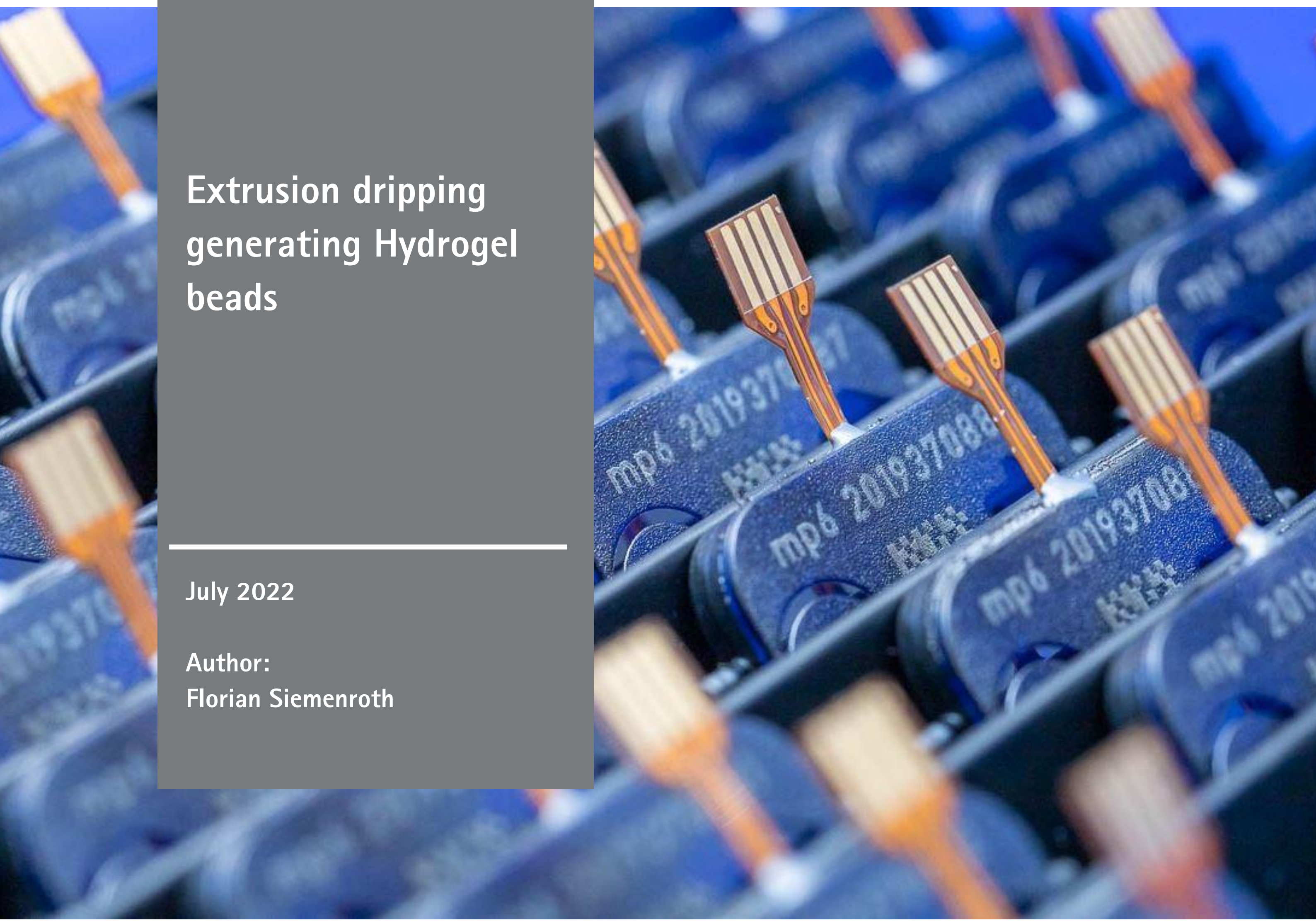
CASE STUDY

Bartels mikrotechnik

with passion for microfluidics



Extrusion dripping generating Hydrogel beads

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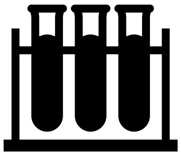
Encapsulating bioactive agents



Emulation of bioactive components

Hydrogel beads is a widely known technology in pharmaceutical or cosmetic development and production. The task of theses droplets is to encapsulate bioactive reagents in stable spheres. Later, they release that material at defined working points on the patient or consumer end.

This case study shall share the idea of generating alginate beads utilizing a microfluidic pressure driven flow setup based on piezo electric micropumps.

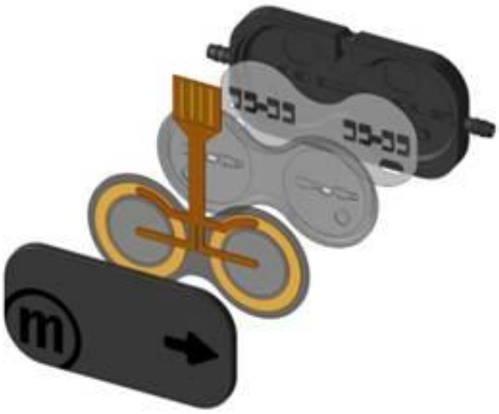
What is microfluidics?

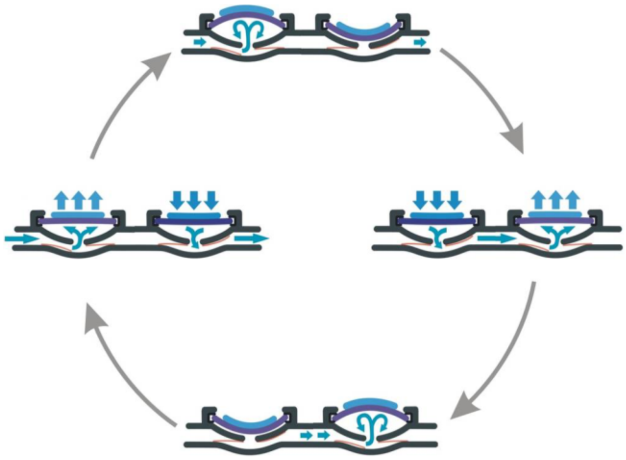
Microfluidics is the fine art of creation and manipulation of small portions of fluids, often realized by flow within small, sub-millimetre-scale channels. These small dimensions allow the fluid flow to be controlled with exquisite precision (Seifert, Thiele; 2020).

About the mp6 micropump

The available, industrialized and commercialized example is the mp6 micropump by Bartels Mikrotechnik GmbH. This micro pump is a positive displacement membrane pump utilizing piezo buzzers. The alternating displacement of the piezo acutators lead to the following typical fluidic values of the pump:

- Liquids (eta = 1 mPas): q = 5 - 8000 µl/min in free flow and p > 600 mbar
- Gas: q > 25 ml/min in free flow and p > 150 mbar





Introduction

Hydrogel microparticles are well-known and often utilized in pharmaceutical applications or the food and beverage industry. They are usually used as a matrix to encapsulate biological and chemical reagents like drugs, proteins or cells for diagnostics, bioreactors or medical treatment. Also, due to its size, shape, deformability and mechanical properties, hydrogel particles are often used to emulate biological components like cells.

Standard, accessible materials for hydrogels are biopolymers e.g., gelatin, agarose, alginate, pectin, etc. Alginate is a preferred material because of its low cost, non-toxicity and the simple methods for the crosslinking options. There are many production procedures, such as emulsification, extrusion dripping or droplet generation by flow focusing or T-junction in microfluidic chips.

I. Alginate hydrogel microparticles

Typical or beneficial Alginate hydrogel characteristics are mainly based on their hydrophilic polymeric networks. The networks can absorb and retain a huge amount of water within the structure and it is generated by polymer crosslinking. There are mainly four different cross-linking options, such as ionic, H-bonding, hydrophobic covalent and vor covalent.

II. Extrusion Dripping

The extrusion dripping method is based on the pendant drop method. The force between a fluid and a nozzle or tubing depends on the diameter d of the nozzle and the surface tension γ of the fluid.

$$F_\gamma = \pi d \gamma$$

Equating this with gravity generates the link to the mass of the droplet.

$$mg = \pi d \gamma$$

Idealizing the shape as spheroid and including the fluid's density ρ one can calculate the radius r of the droplet.

$$\frac{4\pi r^3 g}{3\rho} = \pi d \gamma$$

III. Experiment

For the alginate beads production, a microfluidic pressure driven flow setup is used within the experiments as shown in figure 1. The setup consists of four mp6 micropumps, two in a series setup for an increased pressure and two of those series setups in parallel for an increased flow rate. Now the pressure is generated in Fluid Reservoir 1, which contains Alginate in a liquid form. The liquid is transported to the nozzle where the droplets are generated. Falling into Fluid Reservoir 2, which contains a Ca^{2+}-solution, the cross-linking takes place and Alginate beads are generated as solid spheroids. Changing the diameter of the nozzle leads to different Alginate bead sizes. As shown in figures 3 and 4.

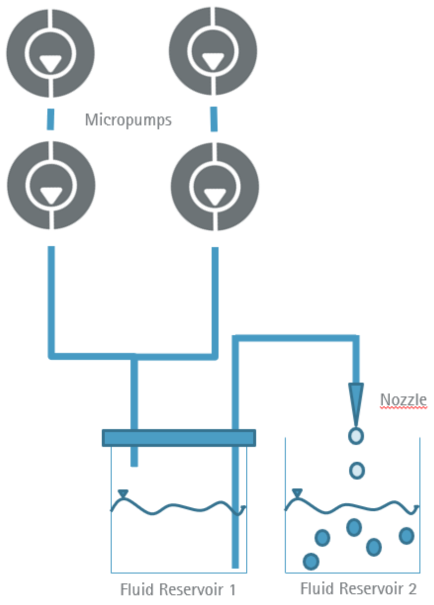


Figure 1 Sketch of experimental setup

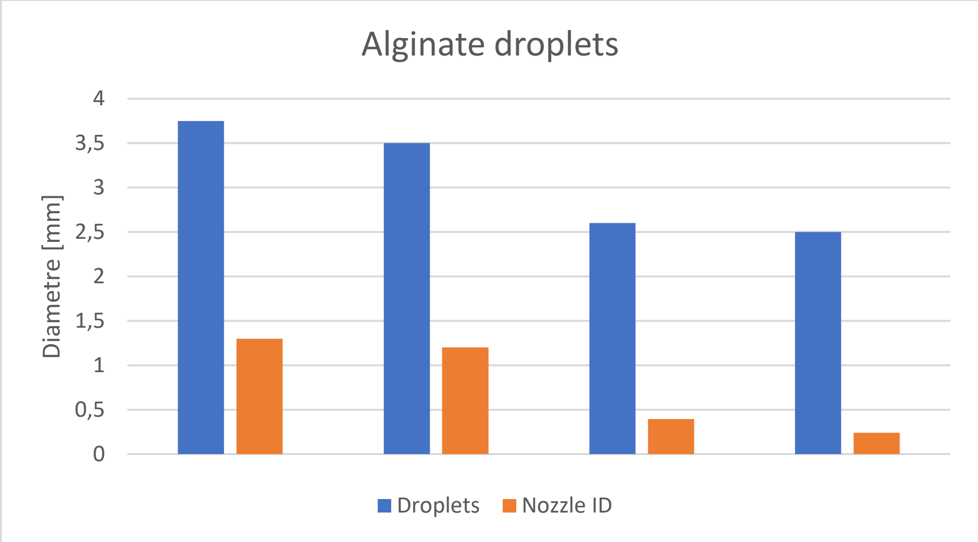


Figure 2 Alginate droplets compared to nozzle diameters

Figure 3 Generated Alginate beads; From left to right: 3.75 mm, 3 mm, 2.6 mm, 2.5 mm in diameter

As a conclusion, a microfluidic pressure driven flow system in combination with the correct selection of nozzle diameters can be a very powerful tool for generating alginate beads of different sizes in high batches decreasing development and production efforts. Due to its small system size the alginate bead generation can take place at the point of need.

Components and systems used:

- mp6 micropump by Bartels Mikrotechnik
- mp-Multiboard2 incl. mp-Highdriver4 by Bartels Mikrotechnik
- Pressurized reservoir
- Dispensing nozzle with different diameter

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Bartels Mikrotechnik is a globally active manufacturer and development service provider in the field of microfluidics. In the microEngineering division, the company supports industrial customers in the modification, adaptation and new development of high-performance and market-oriented product solutions through the innovative means of microsystems technology. The second division, microComponents, produces and distributes microfluidic products and systems, especially for miniaturized and portable applications. Our key products are micropumps that convey smallest quantities of gases or liquids and are used in a variety of ways in biotechnology, pharmaceuticals, medical technology and numerous other applications.

Bartels Mikrotechnik with passion for microfluidics!

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