

FOULING IN A MICRO HEAT EXCHANGER DURING CONTINUOUS CRYSTALLIZATION OF SOLID LIPID NANOPARTICLES

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ABSTRACT

During the continuous crystallization of various solid lipid nanoparticle (LNP) formulations certain formulations led to fouling and blocking of small passages in the applied micro heat exchanger. In order to investigate the fouling behavior of different LNP formulations in detail, integral fouling evaluations by pressure drop measurements were performed. Results show more fluctuations compared to particle fouling experiments in macro devices. These variations in results are due to detached agglomerates from compounds formed in micro devices in the in- and outlet header regions, breaking off randomly due to shear stress. This results in downstream microchannel blockage, the transfer tubings or in subsequent unit operations. During corresponding cleaning experiments different observations compared to macro dimensions are made: Based on significant lower ratios of characteristic dimension of the microchannel to particle or agglomerate diameter agglomerates remain in the microchannels preventing smaller particles from being washed off (i.e. capturing effect).

INTRODUCTION

The handling of solids in micro structured devices offers new opportunities for goods whose production is difficult or not realizable in macro devices [Hartmann, 2010]. Micro process engineering is quite a young research area. However it has attracted significant industrial attention due to multiple advantages such as process intensification and product improvements [Kockmann, 2005]. Microstructured devices are characterized by at least one performance-relevant dimension of $\leq 1000 \mu\text{m}$. Nevertheless the use of these devices for continuous processing is restricted by occurring fouling phenomena. Despite the described market pull fouling phenomena in micro dimensions are investigated rarely.

“As small as necessary and beneficial, not as small as possible” is postulated by Kockmann as a basic design rule to prevent fouling in micro reactors [Kockmann, 2006]. Hartmann and Hessel et al. as well stated that insufficient attention is given to fouling during the different process

development stages of micro systems and identified fouling as the major barrier and greatest challenge to operate micro systems [Hessel, 2004; Hartmann, 2012].

In contrast, fouling phenomena in macro dimensions are meticulously investigated due to high financial losses in all industry sectors, especially within the application of heat exchangers [Bohnet, 1987; Wilson, 1997; Müller-Steinhagen, 1999; Müller-Steinhagen 2000; Augustin, 2006; Geddert 2011].

The present paper describes fouling phenomena occurring within the continuous crystallization of lipid nanoparticles (LNP) in a micro heat exchanger and the cleaning process. Furthermore a comparison to fouling phenomena in macro dimensions is presented.

SOLID LIPID NANOPARTICLES

First mentioned in 1986, based on a patent registration, LNP still offer a high innovative potential for drug delivery applications especially for newly developed lipophilic drugs, e.g. cosmetic products, medical applications or intravenous administrations [Speiser, 1986]. LNP, typically with particle diameters of 100 to 500 nm, consist of a drug containing lipid matrix which is stabilized by emulsifiers in a surrounding aqueous phase. Nowadays most of the newly developed drugs are lipophilic, which are especially well incorporated by LNP due to the lipophilic properties resulting in a wide range of new pharmaceutical applications. Furthermore the lipid matrix acts as a protective shell for the incorporated drug against decomposition due to oxygen, water or light [Müller, 2002]. Further important properties for drug carrying applications are the bioavailability of the incorporated drugs and the physiological degradability of the carrying system. Both are increased by LNP compared to common drug carrying applications, e.g. polymers.

LNP are commonly produced batchwise via high pressure melt homogenization being the most promising preparation process for industrial applications. Following this preparation method the melted lipid phase is emulsified in a surfactant containing aqueous solution. This is subsequently cooled down and crystallized to solid LNP.

Based on polymorphic behavior and thus different crystalline modifications the crystallization step is of great importance. Hence the commonly used batchwise crystallization in a stirred vessel is disadvantageous because poor spatial and time distribution of relevant process parameters result in a variation of product qualities. Altering product properties, within storage or after production, are not acceptable for pharmaceutical applications.

FOULING DEFINITION

The thermal fouling resistance R_f is calculated based on the reciprocal heat transfer coefficients of the clean (k_0) and soiled (k_f) surface:

$$R_f = \frac{1}{k_f} - \frac{1}{k_0} \quad (1)$$

R_f for macro dimensions is classified as follows: $0 \dots 2 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$ no or little, $3 \dots 9 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$ middle and $\geq 10 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$ high fouling [VDI Heat Atlas, 2010]. Alternatively, the fouling resistance may be quantified based on the deposited mass m_d with:

$$R_{f,m} = \frac{m_f}{A_f \cdot \rho_f \cdot \lambda_f} \cong \frac{x_f}{\lambda_f} \quad (2)$$

While the thermal fouling resistance R_f may become negative, the mass based fouling resistance $R_{f,m}$ will always have positive values. This corresponds to the change in pressure drop resulting from fouling depositions [Albert, 2011].

$R_f = 0 \text{ m}^2\text{KW}^{-1}$ defines the initiation phase which ends after the initiation time t_{ini} . The initiation phase as well as the following roughness controlled phase are part of the induction phase which ends at the induction time t_{ind} , followed by the layer growth phase, see Fig. 1.

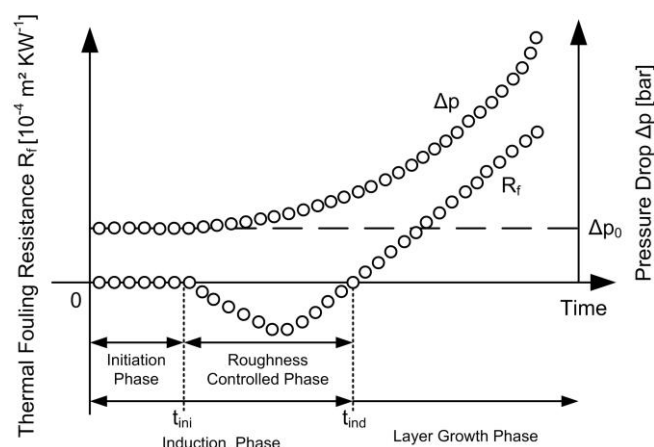


Fig. 1 Development of thermal fouling resistance with regarding fouling phases.

CONTINUOUS CRYSTALLIZATION OF LNP

To overcome disadvantages of the batchwise processing mentioned, a continuous crystallization process in a micro heat exchanger after high-pressure melt homogenization was developed [Jasch, 2009]. Compared to batchwise processing the continuous crystallization leads to improved process control possibilities resulting in well-defined and highly

reproducible product properties. Additionally the scale-up of the continuous process to industrial scale results in an easier transition based on equaling up of the micro device or internal numbering up of the microchannels. Furthermore the continuous process requires lower product quantities and at the same time allows faster preparation of LNP formulations leading to well-defined product properties which are representative for continuous large scale production. This makes the continuous process to a powerful tool for screening purposes.

However continuous crystallization of certain LNP formulations lead to fouling and blocking of small passages in the micro heat exchanger. Obviously, specific interactions between the LNP and the microstructured surface of the device may occur and need to be considered in the process design of the continuous crystallization for different LNP formulations. Continuous processing of LNP recipes with a low fouling tendency resulted in reproducible experiments with constant product properties such as particle size and polymorphic form.

EXPERIMENTAL SETUP

Continuous Crystallization

A micro heat exchanger of the Karlsruhe Institute of Technology (KIT), Germany, was used as crystallization device for continuous crystallization of LNP emulsions. It consists of a stainless steel foil with integrated microchannels on each side positioned between two polymer half shells. The foil had 32 parallel rectangular microchannels with a $200 \times 200 \mu\text{m}$ cross section and a length of 190 mm, see Fig. 2. Jasch et al. investigated the basic process concept for the continuous crystallization [Jasch, 2009]. The experimental setup is shown in Fig. 3. The devices are connected by PTFE tubes with an inner diameter of $1/16''$. Pump P1 was a micro annular gear pump (mzr-7205 by HNP Mikrosysteme GmbH, Germany). The pressure drop was monitored by two stand-alone pressure sensors (WIKA Alexander Wiegand SE & Co. KG, Germany, S-10, 0-16 bar).

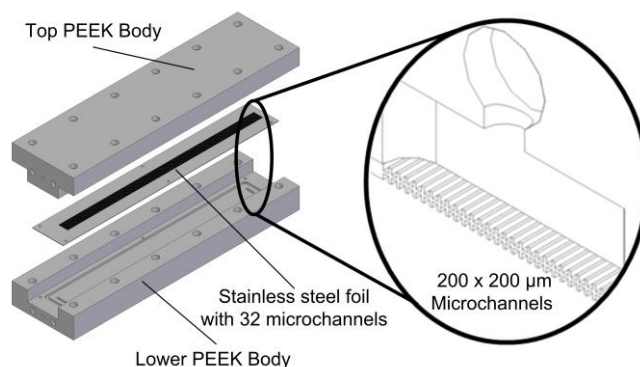


Fig. 2 Micro heat exchanger for the continuous crystallization of lipid nanoparticles

Prior to feeding LNP dispersions to the continuous crystallization equipment a thermal equilibrium was established with water, to reduce the required amount of

LNP dispersions. Water was tempered in a thermostat to 80 °C and was circulated in a loop from the reservoir through the dispersion feed line and the micro heat exchanger.

Once thermal equilibrium was reached the inlets of the three-way valves V1 and V2 were switched. Then the emulsion, stored in a temperature controlled and stirred vessel at 80 °C (20 K above the melting point to ensure that all crystals are melted), enters the micro heat exchanger with a reduced temperature of 60 °C (still all crystals are melted, re-crystallization starts at 58 °C), caused by heat loss within the tubings.

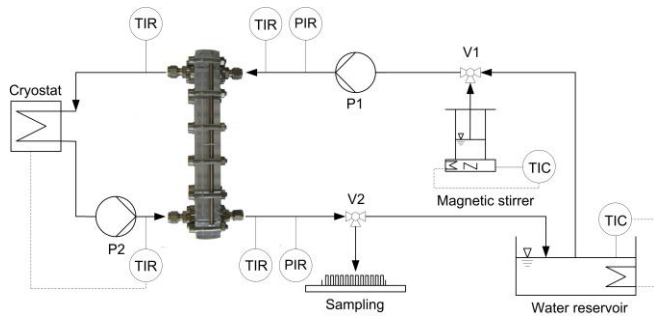


Fig. 3 Experimental setup for continuous melt crystallization of solid LNP in a micro heat exchanger (modified from [Jasch, 2009]).

A LNP formulation prone to build up fouling layers based on decyl oleate and carnauba wax, was used for the experiments, see Table 1. The emulsifier concentration varied from 1 to 3%.

Table 1 Formulation of wax based LNP

Substance	Concentration [wt%]
Decyl oleate	5
Carnauba wax	10
Polysorbate 80	1, 2 or 3
H ₂ O	rest

Cleaning Investigations

LNP suspensions with particle diameters of approx. 250 nm and a polydispersity index of < 0.2, determined by photon correlation spectroscopy, were used as fouling system for cleaning investigations. Fig. 4 depicts the experimental setup.

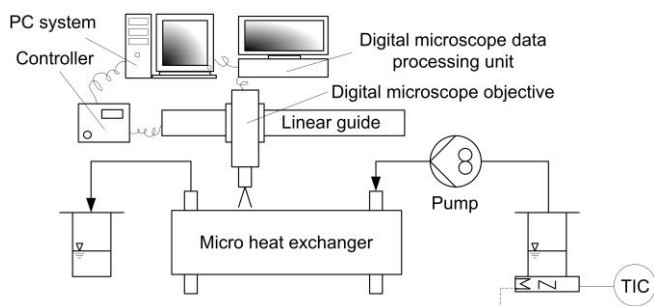


Fig. 4 Experimental setup for cleaning investigations.

To avoid maldistribution in multiple parallel channels, cleaning investigations were performed with a single integrated microchannel (400 x 400 µm, length of 190 mm).

The cleaning detergent was pumped through the micro heat exchanger using a micro annular gear pump.

To allow optical observation the micro heat exchanger was modified at ICTV, see Fig. 5. The top PEEK body had an integrated window for visual access to the underlying microchannel. For cleaning experiments a soiled microchannel foil (400 x 400 µm, length of 190 mm) is adjusted in the modified micro heat exchanger, see Fig. 5.

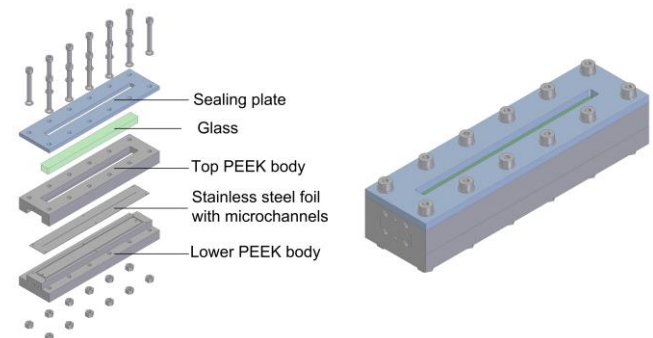


Fig. 5 Modified micro heat exchanger, Left: exploded view, right: assembled view.

In order to decide whether the visual detection method is reliable or not, the cleaning parameters were changed over the cleaning time by changing the cleaning detergent (ethanol to acetone) and the volumetric flow rates, see Table 2. Until approximately 730 seconds ethanol with changing volumetric flow rates of 5 ml min⁻¹ to 25 ml min⁻¹ was used for cleaning. The ethanol cleaning was followed by acetone also with volumetric flow rates of 5 ml min⁻¹ to 25 ml min⁻¹. Three measuring sections were chosen with 100 images taken for each measuring section over the whole cleaning time: (i) in the middle of the microchannel (ii) 8.25 mm upstream and (iii) 8.25 mm downstream the first measuring section.

Table 2 Process parameters for cleaning investigations

Detergent	Image	Flow Rate [ml min ⁻¹]	Re [-]	Process Time [sec]
Ethanol	1 – 10	5	137	0 – 142
	11 – 20	10	274	148 – 289
	21 – 30	15	411	295 – 436
	31 – 40	20	548	442 – 583
	41 – 50	25	685	589 – 731
Acetone	51 – 60	5	508	736 – 877
	61 – 70	10	1016	883 – 1024
	71 – 80	15	1524	1030 – 1172
	81 – 90	20	2000	1177 – 1319
	91 – 100	25	2540	1324 – 1466

Local Visual Fouling Detection

The experimental setup for the local visual fouling detection is shown in Fig. 4. A digital microscope objective (VH-Z 100, Keyence Germany GmbH) with a data processing unit (VHX 100, Keyence Germany GmbH) was used to take images of the microchannels and transfer them to a PC system for image post-processing. The objective

was mounted on a linear guide (Ball Screw Feed Axis LES 4, isel Germany AG). Positioning accuracy (repeatability of linear guide) was ± 0.02 mm. The linear guide was driven by a two-phase stepper motor (MS 135 HT, isel Germany AG) which was connected to a step controller (IT 116 Flash, isel Germany AG). MATLAB® was used to communicate with the linear guide and to traverse the position of the objective automatically to predefined positions. The positions are approached one after another, with an image taken at each one. To realize sharp images for all measuring sections within one experiment with a magnification of 300x, the micro heat exchanger was mounted on a support frame and can be adjusted precisely due to six micrometer screw gauges.

Image Post-Processing

Post processing of the obtained images in the cleaning runs was automated using a MATLAB® code. A schematic drawing of the image post-processing is shown in Fig. 6 with the example of a blocked 400 μm square channel. The algorithm repeats the following stages: The images, using the red, green and blue color model (rgb), are converted into gray scale images with 255 levels of gray (0=black, 255=white). Non interesting parts of the images are cut off, hence just the microchannel itself remained. Subsequently these images are converted into a black and white image.

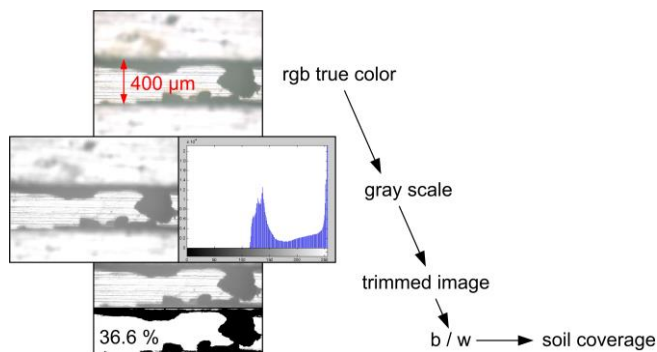


Fig. 6 Image post-processing via MATLAB®, image of a cleaning experiment as example.

For the black and white conversion a threshold value has to be defined (0-255) to convert the gradual gray scale image into a digital black (i.e. covered) and white (i.e. free surface) image. This value is entered as a percentage of the levels of gray (0 – 1). The choice of the threshold value defines the quality of the results and is empirically defined before experiments. The process of choosing the correct threshold is depicted in Fig. 7. An original image with seven different values of the gray scale is shown.

For example with a value of 0.5 all pixels with a scale of gray under 127.5 will be turned into black, causing a loss of information about the soiled surface area. At a threshold of 0.7 traces from the manufacturing process of the microchannel are visible which also is unfavorable.

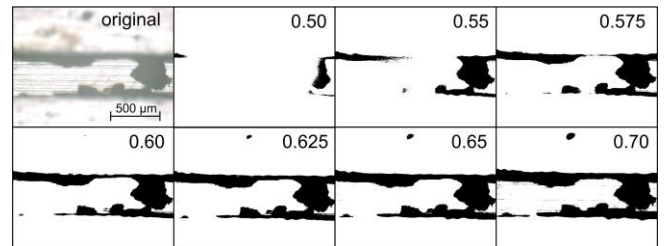


Fig. 7 Original image with varying threshold values for the black and white pixel conversion.

Consequently a value of 0.575 is taken as compromise between wanted and unwanted information for the resulting binary images. The soil coverage is calculated as a percentage value via the ratio of black pixels to the number of all pixels, which is 36.6% for the example in Fig. 7.

RESULTS

Continuous Crystallization of LNP: Fouling Phenomena

Continuous crystallization experiments were carried out for all formulations, undiluted and diluted with demineralized water at 50%, shown in Table 1. As a representative result the thermal (R_f) fouling resistance and pressure drop (Δp) for continuous crystallization in the micro heat exchanger of a 2% emulsifier formulation is shown in Fig. 8. The results for the diluted formulation are shown in Fig. 9.

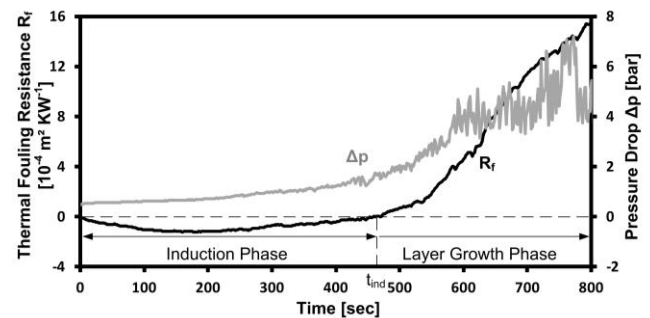


Fig. 8 Thermal fouling resistance and pressure drop for the continuous crystallization of lipid nanoparticles in a micro heat exchanger, characteristic dimension 200 μm , $Re = 30$, 15 wt% lipid in suspension.

The thermal fouling resistance is negative for a process time until 450 seconds with a subsequent increase to approximately $16 \cdot 10^{-4} \text{ m}^2 \text{KW}^{-1}$, see Fig. 8. The pressure drop starts at an initial value of 0.5 bar and increases to approximately 6 bar within processing. Process parameters result in a Reynolds number of 30, thus a laminar flow regime is received.

Fig. 9 shows the thermal fouling resistance and pressure drop in accordance to Fig. 8 for a 50% dilution of the 2% emulsifier formulation (with a 7.5 wt% lipid concentration). The thermal fouling resistance remains negative within the whole process time of the continuous crystallization. The pressure drop was also measured to be constant over the whole process time with approximately 0.4 bar.

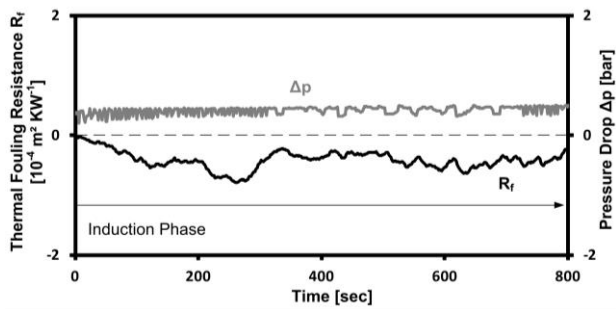


Fig. 9 Thermal fouling resistance and pressure drop for the continuous crystallization of lipid nanoparticles in a micro heat exchanger, characteristic dimension of 200 μm and Reynolds number of 30, 7.5 wt% lipid in suspension.

The results of the continuous crystallization experiments of all formulations are summarized in Table 3.

Table 3 Results for fouling phenomena in continuous crystallization experiments with LNP formulations with varying emulsifier concentrations

Effect\Emulsifier concentration	1%	2%	3%
Induction time [sec]	100	450	>800
Induction time of dilution [sec]	500	>800	>800
Max. pressure drop [bar]	7	5.5	1
Deposits in inlet header regions	high	medium	low
Deposits in microchannels	yes	yes	no

The experiments reveal that the induction time increased from 100 seconds to 450 seconds and at least to > 800 seconds for emulsifier concentrations of 1%, 2% and 3% respectively. For the formulations diluted at 50% the induction time increases significantly to 500 seconds for the 1% formulation and to > 800 s for higher emulsifier concentrations. Especially for low emulsifier concentrations (1%) results with limited repeatability were found. Thus values attained with these formulations should be regarded as indication for the order of magnitude only.

In the inlet header regions attached particles or agglomerates were observed. With increasing concentration of emulsifier blocking and attachment of particles in the header regions decreased. The pressure dropped from 7 to 1 bar over the micro heat exchanger with increasing emulsifier concentration.

The experiments also aimed at creating reproducible fouling layers in the microchannels for subsequent cleaning evaluations. Thus the presence of developed fouling layers in the microchannels was visually observed. For emulsifier concentrations lower than 3% attached particles and agglomerates in the microchannels could be seen, but not for the 3% formulation.

Fig. 10 shows photographs of the inlet header region of the micro heat exchanger after continuous crystallization of LNP suspensions with different emulsifier concentrations (1 to 3%). Attached agglomerates and particles are marked in the photographs. Non marked areas are filled with suspension after disassembling the micro heat exchanger

due to capillary forces. The highest degree of blocking is observed with the 1% emulsifier formulation. The results reveal that fouling phenomena decrease with increasing emulsifier concentration.

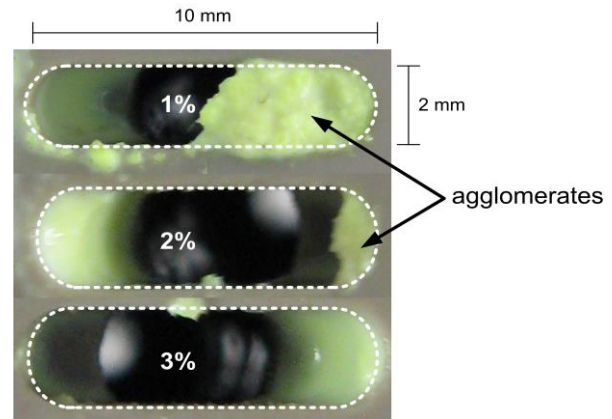


Fig. 10 Inlet header region with attached agglomerates after continuous crystallization of lipid nanoparticles in the micro heat exchanger. The emulsifier concentration of the regarded formulations (1-3%) results in different agglomerate amounts attached at inlet header walls.

Cleaning Experiments

The process parameters for the cleaning experiment are listed in Table 2. The development of the calculated soil coverage, gained from image post-processing via MATLAB®, for three different measuring sections are shown in Fig. 11. 100 images were taken for each measuring section over the whole process time.

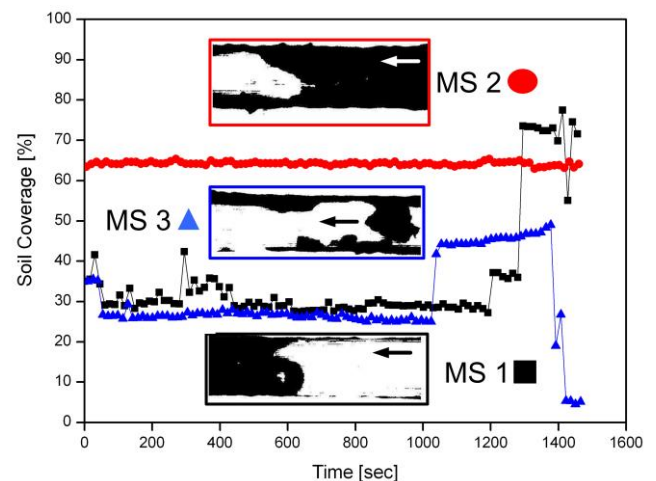


Fig. 11 Soil coverage of the microchannel at three measuring sections (MS 1, MS 2, MS 3) with increasing process time as obtained from image post-processing, arrows displaying flow direction.

Soil Coverage Increase

Curve MS 1 in Fig. 11 depicts the soil coverage development for the first measuring sequence. The soil coverage increases unexpectedly from 30% to 70%. Images of the regarded time frame, approx. 1150 – 1450 s, are shown in Fig. 12, explaining the increased soil coverage

with increased cleaning time. Particles or agglomerates upstream from MS 1 are detached and transported to MS 1 where they are blocked by the already attached agglomerates at this measuring section. Hence this results in an increased soil coverage.

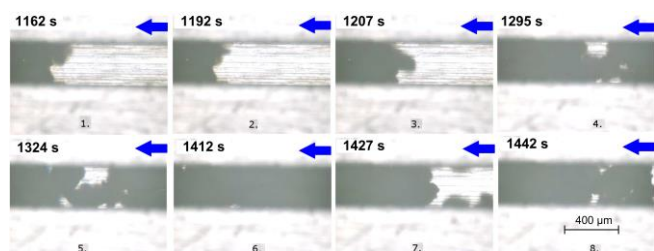


Fig. 12 Capture of agglomerates which were detached upstream of measurement section 1 with increasing cleaning time, arrows indicating flow direction, original images without post-processing.

The evolution of curve MS 1 in Fig. 11 shows several peaks, e.g. at 30 seconds. This can be explained by sudden increases of soil coverage for short periods of time which are evidently induced by gas bubble nucleation and growth at attached particles, see Fig. 13.

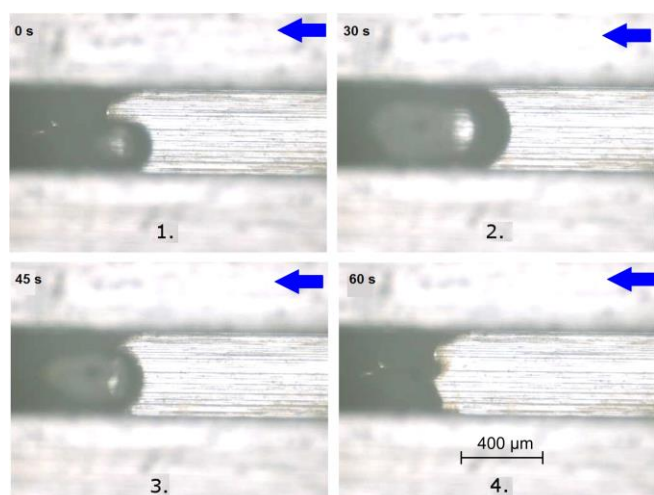


Fig. 13 Gas bubble nucleation and growth at attached particles/agglomerates in the microchannel at measuring section 1, original images without post-processing, arrows indicating flow direction.

Constant Soil Coverage

The soil coverage calculated based on images taken at MS 2 is constant over process time, see Fig. 11. Different cleaning detergents and changing volumetric flow rates do not lead to visually detectable cleaning effects in the two-dimensional plane for this measuring section.

Soil Coverage Decrease

Effective cleaning is found for MS 3, indicated by a decrease in soil coverage, see curve MS 3 in Fig. 11. After an increase from 40% to 50% at 1000 seconds the soil coverage decreases significantly, revealing a cleaned surface after 1500 seconds. In Fig. 14 the progress of increase and

sudden decrease of the soil coverage development, which is described within 1000 to 1500 seconds by curve MS 3 in Fig. 11, is shown.

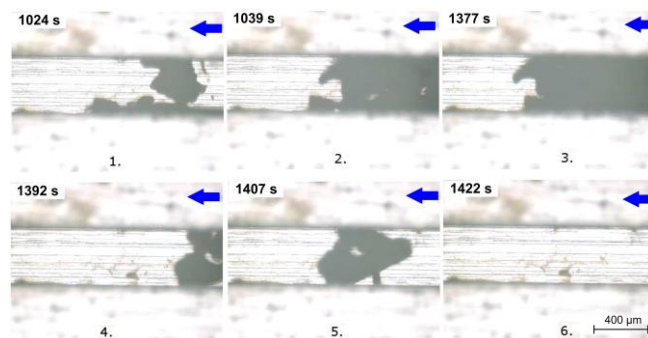


Fig. 14 Measuring section 3: increase and sudden decrease of the soil coverage indicating a cleaned surface, original images without post-processing, arrows indicating flow direction.

The sudden decrease of soil coverage for MS 3 can be explained by an increase of the fluid forces exerted to the attached particles and agglomerates at MS 3 as more blocked particles are deposited. At the point where the fluid forces exceed the adhesion forces of the attached particles and agglomerates these will be detached and washed off. The described process depends on the degree of porosity of the network of attached particles and agglomerates. The denser the network is packed, the greater will be the resulting fluid forces affecting the porous network.

DISCUSSION

Comparing different lipid concentrations (Fig. 8 vs. Fig. 9) significantly lower values for R_f and Δp for lower lipid concentrations are found. This shows a strong dependency between the amount of the disperse phase and the developed fouling layer. This can be attributed to the elevated surface-to-volume ratio. With increasing surface-to-volume ratio the possibility for particle-wall interactions increases significantly.

Table 3 shows a strong dependency between the emulsifier concentration and the corresponding occurrence of fouling. With increasing emulsifier concentration, fouling decreases. This might be due to different levels of lipid surface coverage with emulsifier resulting in stronger particle-particle repulsive forces with increasing emulsifier concentrations. This effect is also observed for the production of LNP: Lower emulsifier concentrations led to aggregation or coalescence caused by hydrophobic attraction between insufficiently covered crystal surfaces [Helgason, 2009].

At lower emulsifier concentration (down to 1%) the repeatability of fouling experiments is decreased. In addition more agglomerates attached to the walls of the inlet header region, see Fig. 10. The more agglomerates are attached in the inlet header region, the more random detachment will take place. This leads to erroneous results with limited repeatability. Random detachment was also reported by Perry and Hartmann [Perry, 2008; Hartmann, 2012]. This

effect is predominant for low emulsifier concentrations as this leads to decreased particle-particle repulsive forces and thus to increased agglomeration.

In order to repeatedly create defined fouled microchannels, the 2% emulsifier formulation is suggested. The buildup of fouling layers directly in the microchannels could be observed visually. Also fewer attached particles in the inlet header region resulting in reproducible conditions for cleaning evaluations in the microchannels were detected.

The local visual fouling detection method works effectively. Changes in local fouling states are observed correctly and quantified by the soil coverage percentage. Constant soil coverage over process time indicates that the regarded cleaning procedure is not effective or that only small amounts of the fouling layers are removed. Since only topview images are taken, the described 2D visual detection method can only distinguish between soiled (i.e. black) or cleaned (i.e. white) areas. Therefore formerly described 3D effects, such as bridging or tunnel build up, cannot be identified separately. In comparison to macro dimensions it is obvious that the ratio of characteristic dimension of the microchannel to particle or agglomerate diameter in micro dimensions are significantly smaller. As an example see Fig. 14, with a ratio of channel to agglomerate diameter of 1.

No dependencies between the observed soil coverage developments in the three different measuring sections were revealed.

Analogies and Differences of Fouling and Cleaning in Micro and Macro Structured Heat Exchangers

The development of the thermal fouling resistance and the pressure drop during continuous crystallization in the micro heat exchanger (Fig. 8) appears similar to known developments from macroscopic dimensions (Fig. 1). Obtained negative values for the thermal fouling resistance, i.e. enhanced heat transfer, are also reported for macro dimensions for turbulent flow regimes. This is due to roughness and constriction effects [Albert, 2011], which also was observed in this work for laminar flow regimes at $Re = 30$ in the micro heat exchanger.

The development of the thermal fouling resistance shows no initiation phase but a clearly developed roughness controlled phase followed by a subsequent layer growth phase. The increase of R_f and Δp compared to macro dimensions is very fast. Within the process time of 800 seconds R_f increases to approx. $16 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$ indicating strong fouling. This results from much smaller ratios of characteristic dimension of the microchannel to particle or agglomerate diameter in addition to significantly higher surface-to-volume ratios.

Fouling affects fluid dynamics as well as thermal performance of heat exchangers. It can be expected that the relative contribution of these effects differs for macro vs. micro dimensions. The thermal effect of fouling is quantified by the fouling Biot number Bi_f [Ishiyama, 2007].

$$Bi_f = k_0 \cdot R_f \quad (3)$$

The fluid dynamics effect of fouling can be quantified by the normalized increase of pressure drop

$$\Delta p^* = \frac{\Delta p_f - \Delta p_0}{\Delta p_0} \quad (4)$$

Thus the relative impairment of fluid dynamics vs. thermal performance due to fouling may be assessed through the **Degree of Fouling Increase**

$$DFI = \left| \frac{\Delta p^*}{Bi_f} \right| \quad (5)$$

For all experiments stated in Table 3 ($\Delta p_0 = 0.28 \text{ bar}$) the DFI varies from 4 to 150. Micro systems with low fouling tendencies ($R_f < 1 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$, see 3% emulsifier concentration in Tab. 3) will result in high DFI values, as Bi_f values are small while Δp^* are high due to fouling based constriction effects. However, low fouling macro systems will show low DFI values. For middle or high fouling tendencies comparable DFI ranges can be found for micro and macro dimensions (for experiments in Tab. 3: 1%: DFI = 14; 2%: DFI = 18). For example Albert stated in his PhD thesis for a double pipe heat exchanger with a characteristic dimension of 30 mm for crystallization fouling experiments a Δp^* of 20.7 ($\Delta p_0 = 0.006 \text{ bar}$; $\Delta p_f = 0.13 \text{ bar}$) and a maximum fouling resistance of $6 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$, which results in a DFI of 19 [Albert, 2010]. Thus absolute values of Δp_f are significantly different (7 bar (micro) vs. 0.13 bar (macro)), but based on the regarding Δp_0 the increase of Δp^* is in the same order of magnitude.

A capturing effect was observed, see Fig. 12, which also is insignificant in macro dimension. Thus it is specific for fouling phenomena in micro dimensions. We assume that the capturing effect is based on the formation of a pore system due to formed fouling layers. In this pore system varying characteristic dimensions based on varying pore dimensions are formed. These constrictions lead to blocking of upstream detached particles/agglomerates.

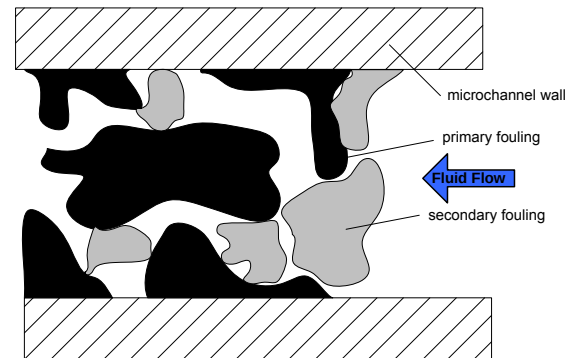


Fig. 15 Primary and secondary fouling effects: adhesive forces to channel walls or attached particles/agglomerates and blocking due to constrictions (i.e. capturing effect).

We define this capturing effect or constriction based fouling in micro dimensions as secondary fouling, see Fig. 15. In contrast, conventional (i.e. primary fouling) fouling describes fouling effects based on particle-wall or particle-particle adhesive forces.

CONCLUSIONS

1. Similar to macro dimensions, a clearly developed induction and layer growth phase, for the thermal fouling resistance and the pressure drop were found for particulate fouling in a micro heat exchanger. The temporary development and increase of R_f and Δp is much faster compared to macro dimensions. The DFI, the ratio of the normalized pressure drop to the fouling Biot number, is for both dimensions in the same order of magnitude, but the absolute pressure drop is much higher for micro dimensions. The resulting values for the thermal fouling resistance are in the same order of magnitude as known for macro dimensions.
2. The repeatability of fouling experiments in micro dimensions varies much more compared to macro dimensions. This is based on random detachment of particles and agglomerates from inlet header regions. In these regions fouling build up is favored because of larger characteristic dimensions and thus increased gravitational forces combined with lower lift forces.
3. The tendency of the LNP system to create fouling layers is highly dependent on the amount of the disperse phase and the emulsifier concentration: Less disperse phase and higher emulsifier concentration decreases fouling.
4. A 2D visual local fouling detection method as presented was successfully developed and applied to measure and monitor the soil coverage percentage during a cleaning process in the micro heat exchanger.
5. The local visual fouling detection during cleaning experiments showed micro dimension specific capturing effects of attached particles/agglomerates which block detached particles/agglomerates from upstream the regarded measuring section.
6. Observed divergent effects compared to known phenomena in macro dimensions for fouling and cleaning experiments are mainly caused by the significantly increased surface-to-volume ratio and thus increased possibility for particle-wall interactions. Also the ratio of the channel dimension to particle diameter in micro dimensions contribute to these divergencies.

NOMENCLATURE

Bi_f	fouling Biot number [-]
DFI	degree of fouling increase [-]
k_0	heat transfer coefficient of clean surface [$W \cdot m^{-2} \cdot K^{-1}$]
k_f	heat transfer coefficient of soiled surface [$W \cdot m^{-2} \cdot K^{-1}$]
λ_f	thermal conductivity of deposited fouling [$W \cdot m^{-1} \cdot K^{-1}$]
m_f	deposited fouling mass [kg]
ρ_f	density of deposited fouling [$kg \cdot m^{-3}$]
Δp^*	normalized pressure drop [-]
Δp_0	initial pressure drop [bar]
Δp_f	pressure drop of fouled heat exchanger [bar]
t_{ini}	initiation time [s]
t_{ind}	induction time [s]
Δp	pressure drop and mass based fouling resistance [bar]
$R_{f,m}$	mass based fouling resistance
R_f	thermal fouling resistance [$m^2 \cdot K \cdot W^{-1}$]
x_f	fouling layer thickness [$m^2 \cdot K \cdot W^{-1}$]

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