chloride.

enter the hardening bath (Figure 5a) or by using a soft-landing method (Figure 5b). For the spinning disk procedure, a reduction in size could be achieved by increasing the rotational speed of the plate and decreasing the volumetric flow rate of the polymer onto the disk, though rotating large disks at high speeds can cause it to vibrate and produce satellites. Smaller capsules can also be obtained by reducing the viscosity of the polymer, but again this can seriously affect the shape of the produced particle.

Challenge 2: High efficiency

The main disadvantage of using the jet-cutting is the loss of product incurred during each cut of the liquid jet. This is known as the cutting loss and can be decreased by re-cycling or applying proper inclination of the cutting tool or nozzle and by also using smaller cutting wires [25]. Whilst these losses can be reduced to negligible amounts for the production of small beads, they do however increase with the increasing size of the produced particles (due to use of thicker cutting wires). The affect of this invasive technique on cells or other encapsulants within the polymer during the cutting process is yet unknown (i.e. within the cutting loss and their ability to be fully re-cycled for future encapsulation without any damage being caused).
Sufficient material (from 5 – 50%) loss can also occur when using the spinning disk and this is a result of the formation of satellite droplets (size range of 60-250 µm) during the break up of the jet. The lighter and smaller satellite particles do not travel as far as the larger particles and for this reason do not reach the collecting/hardeining bath. This can be overcome by increasing the surface are of the gelling bath, but this will increase the overall size distribution and can also cause problems in ensuring sterility of this area during cell encapsulation.

Challenge 3: High production rates

The vibrating jet and jet cutting techniques are usually limited to relatively small production yields of small microcapsules, as they only produce single droplets, one after another at any given time. The production flow rate is mainly dependent on the nozzle diameter with increasing diameters resulting in higher production volumes. However even for the largest orifice diameters, very low production volumes are still achieved.

Increasing the production rates of a vibrating jet encapsulator can be obtained by simply increasing the number of nozzles on the machine [11]. This was shown by Brandenberger and Widmer (1998), when they increased output by adding more nozzles (from one to thirteen) to the nozzle plate of their Encapsulator to obtain a vibrating jet monocentric multi-nozzle Encapsulator [31]. Figure 6 shows a schematic of an eight-nozzle Encapsulator, which represents a system supplied by EncapBioSystems, and is similar setup to the device used by [31], the main difference being the presence of an electrostatic device on the EncapBioSystems model.

The flow rate can be kept constant on the multi-nozzle Encapsulator by pumping the polymer through a concentric split (Figure 6) placed before the nozzles. When using this spilt, Brandenberger and Widmer (1998) were able to obtain a relative flow difference of ← 2.0% between all thirteen nozzles on their Encapsulator. Before extrusion, the polymer solution passes through a vibrating chamber which transmits a disturbance onto the solution, hence resulting in the break up of all jets into droplets of equal size. Whilst differences in droplet size can be obtained; this can be attributed to small differences in the diameters of the nozzles. Subjecting all liquid jets with the same sinusoidal force would pose a difficult engineering challenge and this is another reason for using a pulsating chamber to exert the perturbation onto the extruded jet, compared to vibrating each nozzle individually.

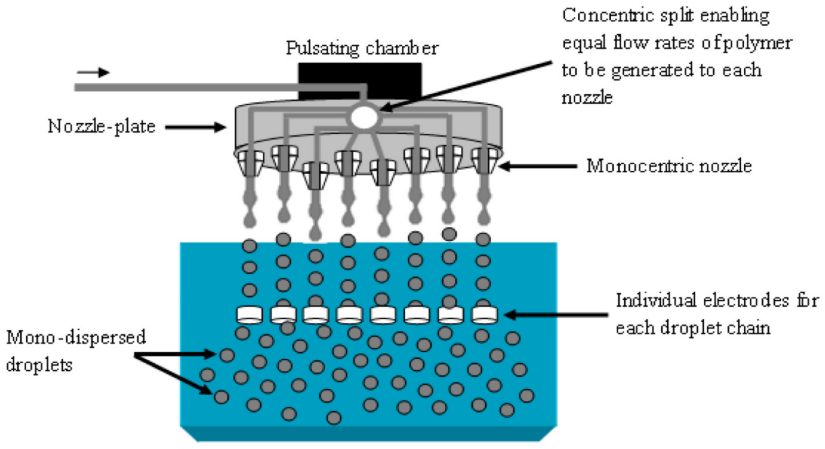


Figure 6: Monocentric multi-nozzle Encapsulator, representing a device supplied by EncapBioSystems, in which eight nozzles are present on the nozzle-plate.

Challenge 4: Extrusion of viscous solutions

This problem of only being able to use solutions containing low concentrations of the polymer (i.e. alginate), which only allows the production of particles with limited mechanical strength, can be resolved by reducing the viscosity of the alginate solution. This can be achieved by increasing its temperature during extrusion through the nozzle(s). Recently an apparatus has being developed (by EnCapBioSystems), for heating and/or maintaining polymers solutions at controllable temperatures as they pass through the pulsation chamber, before extrusion and break-up. This apparatus, termed a heating nozzle/pulsating-head device (Figure 7), consists of a temperature control unit connected to a heating element placed adjacent to a circular aluminum casing, which conducts the heat from the element. The pulsating chamber with the nozzle holder attached sits within the heating device and is completely enveloped. The casing itself can be fastened tightly to the nozzle housing to improve heat transfer and enables a more precise temperature control. The heating apparatus can supply a controllable temperature of up to 60 °C ± 1 °C to the chamber which subsequently heats and/or maintains the temperature of the polymer during extrusion and jet break-up. The shell and/or core liquid can be heated in their reservoirs to the desired temperature using standard water baths before being pumped along insulted tubing to the pulsating chamber. At present only preliminary experiments have being preformed in regard to using this device and as of yet, no concrete conclusions can be made. However initial experiments have being performed and have shown the device to enable concentrations of alginate of ↗ 4% (w/v) to be successfully produced into microcapsules which showed considerably improvements in mechanical strength compared to lower concentrations of alginates.

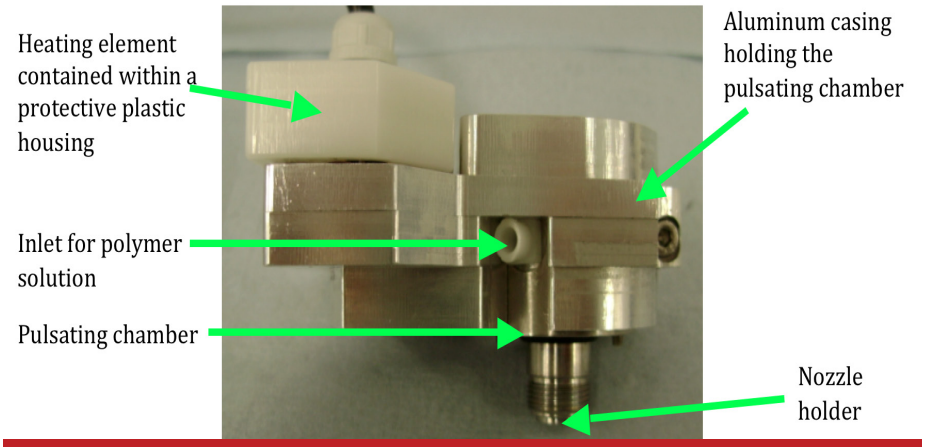


Figure 7: Image of the heating nozzle/pulsating-head device for the Inotech Encapsulator IE-50R.

SUMMARY

Capsules in the micron size range have played a very important role in a vast variety of industries such as, pharmaceutical, cosmetics, agricultural and food since the early to mid-twentieth century, with the food industry being one of the biggest benefactors. Such has being its success; that in the 70s scientists set-about in implementing the versatile technology to medical and biotechnological fields. Originally it was anticipated that similar achievements could be obtained in comparison to the aforementioned industries, when it came to developing new products, improving existing ones, or in some situations completely re-defining the role of a commodity.

Unfortunately in this period of time the technology has not reached what many would perceive as its full potential when being applied to these areas. This point is exemplified by the few medical and biotechnological products available commercially which make use of the technique. The problem has being mainly attributed to the slow development of methodologies needed to manufacture the particles at a large scale-level and meeting the required properties. This has culminated in many situitions whereby a potentially successful product incorporating encapsulation technology has been developed, but no method is available to carry out production.

In recent time techniques based on dripping and jet break up have been extensively studied on their capabilities to produce microcapsules for biotechnology and medical applications. Unfortunately, these methods possess the characteristic problems of being unable to produce small (← 100 µm) and homogenous shaped microspheres/microcapsules at a large scale level using highly viscous (up to several thousand mPas) materials.
Of all six techniques discussed, the vibrating jet and the jet cutting techniques seem the most capable of overcoming these obstacles. The problem of extruding highly viscous solutions through the nozzle(s) and ensuring their optimal break-up when subjected to vibrational frequencies can be achieved by heating the polymer using a heating nozzle/pulsating-head device.

Whilst elevated temperatures (↗ 45 °C) can be detrimental to certain animal cells, aroma compounds and bioactives, it must be noted that use of these temperatures at the short period of time required for the process to be successful, should not affect most materials. For heat sensitive encapsulants temperatures of 35-45 °C can be employed. This heat should be adequate to reduce the viscosity to the necessary level to obtain extrusion and adequate jet breakup, whilst not damaging the encapsulated product.
Use of the heated nozzle apparatus should provide an optimal method to encapsulate a large range of materials within the desired membranes, especially when viscous materials like gelatin's and gums are required.

Large scale production can be achieved by increasing the number of nozzles on the head plate of the encapsulator. For this to be successful, each nozzle must obtain identical production conditions, such as frequency, amplitude, etc., which can be accomplished in a relatively simple manner. However, obtaining similar liquid flow rates is somewhat more problematic. Fortunately this can be overcome by employing a concentric split, which enables an equal flow to be distributed to all nozzles. Provided that all orifice diameters are identical, the relative flow difference between each nozzle should be negligible.
It is envisaged that future use of the multi-nozzle system will enable the production of required quantities of microspheres/microcapsules for industrial use.

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UPCOMING EVENTS

SOUTH AMERICAN SYMPOSIUM ON MICROENCAPSULATION

Limeira, Brasil - April 30 - May 2, 2012

Organized in collaboration with

UNICAMP

APRIL 30, 2012

Session 1 : Methods

- Microencapsulation Introduction & Applications - Denis Poncelet, Oniris, France
- Particle engineering using spray drying - Maria Inès Ré, EMAC, France
- Nanobiotechnology : strategies to medical , environmental and agricultural encapsulation - Nelson Duran, UNICAMP, Brazil
- Coacervation and hydrogel encapsulation - Carlos Grosso, UNICAMP, Brazil

Session 2 : Case studies

- Encapsulation technologies for herbal products- Wanderlei P. Oliveira, USP, Brazil
- Liposomes - Maria H. Santana, UNICAMP, Brazil
- Electrospinning process: A versatile method for the encapsulation technology - Maria Helena Ambrosio Zanin, IPT, Brazil
- 3 open lectures

MAY 1, 2012

Session 3 : Industrials

- Encapsulation Challenges and Future - James Oxley, SwRI, Texas
- Engineering aspects of microencapsulation - Denis Poncelet, Oniris, France
- Microencapsulation: applications for cosmetic industry - Jenny Ling, Natura, Brazil
- Microfluidic devices applications to Microencapsulation - Mário Gôngora, IPT, Brazil
- Microencapsulation of Functional and Nutraceutical ingredients: challenges and achievements - Eduardo Cárita, Mikron, Brazil

Session 4 : Demonstrations

- Hydrogel beads and microcaspule, Denis Poncelet, Oniris, France
- Coacervation, Carlos Grosso, UNICAMP, Brazil
- Polymerisation, Nelson Duran, UNICAMP, Brazil
- Spray drying, Izabela Alvim, UNICAMP, Brazil
- Spray coating, Ana Siliva Pratas, UNICAMP, BrazilMay 1st, 2012

MAY 2, 2012

Session 5 : Applications

- History, challenges and perspectives of cell microencapsulation - Paul de Vos, UMCG Groningen, Netherlands
- Applications of encapsulation for food ingredients - Gary Reinecus, University of Minnesota, USA
- Aquaculture: microdiets for fish larvae - Maria Cella Portella, UNESP, Brazil
- Cosmetic: particles for skin applications - Silvia Guterres, DF/UFRGS, Brazil
- Environment: Ecosystem protection by effluent bioremediation - Oswaldo L. Alves, IQ/UNICAMP, Brazil

Session 6 : Applications

- Medicine: Microencapsulation of pancreatic islets- Thiago Mares Guia, USP, Brazil
- Nutrition: Probiotics microencapsulated- challenges applications- Carmem Favaro, USP, Brazil
- Nutrition: Probiotics in dairy products - Mirna Gigante, UNICAMP, Brazil
- 3 opens lectures

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JOURNAL

Journal of Microencapsulation Volume 28, Number 6 (2011)

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- **Formulation and optimization of alkaline extracted ispaghula husk microparticles of isoniazid – in vitro and in vivo assessment** D.P. Maurya, Yasmin Sultana, M. Aqil, D. Kumar, K. Chuttani, A. Ali, and A.K. Mishra, Journal of Microencapsulation 2011, Vol. 28, No. 6, 2011: 472-482.
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Functional Filmcoating
September 27 - 29, 2011, Weimar, Germany
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http://bioencapsulation.net/2011_Amboise

Microencapsulation and Particle Coating - An Introductory Course
October 19-21, 2011, New Brunswick, NJ
http://www.cfpa.com/201110190774-10a/774/d/courseSummary.aspx

Exosomes and Microvesicles 2011
October 15-17, 2011, Lake Buena Vista, Florida 32830, USA
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AUS-CRS 5th Annual Meeting
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http://www.crsaustralia.org/

XXVIièmes SCIENTIFIC GTRV MEETING
December 5-7, 2011, Bruxelles, Belgium
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9th International Conference on Biological Barriers
February 29 - March 9, 2012
http://www.uni-saarland.de/info/wirtschaft/kwt/messe-kongresse/biologicalbarriers-2012.html

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Graduated in Chemistry (BSc) from Gadjah Mada University in Indonesia, I work several months as technical support for Buckman Laboratories in Singapour. In 2010, I got a PhD from Ecole Nationale Supérieure de Chimie de Montpellier (ENSCM) and Ecole Des Mines d'Alès (EMA) in collaboration with Bluestar Silicone. My scientific skills include composite formulation skills including mineral filler, flame retardant, polymer and formulation process, encapsulation of active ingredients and analytical chemistry. For reference, please contact Prof Denis Poncelet (denis.poncelet@oniris-nantes.fr), Dr.François Ganachaud (francois.ganachaud@enscm.fr).

Should you have any questions, please feel free to contact me: Siska Hamdani-Devarennes (siskahd@gmail.com)

ARTICLE

PREPARING FUNCTIONALIZED THREADS, SCAFFOLDS AND MICRO BUBBLING/FOAMING WITH ADVANCED MATERIALS

Dr. S. N. Jayasinghe, University College London, and N. Suter, Nisco Engineering Inc.

The unique and versatile aerodynamic and pressure driven technologies [Fig.1] possess the ability to form not only droplets, but also threads, scaffolds, micro bubbles and micro foams. These new approaches offer several advancements over existing technologies, while both operating in stable and continuous operation, with a significantly reduction in their hazardousness to the operator.

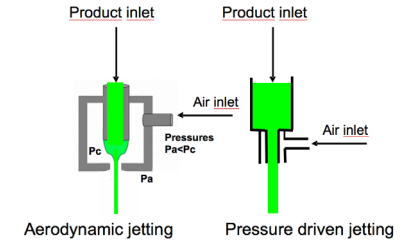

Figure 1: Aerodynmic and pressure driven technologies

It is seen from the operational map that there are two defined regions where droplets and threads are formed (Fig. 2,3). Threads can also form a scaffold/membrane, which is very important for applications in regenerative medicine (Fig. 4).

At given operational conditions it is possible to create micro bubbles/ foams. Figure 5 shows such multi-composition structures.

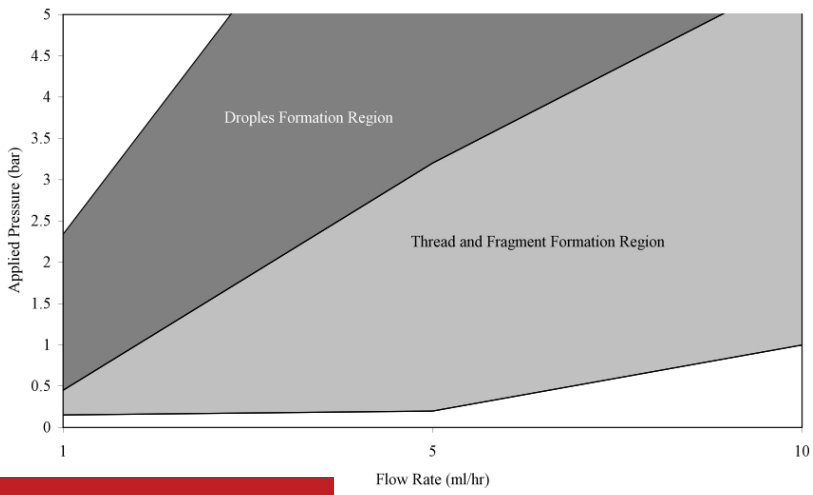

Figure 2: Operational map

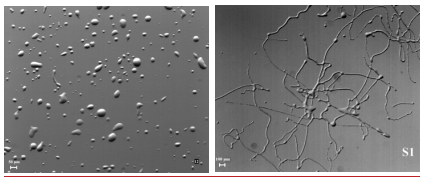

Figure 3: Droplet and tread regions

These techniques have been demonstrated for handling multi-compositional suspensions containing micro/ nanomaterials combined with living cells. It is also possible to convert this approach into a high-throughput method by incorporating an array of needles and thus increasing production volumes.
Generally, these new structural entities could be useful for tissue engineering, regenerative medicine and controlled and targeted cellular advanced therapeutics.

PUBLICATIONS

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[2] S. Arumuganathar, S. N. Jayasinghe, N. Suter, Unique Aerodynamically Driven Methodology for Forming Droplets, Threads to Scaffolds, Journal of Applied Polymer Science, Vol. 104(2007), 3844-3848Fig.2a Droplet region Fig.2b Thread region

Figure 4: Scaffolds

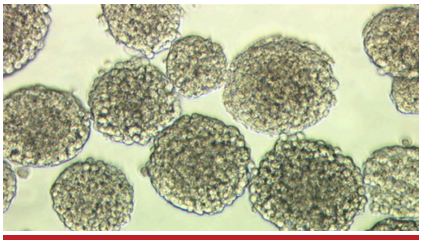

Figure 5: Microbubbles foams

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Prof. Suwan Jayasinghe has got in 2003 a PhD from the Department of Materials in Queen Mary, University of London, London where is now appointed as Academic Fellow investigating Materials Science and Engineering as applied to biological and medical fields of research, funded by the EPSRC and Research Councils (UK). He was Awarded the 2002 De Montfort Medal for "Excellence in Science, Engineering, Medicine and Technology" and the 2002 Leonardo Da Vinci Gold Medal for "Excellence in Engineering Sciences". He has over 120 status papers.

Immobilisation of porcine pancreatic lipase in liquid-core capsules

Sariah Abang

Supervisor : Denis Poncelet

Presentation : Oniris, Nantes, France - October 2011
Keywords: Liquid-core capsules, lipase, enzyme immobilisation, alginate, pectin
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Abstract : Liquid-core calcium-alginate capsules were prepared by dripping calcium chloride-in-oil emulsion into an alginate solution. The operating condition impacts on the membrane thickness and mechanical strength of capsules were evaluated.
Capsules were applied in the porcine pancreatic lipase immobilization. Encapsulation efficiency was 60% without losing their enzyme activity. Biocatalyst showed higher catalytic activity relative to free enzyme. However, leaching of lipase from the capsules membrane occurred after repeated use and low storage stability at room temperature and 4°C.
Porosity of the calcium-alginate membrane was reduced by applying a composite membrane of alginate and pectin. Alginate-pectin capsules demonstrated higher encapsulation efficiency and reduced the leaching of lipase from the capsules. Storage stability of the immobilised lipase in calcium-alginate-pectin capsules was improved by storing them in low water activity environment.

Encapsulation of probiotics for improved stability and bioavailability

Sinéad B. Doherty

supervisor : André Brodkorb
Presentation : Moorepark Food Research Centre, Fermoy Co. Cork and University College Cork, Ireland, October 2011
Keywords: droplet encapsulation, probiotics, whey proteins, delivery, gastro-intestinal digestion
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Abstract : The concept of protection and controlled release of an encapsulated ingredient at the right place and the right time has become a key competitive technology. The ability of milk proteins to form cold-set gels opens interesting opportunities for whey proteins as cost-effective probiotic-carriers. A novel encapsulation technique was developed for probiotic protection using gelled protein micro-beads of defined shape and size. Process optimization created high encapsulation efficiencies (←98) and minimum micro-bead diameters (180?m), while coated micro-beads were designed for delayed cell-release. Probiotic protection was validated during in vivo animal studies with probiotic viability highest in the intestine of animals fed encapsulated probiotics (7.2 log10cfu/ml) relative to free probiotics (3.0 log10cfu/ml). Hence, cell encapsulation in whey protein micro-beads created suitable matrices for cell stability and bioavailability during gastric delivery.

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Fabrication and characterization of microcapsule populations with a microfluidic technique

Thi Xuan Chu

Supervisor : Dominique Barthès Biesel ; Eric Leclrec ; Anne-Virginie Salsac
Presentation : 09/30/2011 at the University of Technology of Compiègne
Links: eric.leclerc@utc.fr

Abstract : An inverse analysis method which combines the microfluidic technique with the numerical simulation has been developed for the determination of the shear modulus of microcapsule populations. This method allows the discrimination between various ovalbumin microcapsule populations fabricated under different physico-chemical conditions. The elasticity of microcapsule membrane was successfully correlated with the reticulation degree of the fabrication.
For online fabrication and characterization, a microsystem was designed. It consisted in three parts: a double flow-focusing system for controlling the microdroplets and microcapsules fabrication, a wavy microchannel for controlling the reticulation time and a cylindrical microchannel for online characterization using the inverse analysis method. We found that the droplet size is increased with the flow rate ratio of continuous and dispersed phases, but did not change with the flow rate of reticulation phase. The online reticulation has been demonstrated by the wrinkles on the membrane, and the membrane properties were extracted successfully.

ARTICLE

FLOW FOCUSING® MICROENCAPSULATION: MUCH MORE THAN DRIPPING

Flores-Mosquera, M.; Jurado, G; Chávez, S.; Gañán-Calvo, A.M. (INGENIATRICS, Seville, Spain).

INTRODUCTION

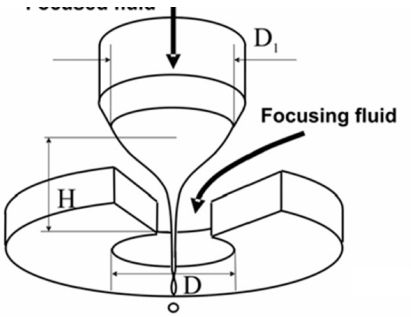
Numerous strategies and processes have been developed to obtain microparticles; the determinant step being the drop formation, which fixes the size distribution of the resulting microparticles. Depending on the physical properties of the fluids, different techniques or mechanisms are used to produce monodisperse drops. One of the more straightforward strategy is the formation of a single drop at a time, as in dripping processes [1-4]. Notwithstanding the very uniform microparticles obtained by this technique, it has some disadvantages as the drop-production rate is very low and the drop diameter scales with the diameter of the capillary or the pore, which makes it difficult to produce microparticles of a few micrometers or less.

The second strategy is the formation of numerous drops at a time, as in mixing or stirring processes[5], with scarce size predictability and homogeneity, or jet-disintegration techniques, in which a wide range of drop sizes is obtained, with different distributions depending on the Reynolds and Weber numbers of the jet. In particular, in laminar-jet disintegration or Rayleigh breakup [6] , the jet breaks up into uniform droplets due to capillary instability. One of the main features is that capillary jetting from a fluid source gives rise to droplets significantly smaller than dripping under the same operating conditions.

FLOW FOCUSING®

Flow Focusing® (FF) is a laminar-jet disintegration technology that uses the combination of a specific axisymmetric geometry and hydrodynamic forces to generate, under certain conditions, a microjet much smaller than the nozzle orifice, making the drop size independent of any geometrical dimension of the device: see Figure 1. One advantage of FF is the precise control of the microjet diameter that is achieved, and consequently of the droplet diameter, when the ratio of the jet inertia forces over the surface tension forces (i.e., the Weber number) is below a certain limit.

Figure 1. A schematic of the experimental flow-focusing setup. The disperse fluid is injected, with a syringe pump, through a capillary tube inside a chamber and pressurized by a continuous fluid supply. As the exit orifice of the chamber is facing the tip of the feeding tube, the focusing fluid stream forces the injected liquid (focused fluid) to exit the chamber through the orifice, producing a microjet much smaller than the exit orifice. The microjet proceeds downstream until it breaks up into a chain of nearly uniform drops.



Flow Focusing® was discovered in 1994 by Professor Alfonso Gañán-Calvo and developed by his research team. Since then, this micorfluidic technology has become the main business line of Ingeniatrics (Seville, Spain).
Based on this Proprietary Technology, Ingeniatrics has developed different tailor-made encapsulation processes of active substances, in order to stabilize them and provide protection from their external environment, as well as for controlled-release dosage, combination of mutually incompatible substances, etc.

Flow Focusing® is able to very gently produce and process aerosols and emulsions which, after the solidification process best suited to each system, gives rise to microparticles of the required composition and dimension, all the same as each other, something difficult to achieve by other technologies without further treatment.
In particular, here we show successful examples of the Flow Focusing® technology for the microencapsulation of different types of cells in monodisperse hydrogel microspheres using a Cellena® Flow Focusing® microencapsulator (Figure 2).

Figure 2. Cellena® User-friendly portable lab equipment for homogeneous encapsulation of living cells and microorganisms with sterile disposable nozzles.

CELL ENCAPSULATION BY CELLENA®

Cell encapsulation is an increasingly prominent and innovative technology that can provide solutions to complex problems within the area of biotechnology. In general, cell microencapsulation provides varying degrees of protection and isolation from their environment. It uses porous materials for the outer capsule which allow not only the diffusion of nutrients from outside to inside so that particles receive the necessary supplies for cell viability, but also permits the elimination/release of secretory products, both toxic and/or active substances, from cell metabolism.

Cellena® is the first bioencapsulation equipment developed by Ingeniatrics that is based on the Flow Focusing® technology. Its design allows encapsulation of cells / organisms in sterile conditions in the particle size required depending on the application type. Main features are:

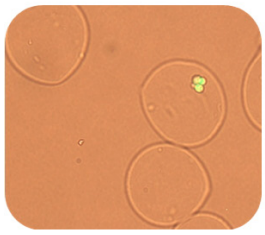
- Methodology in sterile conditions.
- Choice of particle size depending on the application, i.e. 90µm, 120 µm, 200 µm, 300 µm ... up to 500 µm
- Individual encapsulation of microorganisms in very small particle sizes.
- Uniformity of particle size, with reproducible composition.

- Very gentle technology that does not compromise cell viability.
- Validated for polymers solidified by ionic gelation: alginate, cellulose, etc

By means of Cellena® it is possible to produce monodisperse alginate microparticles containing individual bacteria, yeast and human stem cells (Figure 4). Alginate particle sizes were reproducibly selected from less than 100 µm to over 600 µm depending on the final application. Some of the main applications are:

- Cell susceptibility studies and microbial analyses
- Identification of potential biodiversity libraries
- Discovery of new, strong activity molecules
- Cell therapy
- Logistics
- Culture alternative for non-cultivable cells and organisms

One of the most important specific advantages of Cellena® is its unique ability to non-aggressively generate particles/micro-reactors of uniform and very small size that can be employed to address certain areas of microbiological research, in which it is essential to investigate microorganisms individually, without interference from other cells or strians present in the sample and speedily assessing the influence of various external factors (temperature, additives in the matrix like salts, antibiotics, cytotoxins, antibodies, enzymes, etc.) during a short number of division cycles. Some applications of individual cell-microencapsulations are:



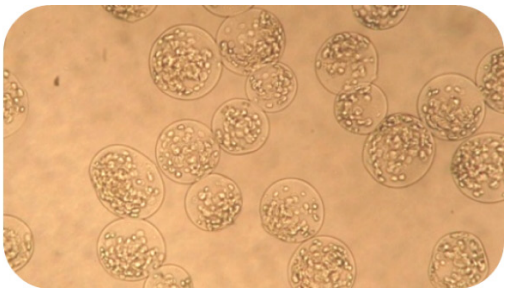


Figure 4. Left: Individual cell microencapsulation (fluorescent); Right: microencapsulated cells after growth.

- Evaluate the effect of a substance individually.
- Permit the individual growth of microorganisms while interacting with each other and with their external environment through extracellular signals.
- Discriminate rapidily the proliferation capacity of each cell within a population.
- Provide a highly sensitive detection method that can easily distinguish microcolonies of 30-100 individuals by flow cytometry.
- Reduce test times, speeding up and increasing the number of tests.

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Maria Flores is an Organic Chemistry (with a degree from UAH) and a PhD from Universidad Autónoma de Madrid (Spain). Since her PhD on inositolphosphogycans as insulin second messengers, she has been working in Medicinal Chemistry including Chemical Synthesis, Structure Activity Relationships and Molecules of Biological Interest. She joined PharmaMar in 2001 to continue working with Active Molecules, marine compounds with cytostatic activity. In 2004 she moved to Seville and joined Ingeniatrics becoming the Director of Research and Development. Ingeniatrics' R&D Department is focused on the development of microencapsulation applications of own proprietary technologies Flow Focusing® and Flow Blurring®. Main sectors of interest are Pharma, Food and Biotech industries.

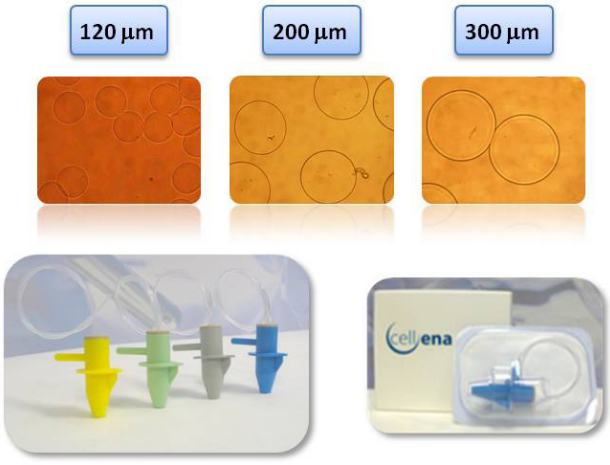

Figure 3. TOP: Examples of alginate microparticles obtained sterile disposable nozzles. BOTTOM: Disposable nozzles packed into sterile blisters designed for a fast and comfortable use preventing contamination.

ARTICLES

HOW TO OBSERVE A DRIPPING PROCESS ?

Poncelet D. , Davarci F. , Sayad M., Guessasma S. #, Oniris and INRA#, Nantes, France

INTRODUCTION

While developing an encapsulation process, we are often limited in our observations to measure initial state (concetration, viscosity ...) and the resulting microcapsules (size, membrane tichness ...). From this information, we tends to build theories explaining how capsules are formed. Our explanantions look more often more to hypothesis then facts.

However, things are changed. For example, micro- and minifluidics may allow to follow dropplets along the tube and then curing time. The purpose of this contribution is related to observing droplets during a dripping pocess taking profit of high speed camera..

Many encapsulation methods consist in extruding drop per drop a liquid in an other liquid. The contact of the droplets with the receipting bath lead to a solidification or membrane formation at the interface of the droplets.

Encapsulation by dripping may been divided in four steps:

- Droplet formation at end of the needle,
- Fall of the droplets in air,
- Droplet penetration in the liquid,
- Microcapsule formation it-self.

In this study, alginate bead production is considered as simple and fast way to solidify the droplets. The observations concerns the 3 first steps of simple drop-per-drop method under gravity.

MATERIAL AND METHODS

Alginate bead production

Alginate solution (20 g/L) is dropped in a 20 g/L CaCl2 solution (Panreac, Spain) using a syringe pump and 30 ml syringe connected to a tronconique tip (EFD, France). Glycerol (Labogros, France) is added into CaCl2 solution to modify the viscosity and Tween 20 (Sigma Aldrich, USA) is added into CaCl2 solution to modify the surface tension. Beads are cured for 30 min, filtered and observed under microscope to determine their shape and size.

High speed video observations

Images of the droplet formation, fall and bath penetration are recorded using a Phantom v7.3 high-speed camera (Vision Research, USA) at a rate of 400 fps.

RESULT AND DISCUSSION

Droplet formation at the tip

Figure 1 presents different steps of the droplet formation

- Liquid flows forming a suspended pear shape droplet,
- The droplet is maintained on tip through a neck,
- The neck elongates until it breaks,
- Droplet falls and changes to a spherical form.

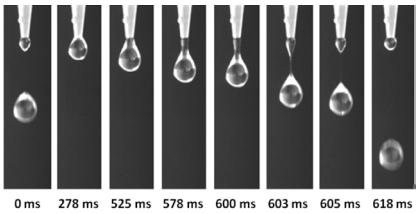

Figure 1: drop formation sequence

The neck diameter is mainly equal to the external tip diameter (Figure 2) and the size of the droplet is linked to the external tip diameter but also to the liquid flow. The last effect may be due to a longer neck at breaking time for higher flow (data not shown). Part of the neck is be-ing incorporated in the droplets.

Conditions to get spherical droplets

With help of the video recording, it is also possible to define the distance

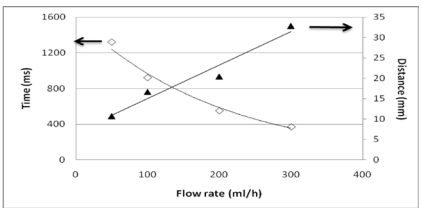

Figure 3: Time and distance to obtain spherical droplet for different nozzles.

and period to get spherical droplets (Figure 3 and 4) as function of the nozzle diameter and alginate flow. Even with large tip diameter and high

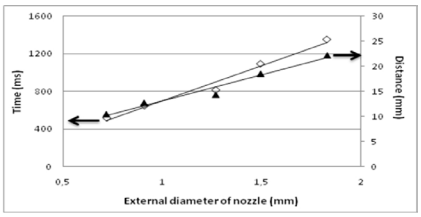

Figure 4: Time and distance to obtain spherical droplets for different flowrates

flow, the distance to obtain spherical droplet is limited to 4 cm and the time to less than 1 s.

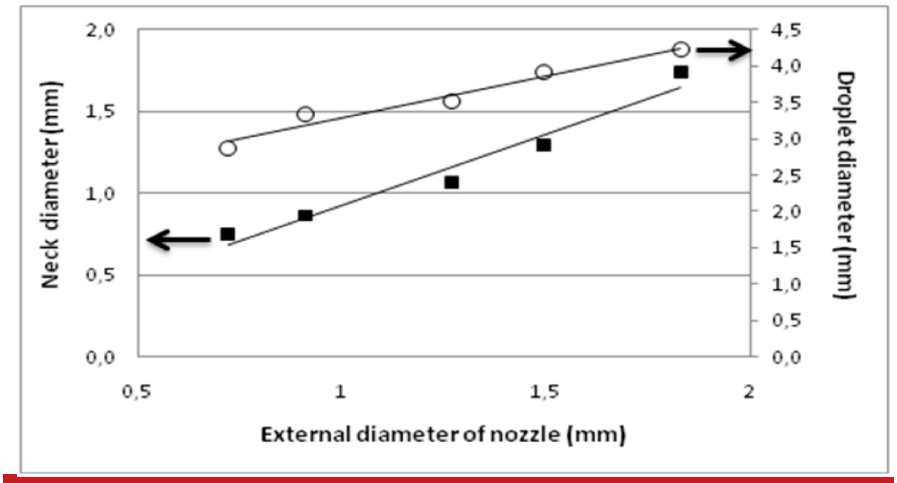

Figure 2: Diameter of the neck and droplet versus nozzles diameter

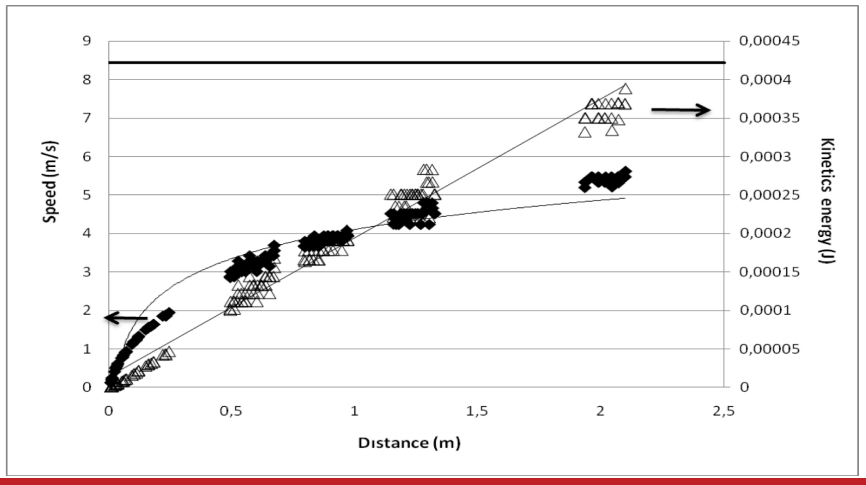

Figure 5. Droplet velocity and kinetics energy

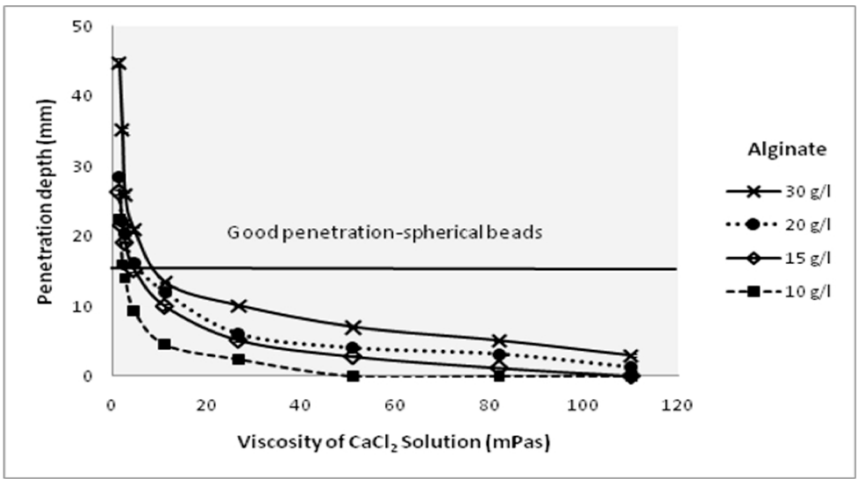

Figure 6. Effect of viscosity on droplet penetration in the bath

Droplet falling velocity and kinetics energy

By measuring the distance covered by the droplets during a certain time (certain number of frames), it is possible to draw the droplet velocity and the kinetics energy (E = ½ m v2) profiles (Figure 5). Terminal velocity is calculated as 8.4 m/s (Chan et al.,2009). In most laboratory experimental set-ups, the droplet would penetrate the solidifying bath at a speed between 25 and 33 % of the terminal velocity.

Droplet penetration into liquid

The droplet (or bead) deforms the surface of the receipt-ing bath until it breaks it allowing full penetration. If their kinetics energy is too low, the droplet is rejected. Pene-tration depth required to get incorporation is mainly func-tion of the viscosity and surface tension of the receipting bath (Figures 6 - 7) but generally it is around 1.5 cm.

Even if the droplet penetrates correctly the receipting bath, resulting beads may not be spherical. The droplet viscosity, at some extend of the receipting bath, deter-mine the sphericity of the beads (Pregent et al.,2009). (Figures 8 and 9)

CONCLUSIONS

Our preliminary experiments show that high-speed cam-era really helps to define optimum conditions for a good dripping techniques. Future work

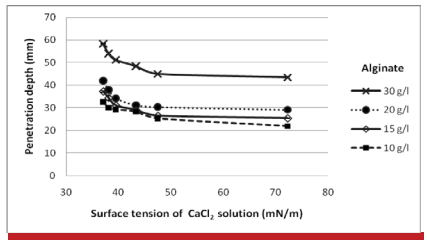

Figure 7: Effect of surface tension on droplet penetration in the bath

will be undertaken to analyze more deeply the process and extend the study to more complex process like electrodripping or even co-extrusion with nozzle resonance.

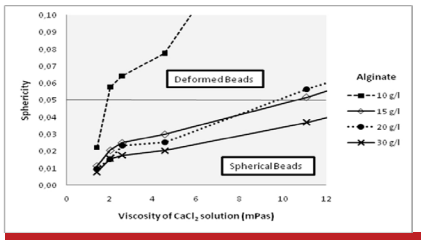

Figure 9: Sphericity factor of the beads

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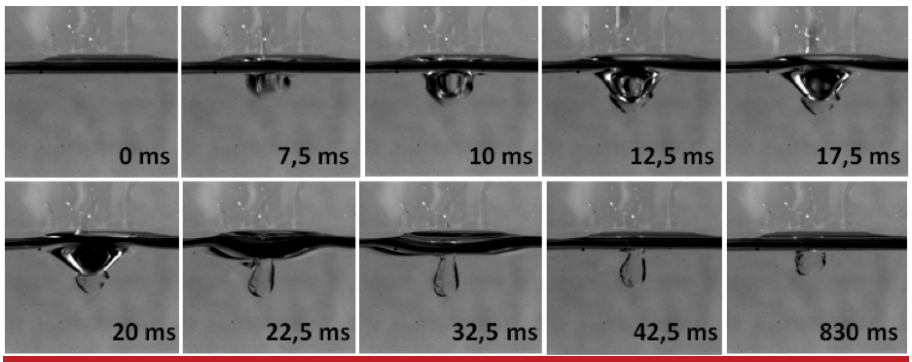

Figure 8/ Shape deformation of droplet (bath viscosity 111mPa.s)

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