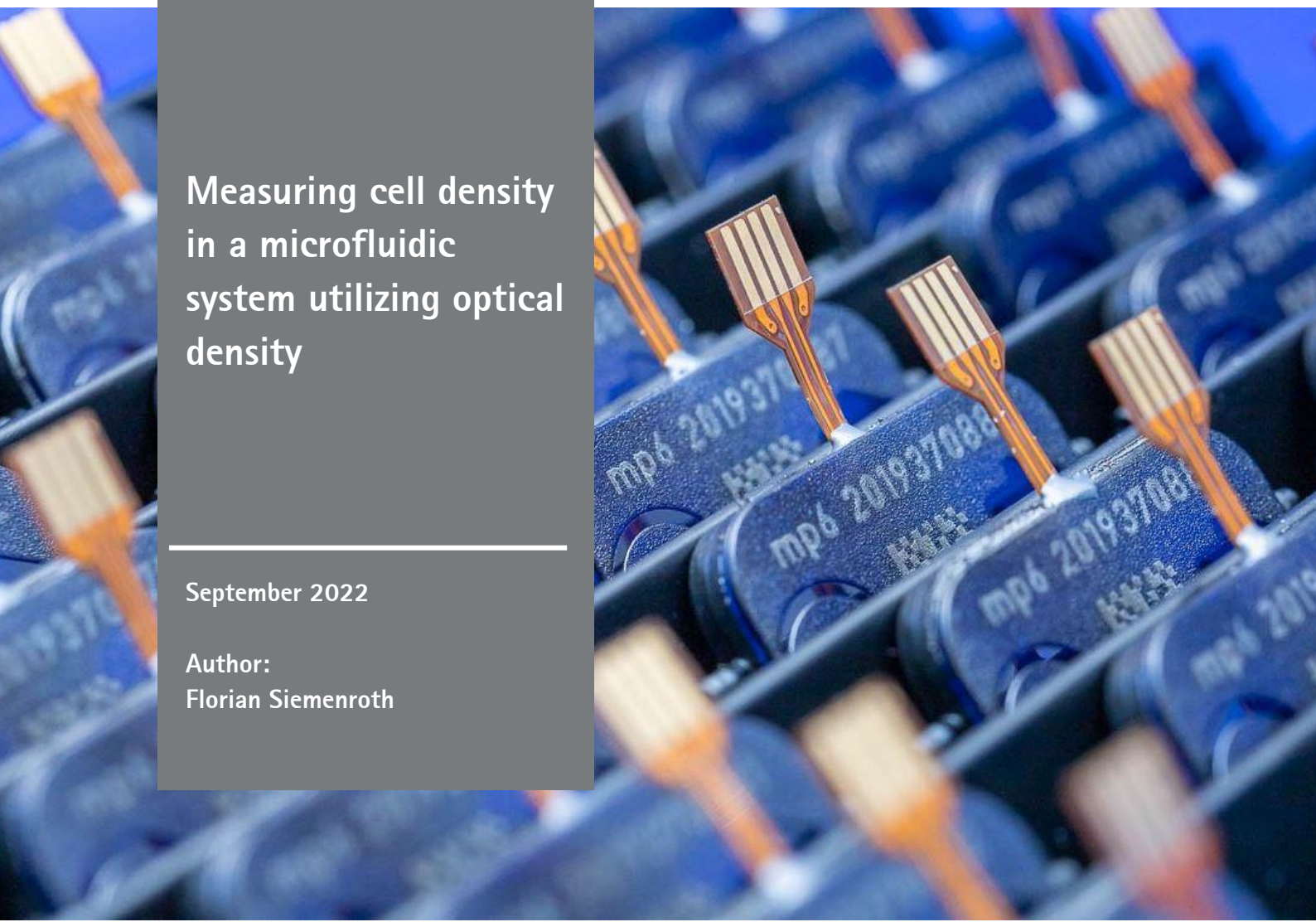
CASE STUDY

Bartels mikrotechnik

with passion for microfluidics

Measuring cell density in a microfluidic system utilizing optical density



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Parallelization & scalabibilty

Increased efficiency (time & reagents)

Inline monitoring

Microfluidic systems become more and more important in biotechnological applications in the pharma, cosmetics and food & beverage markets due to its small footprint. Therefore, these systems are an easy option for parallelization, modularity and scalability as well as low power and reagent consumption.

Culturing cells is a highly sensitive procedure. Some important parameters need to be monitored closely and accurately, i.e. temperature, dissolved oxygen, CO_2, pH, concentration of feed, VOC and cell density.

The cell density is often measured by an optical measuring principle taking the optical density (OD) value generated by turbidity in the cell suspension and its potential for transmitting respectively absorbing light.

This case study shall share the idea of a cost-efficient, microfluidic setup for microbioreactors in cell culturing processes taking the OD and monitoring the cell growth.

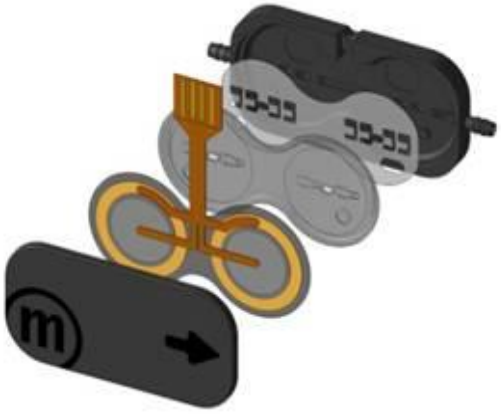
What is microfluidics?

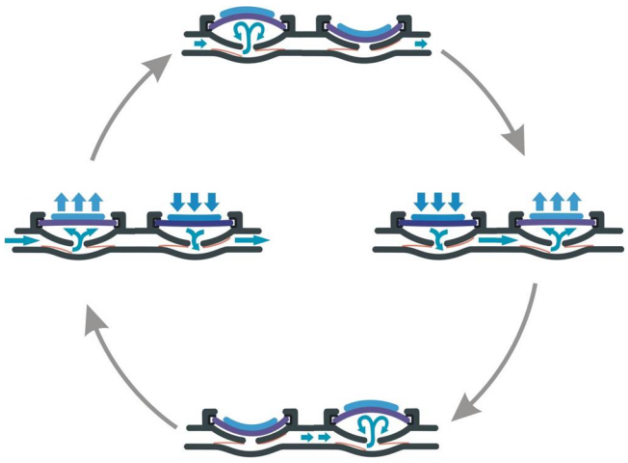
Microfluidics is the fine art of creation and manipulation of small portions of fluids, often realized by flow within small, sub-millimetre-scale channels. These small dimensions allow the fluid flow to be controlled with exquisite precision (Seifert, Thiele; 2020).

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

Especially the upstream process in batch, feed batch or even perfusion processes in biotechnological applications, e.g. pharmaceuticals research, development and production or food and beverage, is a very important part. Within this process, cells are grown at a very high level and affect later processes. Therefore, the upstream process needs to be monitored and adjusted at all times offering the best circumstances for growing cells being as efficient as possible. Reagents are often expensive and time is short, so a wasting behaviour should be avoided as much as possible. Monitoring the temperature, dissolved oxygen, CO2, pH, concentration of feed, VOC and cell density is essential.

I. Cell Density

The cell density is the number of cells in a defined volume. An increasing cell density, i.e. a higher number of cells in the same volume, gives a good input on the behaviour of cells is especially on their growth. In most cases the goal is that the cell growth is defined by a low time and feed or reagent consumption. That leads to an adjusted feeding process depending on the cell growth. The higher the cell density, the higher the turbidity and therefore the absorbance of light.

If one measures the cell suspension optically, the gradient of absorbance can be higher or lower, which describes a higher or lower cell growth and the operator or even the bioreactor system itself can react to the cell culture circumstances. This measuring principle is based on the optical density (OD).

II. Optical Density (OD)

The optical density in cell culturing applications is defined as:

$$E_\lambda = \log_{10}(\frac{I_0}{I})$$

At a wavelength of λ = 260 nm. Here [E_λ]is the absorbance and [I] is the intensity. In this case an optical sensor incl. light source is used working at a wavelength of λ = 350 nm.

III. Experiment

The experiment set-up is shown in Fig. 1. A recirculation setup including the mp6 micropump driven by the mp-Multiboard2 and a mp-Highdriver4 running the cell suspension from a microbioreactor in a loop. The optical sensor, Optek OPB350, is monitoring the absorbance respectively intensity inline but without being in contact with the liquid.

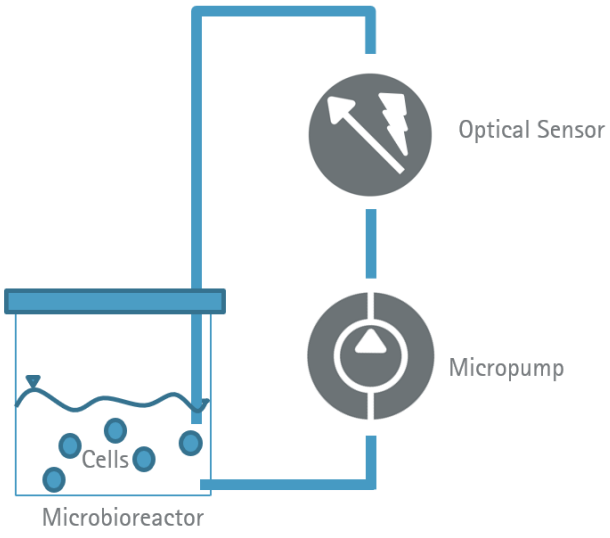


Figure 1 Sketch of experimental setup

In this experiment yeast is used as cell material. It has a number of cells related to its weight of 1010 cells/mg. For the suspensions 150 mg is dispersed in 50 ml, which leads to 1.5*1010 cells in total and 3*107 cells/ml. Fig. 2 shows three differently dispersed suspensions.

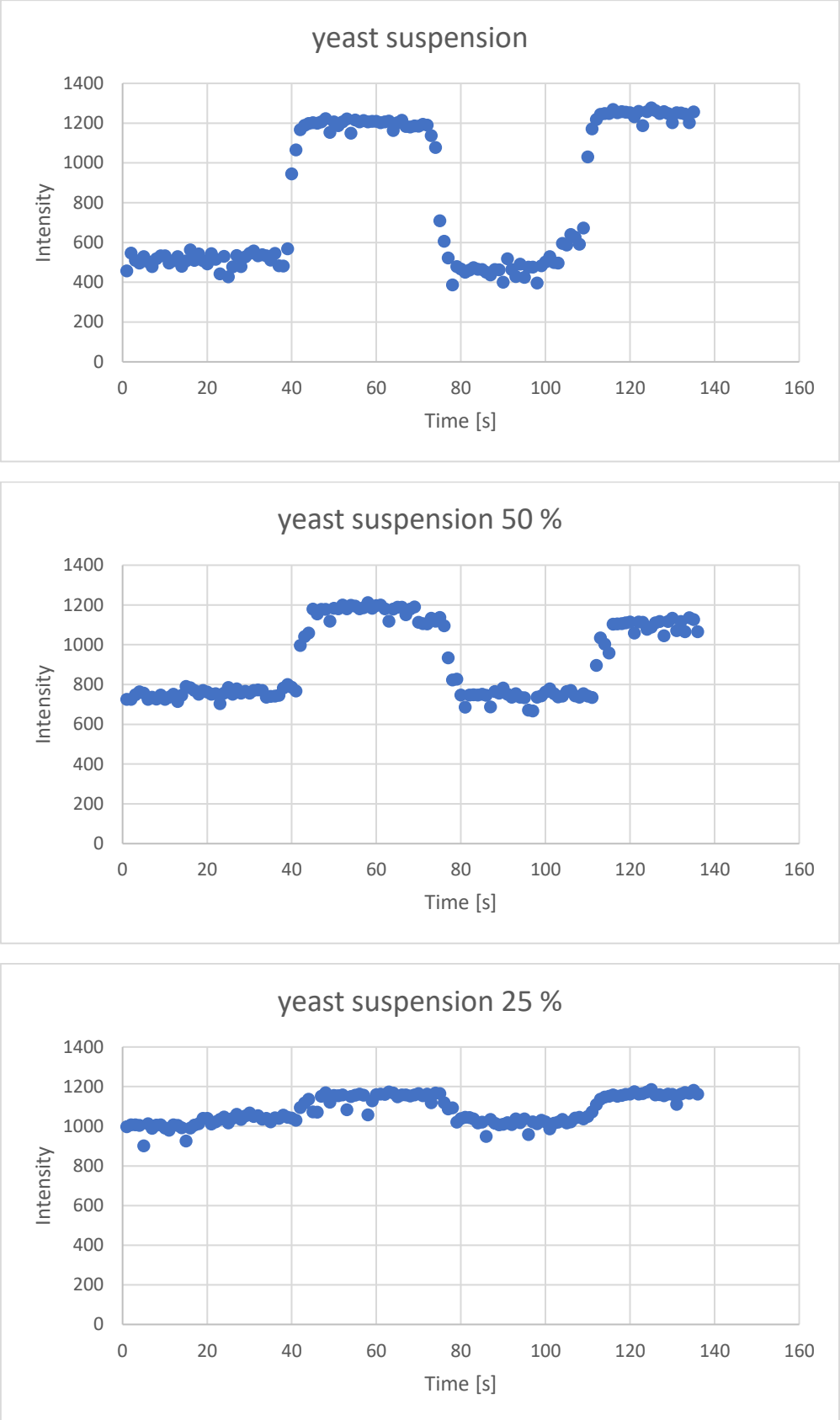


Figure 2 Absorbance of differently dispersed yeast suspensions always compared to pure water

One can see the increasing intensity for less dense suspension. Also, the OD for the densest suspension 0.38, the OD for the second suspension is 0.17 and the OD for the suspension with the smallest density is 0.08. So, the transparency increases which fits to the fact of more and more less dense suspension. In addition, the comparison between the cell suspension and pure water shows a decreasing gap from densest to lowest density and shows the plausibility of the principle at the same time as the intensity value for pure water is constant at 1200.

In addition to this case study, we have created a video that further shows what a microfluidic system measuring cell density can look like. You can find it on the Bartels Mikrotechnik YouTube channel: https://www.youtube.com/watch?v=T0hh2LR3gNQ

Components and systems used:

- mp6 micropump by Bartels Mikrotechnik
- mp-Multiboard2 incl. mp-Highdriver4 by Bartels Mikrotechnik
- Microbioreactor
- Optek OPB350

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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