Published online www.heatexchanger-fouling.com

FOULING IN MICROSTRUCTURED DEVICES: A REVIEW ON THE CURRENT STATE OF EXPERIMENTAL WORK

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ABSTRACT

Process intensifying microstructured devices are widely used for processing of products, which do not contain any particles. However the handling of particulate flows in microchannels is challenging, due to the very high surfaceto-volume ratio (up to 100,000 m²/m³). This results in increased fouling and specifically blocking in microchannels compared to macro equipment. To overcome these restraints and to increase the applicability of micro devices, a better understanding of the underlying processes and phenomena is necessary. This work reviews experimental fouling investigations in microchannels in order to evaluate the level of research for all types of fouling in micro-dimensions, with a focus on identifying differences and analogies of fouling in micro- and macro-dimensions.

INTRODUCTION

The use of microstructured devices with characteristic dimensions of $\leq 1000 \ \mu m$ results in process intensification. This process intensification, based on increased heat and mass transfer coefficients, is advantageous for many applications of the pharmaceutical or fine chemicals industry. The innovative character of the micro process technology is also expressed in an exponential growth of the market forecast for microstructured devices, see Fig. 1.



Fig. 1 Market forecast for microstructured devices, adapted from [Körsten, 2009]

The mentioned advantages are countered by certain disadvantages and restraints:

- (i) Compared to typical capacities of the chemical industry achievable capacities of micro process plants are significantly lower (≤ 1000 t a⁻¹).
- (ii) Existing microstructured devices often represent a highly specialized solution for one specific application. A toolbox of standardized and commercial available microstructured devices is still missing [Grundemann, 2012].
- (iii) Fouling and blocking issues when the micro process involves the handling of particulate flows.

In 2003 Hessel et al. stated, that fouling issues are "only said in a whisper among micro chemical engineers" [Hessel, 2003]. Still in 2007 "fouling and blocking issues are not yet solved" [Brandner, 2007] and still in 2012 Hartman identified fouling in microstructured devices as the "major barrier and greatest challenge to operate micro systems" [Hartman, 2012]. Fundamental research of fouling in microstructures is published rarely; just basic anti-fouling design rules are given ("as small as necessary and beneficial, not as small as possible" [Kockmann, 2006]). Chen et al. from Novartis-MIT center for continuous manufacturing even stated, that a "successful resolution of these problems (...) would provide a new route ..." for processing of many applications, especially crystallizations [Chen, 2011].

In 2009 Wilson analyzed the research progress of fouling in heat exchange equipment by using Epstein's 5 x 5 fouling matrix [Wilson, 2009; Epstein, 1983], indicating that progress had been made for all research topics (see Fig. 2). For structuring purposes, this matrix and approach for assessing research progress is applied here as well as for microstructured systems.

An in depth review about fouling in microchannels is published by Schoenitz et al. [Schoenitz, 2015]. This contribution aims to give an overview about fouling investigations in microstructures in order to assess underlying processes for a better understanding of the differences between fouling in macro and micro equipment. Therefore, exemplarily results of published experimental research work is shown here with a focus on a concluding comparison between fouling in micro and macro devices.



Fig. 2 Wilson's approach to summarize research progress for all fouling categories and fouling events [Wilson, 2009]. Survey amongst attendees of the 8th HXFC in 2009, ranking their personal level of understanding between 0 (no) and 5 (high).

Membrane fouling is, however, excluded from this review for it differs significantly from microchannels due to the porous nature of the fouled surface combined with the influence of transmembrane flow on the fouling process.

FOULING MECHANISMS

Crystallization fouling

Fouling by crystals, which are formed in the bulk solution without contact to the heat exchanger surface, is not considered as crystallization fouling and will be discussed in the chapter about particulate fouling.

Only two research groups did research on crystallization fouling in microstructures. Both used $CaCO_3$ as fouling system. The experiments were performed in parallel microchannels in the laminar flow regime.

Benzinger et al. investigated crystallization fouling in an oval shaped micro heat exchanger with 17 parallel microchannels (25 mm length x 800 μm width x 100 μm height), see Fig. 3, and presented the results on the 7th HXFC in 2007. They investigated the influence of different surface coatings (DLC: diamond like carbon, FEP: fluorinated ethylene propylene) on the fouling process in the micro heat exchanger. Within a process time of 5.5 h they found no significant difference of the fouling behaviour, the thermal fouling resistance slightly increased to approximately $R_f = 1 \cdot 10^{-4} \text{ m}^2\text{KW}^{-1}$ for all experiments. The disassembled micro heat exchanger after experiments at Re = 110 is shown in Fig. 4, also showing crystals on the surfaces of the transparent microstructured device and not only on the heat transfer surface (metallic foil).

Benzinger et al. concluded, that microstructured heat exchangers are prone for fouling because of their narrow channels and especially of their high heat transfer coefficients ($\alpha = 7,700$ W m⁻²K⁻¹ for the presented experiments).



Al-block microstructured device metallic foil in between Fig. 3 Oval shaped micro heat exchanger with 17 parallel microchannels (25 x 0.8 x 0.1 mm) [Benzinger, 2007].



Fig. 4 Microstructured device with integrated microchannels (left) and metallic foil (right) with different coatings (A: no coating, stainless steel; B: DLC; C: FEP) of the disassembled micro heat exchanger after the experiments [Benzinger, 2007].

In contrast, Geddert found significantly different behavior for crystallization fouling on different surface coatings at turbulent flow regimes in macro-scale [Geddert, 2009].

Mayer et al. investigated the influence of different Reynolds numbers on the fouling behavior of CaCO₃ in a micro heat exchanger [Mayer, 2015], which was similar to the one shown in Fig. 3. The time dependent behavior of the thermal fouling resistance varied for different Reynolds numbers (Re = 66, 198 and 264), showing an increase with decreasing Reynolds number. $R_{f,max}$ was $2.5 \cdot 10^{-4}$ m²KW⁻¹ at Re = 66, see Fig. 5.

Mayer et al. also investigated the influence of crystallization fouling on the heat transfer performance [Mayer, 2012]. They summarized, that the impact of crystallization fouling on the heat transfer shows a similar behavior as for fouling in macro-dimensions. The impact on the pressure drop was much higher than known from macroscopic experiments, which the authors attributed to the much smaller dimensions. Increased flow rates resulted in decreased fouling and pressure drop, as known from macro-heat exchangers.



Fig. 5 Thermal fouling resistance for CaCO₃ different Reynolds numbers. [Mayer, 2012]

Chemical reaction fouling

No research work was found which fits the definition of chemical reaction fouling: Fouling based on reactions with the wall materials (polymerization, decomposition) or products of such processes, depositing on the channel walls. Fouling based on chemical reactions in the bulk flow with inert wall materials is classified as particulate fouling, which is addressed below.

Particulate fouling

Particulate fouling represents the most common fouling category for fouling investigations in microchannels. Hartman et al. categorized particulate fouling phenomena in micro dimensions in three mechanisms: clogging by constrictions, bridging and random detachment [Hartman, 2012]; examples are given in the following.

Constriction and bridging

The sudden enlargement or narrowing of channels are in the majority of cases unavoidable when microstructured devices are designed to form an integral part of a process chain. They are present at the device's entrance or exit or even within the micro device, for instance in flow distribution headers. Hydrodynamic bridging, or blocking by arching, occurs when particles flowing in a streamline get in contact with each other. This effect is quite similar to particle-based bridging in macroscopic silos (e.g. grain silos). Bridging occurs when particles are growing in size (for example due to agglomeration) or at constrictions, i.e., at reduced flow path cross-sections.

An example, which contains both, constriction and bridging based fouling, is the Pd-catalyzed C-N bond formation in microchannels. It is an important reaction for the production of active pharmaceutical ingredients, natural products and special chemicals [Hartman, 2010]. The reaction is carried out in nonpolar solvents resulting in precipitation of products and byproducts, making this reaction suitable for investigations about fouling mechanisms in microchannels. The used serpentine microchannel $(0.4 \times 0.4 \times 875 \text{ mm})$ was made of silicone with a low-stress silicon nitride coating, see Fig. 6 [Hartman, 2010].



Fig. 6 Silion microreactor with serpentine channels $(0.4 \times 0.4 \times 875 \text{ mm})$ for particulate fouling investigations [Hartman, 2010]

For low flow rates (20 μ L min⁻¹) the reactor started to block after six reactor volumes injected, being totally blocked after nine (Fig. 7, A). Blocking occurred mainly in the 180° turns of the serpentine microchannel (Fig. 7 B). An expanded view is showing accumulated white solids, having the same dimension as the microchannel (400 μ m), see Fig. 7 C.

Increasing the flow rate by a factor of 3.5 (70 μ L min⁻¹) resulted in a gradually increasing pressure drop (Fig. 7 D). The microchannel was also blocked after a few reactor volumes injected. White solids accumulated or grew at the channel walls, not directly in the microchannels, see Fig. 7 E in contrast to Fig. 7 B. The different clogging mechanisms, initiated by different flow rates, are illustrated in Fig. 7: clogging by bridging (F) and by constriction (G), with D₁ > D₂.

Random detachment

The effect of random detachment is based on different shear stresses in header regions (in- and outlets) compared to the microchannels of microstructured devices. Perry and Kandlikar found 11 times higher shear stresses in the microchannels compared to the headers, resulting in 24 times higher gravitational forces compared to corresponding lift forces in the header regions [Perry, 2008]. This coupled effect, low shear stresses in combination with low lift forces, results in high fouling tendencies especially in the header regions.

Consequently, fouling builds up preferentially in the header regions. These agglomerates break off randomly and will then be transported by the fluid into the microchannels, resulting in blocking of the corresponding microchannels. Based on that random effect, fouling investigations in microchannels show poor repeatability. For example Perry and Kandlikar found relatively high standard deviations for pressure drop-based fouling investigations for silica dispersions. In three repetitions with identical conditions, the standard deviation was 60 % [Perry, 2008].



Fig. 7 (A & D) Dimensionless pressure drop as a function of reactor volumes injected (B & E) photographs showing the accumulation of white solids (C) expanded view of B (F & G) schematically drawing of bridging (F) and constriction (G) effect [Hartman, 2010]

Schoenitz performed continuous crystallization experiments in a micro heat exchanger with 32 parallel microchannels (0.2 x 0.2 x 190 mm). To evaluate the repeatability of these experiments, the lipid concentration was varied between 5 % and 25 % in three independent runs, respectively [Schoenitz, 2015a]. The resulting maximum pressure drop and R_f of the corresponding experiments are shown in Fig. 8.

Only for a lipid concentration of 5 % repeatable experiments are possible, because the fouling tendency is low. With increasing lipid concentration, the results vary significantly for each lipid concentration (7.5 % - 25 %). The random detachment is also quantified by the photographs of the inlet header region (see Fig. 8): For low fouling tendencies (5 % lipid concentration) the accumulated white solid is small, whereas for higher concentrations (picture shown is for a lipid concentration of 25 %) just a small non-blocked area is left.

Biological Growth Fouling

Fouling layers composed of micro- or macro-organisms are classified as biological growth fouling. Aside from direct contamination from micro- or macro-organisms, their metabolic products and extra cellular polymeric substances,



Fig. 8 Maximum pressure drop and R_f while continuous crystallization of lipid nanoparticle formulations with varying lipid concentrations.

mainly proteins, can cause fouling issues in many applications. These include clinical monitoring, environmental monitoring and food quality control, either before or during processing. Metabolic products are of great importance for lab-on-chip systems, e.g., for blood analysis at point of care, and are essential for the buildup of biofilms.

Fig. 10 depicts results for the detachment percentage, see equation (1), for the three different coatings and for the microchannel with no coating.



Fig. 9 (a) Micro-Chip with tubing, valves and (b) channel network [Zhang, 2008].

Zhang et al. investigated the attachment/detachment of living cells on modified microchannel surfaces with the aim to keep cells attached to the channel walls for lab-on-a-chip analysis with different carrier media. The microchannel network is shown in Fig. 9. The width of the microchannels was $320 \,\mu$ m, the depth $60 \,\mu$ m. Different coatings were used: silane, glutaraldehyde and collagen. The used cell culture was chinese hamster ovary (CHO-K1) [Zhang, 2008]. Cell suspension was delivered from inlet B to outlet C while A and D were closed, followed by a settlement period for the cells of 30 min with closed channels, see Fig. 9. Detachment experiments were performed with fluid flow from A to D with incrementally increasing flow rates of $1 - 10 \,\mu$ L min⁻¹.

$detachment(\%) = \frac{initial cell number - remaining cell number}{initial cell number} \cdot 100 \quad (1)$

With increasing shear force the number of detached cells is increasing. The results show, that the modified surfaces led to a retention of cells compared to the unmodified surface. For higher shear forces the detachment percentage reaches a stable level indicating strong adhesive forces of the left cells.



Fig. 10 Detachment percentage of CHO cells from the four types of modified microchannel surfaces as a function of shear stress [Zheng, 2008].

Fig. 11 shows a single CHO cell under different flow conditions. When the cell was delivered to the attachment region by injection flow, micrograph (a) was taken, followed by settling for 40 min (b). The effect of shear stress is also shown: the cell under low shear stress of 110 μ N cm⁻² (c) and high shear stress of 2,740 μ N cm⁻² (d). With higher shear stress cell deformation is increasing, being more flat to the surface oriented in the direction of the flow.

The authors also fitted the experimental data with a theoretical model, taking into account shear stress, surface adhesion bonds and hydrodynamic viscous stress. With this approach, different surfaces were investigated for their attachment/detachment behavior to a wide range of living cells in an easy and controlled fashion.



Fig. 11 Micrographs of a single CHO cell in a microchannel under different flow conditions: (a) cell was delivered to position by injection flow, (b) followed by 40 min settling, (c) under low shear stress of $110 \,\mu\text{N cm}^{-2}$ and (d) under high shear stress of 2,740 μ N cm⁻² [Zheng, 2008].

Corrosion and erosion fouling

If fouling layers are composed of corrosion products, this is referred to as corrosion fouling. Thus, the products of the preliminary phenomena, erosion and corrosion, will cause fouling issues in devices downstream. Corrosion fouling often is an issue in long term experiments of several 1,000 hours of operation, whereas in microstructured devices experiments are comparable short. Therefore, no research is published about corrosion fouling in micro dimensions, occasionally about the preliminary phenomena erosion and corrosion. Additionally, wall thickness in microsystems frequently is in the order of 100 to 500 μ m. Corrosion would thus lead to a mechanic breakdown of the system disabling long time operation.

Clogging by gas bubbles

The unwanted accumulation of gas in process equipment is a serious issue, regardless of the dimension. For micro dimensions, gas bubble diameters are in the range of the characteristic dimension of the microchannels, blocking the whole cross sectional area. This results in an equivalent operational misbehavior of the affected devices as the abovementioned fouling categories. For example, in parallel microchannels the blockage of single microchannels result in a maldistribution of the process fluid which may result in inhomogeneous product properties.

At the initial state of experiments, microchannels usually contain air. While filling the microchannels with the process fluid, air bubble entrapment can occur. Also during processing gas bubble clogging due to rapid coalescence and therefore growing gas bubbles can appear.

Goldschmidtböing identified the following wetting characteristics while the filling process of the microchannels as the main reason for gas bubble entrapment [Goldschmidtböing, 2003]: Edges are preferentially wetted prior to plane microchannel walls, which results in a splitting of the fluid in micro cavities at cross-sectional extensions and gas inclusions as illustrated in Fig. 12. Capillary and viscous forces dominate while filling the microchannels. Based on numerical simulations, they provided design rules which are independent from experimental fits and can hence be applied to identify "filling-friendly" microfluidic structures. [Goldschmidtböing, 2003]



Fig. 12 Mechanism of gas inclusion via an unstable meniscus in micro cavities or cross-section extensions [Goldschmidtböing, 2003].

Once the process is operating, clogging by gas bubbles may be caused by rapidly growing gas bubbles, gas emissions of the fluid due to reactions, degassing downstream of pressure reductions or an unintentional wash-in of gas bubbles. In this case, the mobility of gas bubbles in the microchannel should be high in order to wash them off as fast as possible. Aiming at maximum bubble mobility, Litterst et al. investigated an optimized design of T-shaped microchannels [Litterst, 2008]. The dimensionless maximum velocity of gas bubbles in a given setup was introduced to describe the tendency for bubble movement, hence the tendency for clogging by gas bubbles. Their presented graphs can be used to design non-clogging T-shape microchannels with height to width ratios of 0.2 - 5.



Fig. 13 Possible bubble configuration: (a) vertical (b) blocked (c) horizontal [Litterst, 2008].

Possible bubble arrangements in optimized microchannels are shown in Fig. 13, showing configurations for partial blocking (a and c) and complete blocking by gas bubbles (b).

ANALOGIES AND DIFFERENCES OF FOULING IN MICRO- AND MACROSTRUCTURED DEVICES

Conducting chemical processes in microstructured rather than macrostructured devices results in altered geometrical and flow conditions, which also affect the fouling behavior of these devices. The differences are (i) the characteristic inner tube/channel diameter is smaller than 1 mm, whereas in macro equipment dimensions of more than 10 mm are typically applied, (ii) this results in a surface-to-volume ratio of up to 100,000 m²m⁻³, more than 100 times higher than for macrostructured devices, and (iii) the flow regime is usually laminar.

At these typical laminar flow regimes in micro devices paired with low wall shear stress affecting the fouling layers, fouling build-up increases whereas the detachment of matter decreases. Therefore, microchannels are very prone to fouling and complete blockages, resulting in a maldistribution of the fluid flow in parallel channels. Blocked channels also cause altered cleaning mechanisms compared to non-blocked channels, as Schoenitz et al. pointed out: In "For nonblocked microchannels, cleaning is induced by wall shear stresses. In contrast, blocked microchannels lead to dead zones up-stream of the blocked areas, resulting in pressure forces instead of shear stresses. Thus especially for these blocked channels, chemical cleaning becomes more important" [Schoenitz, 2014].

In operating microstructured devices a capturing effect has been observed for microstructured devices [Schoenitz, 2015b]. The effect is due to porous fouling layers with internal pores of various sizes acting as obstacles for particles or agglomerates, which have been detached upstream of the pore system. Blockages may then occur as a consequence of this capturing effect and may consequently be attributed as "secondary fouling". "Primary fouling", on the other hand, is based on particle-wall or particle-particle adhesive forces. In macrostructured equipment, "secondary fouling" is very rare since the characteristic dimensions are much larger [Schoenitz, 2014].

Heat exchanger fouling

Heat transfer is a frequently used unit operation in process engineering, thus fouling investigations in heat exchangers are widespread, no matter of the underlying dimension. In micro heat exchangers, the predominant fouling types are crystallization and particle fouling. For these fouling types, Schoenitz et al. and Mayer et al. found qualitatively similar trends to what is known for macroscopic dimensions for the thermal fouling resistance and the pressure drop during continuous processing in microstructured devices [Mayer, 2012; Schoenitz, 2015b]. During continuous processing of lipid nanoparticles in the micro heat exchanger, the thermal fouling resistance showed no initiation phase but

went through a clearly developed induction phase with a subsequent layer growth phase [Schoenitz, 2015b].

In general, the development and the defined fouling phases known from macro-dimensions also appear in micro-dimensions, but the relevant time scales (minutes) are much shorter compared to macro dimensions (hours). These shorter characteristic time scales mainly arise due to significantly higher surface-to-volume ratios combined with characteristic dimensions in the micro scale, and thus small flow cross sections for microstructured devices compared with macro devices. This drastically increases possibilities for particle-towall attachment.

These short time scales for fouling events may also give rise to the observed absence of aging phenomena in microsystems. If encountered, fouling in microstructured devices requires immediate measures thus preventing any deposit from a long-term aging process.

Negative values for the thermal fouling resistance, i.e. enhanced heat transfer, are reported for turbulent flow regimes in macro dimensions. This is attributed to roughness and constriction effects due to the fouling layers. This effect was also observed by Schoenitz et al. for micro devices, although at laminar flow regimes [Schoenitz, 2015]. In their investigations the maximum absolute values of thermal fouling resistance (thermal effect) and pressure drop (fluid dynamic effect of fouling) are much higher in micro dimensions, whereas the normalized increase of these fouling indicators is in the same order of magnitude compared to macro devices. The "Degree of Fouling Increase" (DFI) may be employed for the comparison of fouling processes in micro and macro devices, see equation 2 [Schoenitz, 2015b]:

$$DFI = \frac{\left|\frac{\Delta p_{f} - \Delta p_{0}}{\Delta p_{0}}\right|}{\left|\frac{k_{0} \cdot R_{f}}{k_{0} \cdot R_{f}}\right|} = \left|\frac{\Delta p^{*}}{Bi_{f}}\right|$$
(2)

The equation relates the fluid dynamic effect of fouling (f = fouled; 0 = clean) to the thermal effect. The latter is expressed by the fouling Biot number, defined as the product of the overall heat transfer coefficient at the clean state k_0 with the thermal fouling resistance R_f . low fouling Micro systems with tendencies $(R_{\rm f} < 1~\cdot~10^{\text{-4}}~m^2 K W^{\text{-1}})$ are characterized by high DFI values since Bi_f values are low while Δp^* values are high due to fouling-based constriction effects. However, low fouled macro systems will show low DFI values. For systems with moderate or severe fouling tendencies, comparable DFI ranges can be found for micro and macro dimensions [Schoenitz, 2015b].

CONCLUSIONS

This work provides a brief review on fouling research in microstructures, based on a more detailed review by Schoenitz et al [Schoenitz, 2015]. The focus of this paper is presentation of exemplary examples of experimental findings for the different fouling mechanisms. The majority of the reviewed papers may be grouped as follows: (i) intensified processes were described, resulting in higher yields or increased product properties compared to macro-scale processing, (ii) fouling/blocking occurred during processing, and (iii) a solution to mitigate or prevent fouling altogether was developed for the specific process and microstructured device employed. Most of the presented papers offer very specific fouling investigations making it difficult to derive general rules and/or parameter dependencies, thus comparative or critical considerations of the reviewed papers are not possible. Thus, in the following a statistical approach was used to evaluate the research in the field of fouling in microchannels.

Traditionally, macro scale fouling phenomena can be classified based on Epstein's 5 x 5 matrix [Epstein, 1983]. For fouling in micro dimensions, a sixth fouling category may be added to that matrix: clogging by gas bubbles. Although this type of clogging does not follow the macroscopic definition of fouling ("unwanted deposition on surfaces"), it results in comparable effects with respect to heat, mass and/or momentum transport to the affected devices. Thus, gas bubble clogging can be considered as a micro-specific fouling category, resulting in a 5 x 6 micro fouling matrix.



Fig. 14 5 x 6 Matrix: Published papers for categories and sequential events of fouling in micro scale devices. Multiple occurrences were accounted for.

Following Wilson's approach to quantifying the research progress in macro scale fouling [Wilson, 2009], experimental-based papers (70 of all reviewed papers) dealing with fouling in microstructured devices were assigned to the respective fouling category as shown in Fig. 14, multiple events were accounted for.

It is obvious that the majority of papers within the 5 x 6 micro-fouling-matrix were dealing with "*particulate fouling*". This is mainly due to the fact that microstructured devices offer great advantages, specifically for reactions involving particle precipitation: based on intensified mixing on the micro-scale, the resulting particle size is decreased as well as the particle size distribution narrowed in many

applications. Such reactions were among the very first examples studied in microstructured devices and are still being investigated. As corrosion fouling is a matter of correct choice of material and oftentimes of long-term experiments, only papers dealing with the preliminary effects erosion and corrosion were found. Similar to this fouling category, the number of papers studying "clogging by gas bubbles" also was small. However, many papers dealt with the crystallization of solids, which were allocated to "particulate fouling". "Crystallization fouling" itself requires the formation of nuclei and their subsequent growth on the surface. Fouling due to biological systems in microstructured devices was studied only rarely, as biotechnological processes - aside from lab-on-a-chip or biomedical applications - just occasionally employ micro devices. The investigations mainly aimed at preventing fouling by observing and tackling the "initiation" and "attachment" phases. "Aging" of depositions in microstructured devices was not addressed in any of the reviewed papers. This might be due to the fact that fouling in these dimensions is not tolerable for most applications, therefore processes are directly shut down when fouling occurs.

Revealing the fundamentals of fouling in microchannels, however, requires experimental studies of all sequential events and all influencing factors.

NOMENCLATURE

Latin symbols

$\operatorname{Bi}_{\mathrm{f}}$	fouling Biot number	
R_{f}	thermal fouling resistance	$m^{2}KW^{-1}$
D	diameter	m
DLC	diamond like carbon	
FEP	fluorinated ethylene propylene	
k	overall heat transfer coefficient	$Wm^{-2}K^{-1}$
Re	Reynolds number	

Greek symbols

α	film heat transfer coefficient	Wm ⁻² K ⁻¹
u		** 111 15

Subscript

0	clean
f	fouling
max	maximum

REFERENCES

Brandner, J.J., Bohn, L., Henning T., Schygulla, U., Schubert, K., 2007, Microstructure Heat Exchanger Applications in Laboratory and Industry, *Heat Transfer Eng.*, vol. 28, pp. 761-771. Benzinger, W., Brandner, U., Schygulla, U., Schubert, K.,

2007, Influence of different surface materials on the fouling process in a microstructured heat exchanger under laminar regime, *Proc. of 7th HXFC*, Tomar, Portugal. Chen, J., Sarma, B., Evans, J.M.B., Myerson, A.S., 2011, Pharmaceutical Crystallization, *Cryst. Growth Des.*, vol. 11, pp. 887-895.

Epstein, N., 1983, Thinking about heat transfer fouling: A 5 x 5 matrix, *Heat Transfer Eng.*, Vol. 4, pp. 43-56.

Geddert, T., 2009, Einfluss von Oberflächenmodifikationen auf die Induktionszeit beim Kristallisationsfouling, Diss., Technische Universität Braunschweig.

Goldschmidtböing, F., Schlosser R., Schonhardt, S., Woias, P.,2003, Capillary filling of micro-reservoirs with various cross sections, *Proc. of 12th International Conference on Solid State Sensors, Actuators and Microsystems*, pp. 1883-1886.

Grundemann, L., Schoenitz, M., Scholl, S., 2012, Shorter timeto-market with micro-conti processes, *Chem. Ing. Tech.*, vol. 84, pp. 685-693.

Hartman, R.L., Naber, J.R., Zaborenko, N., Buchwald, S.L., Jensen, K.F., 2010, Overcoming the Challenges of Solid Bridging and Constriction during Pd-Catalyzed C-N Bond Formation in Microreactors, *Org. Process Res. Dev.*, vol. 14, pp. 1347-1357.

Hartman, R.L., 2012, Managing Solid in Microreactors for the Upstream Continuous Processing of Fine Chemicals, *Org. Process Res. Dev.*, vol. 16, pp. 870-887.

Hessel, V., Löwe, H., 2003, Micro chemical engineering: components – plant concepts – user acceptance: Part III, *Chem. Eng. Technol.*, vol. 26, pp. 531-544.

Kockmann, N., 2006, Transport Processes and Exchange Equipment, in *Micro Process Engineering: Fundamentals, Devices, Fabrication and Applications*, Wiley-VCH, Weinheim, pp. 102.

Körsten, S., 2009, Entwicklung von mikroreaktionstechnischen Modulen für die Anwendung im chemischen Labor, PhD Thesis, Friedrich-Schiller-Universität Jena.

Litterst, C., Metz, T., Zengerle, R., Koltay, P., 2008, Static and dynamic behavior of gas bubbles in T-shaped non-clogging microchannels, *Microfluid. Nanofluid.*, vol. 5, pp. 775-784.

Mayer, M., Bucko, J., Benzinger, W., Dittmeyer, R., Augustin, W., Scholl, S., 2012, The impact of crystallization fouling on a microscale heat exchanger, *Exp. Therm. Fluid Sci.*, vol. 40, pp. 126-131.

Perry, J.L., Kandlikar, S.G., 2008, Fouling and its mitigation in silicon microchannels used for IC chip cooling, *Microfluid. Nanofluid.*, vol. 5, pp. 357-371.

Schoenitz, M., Augustin, W., Scholl, S., 2014, Challenges in Cleaning Microstructured Devices, *Proceedings of Cleaning & Disinfection in Food Processing*, Cambridge, UK, pp. 166-173.

Schoenitz, M., Grundemann, L., Augustin, W., Scholl, S., 2015, Fouling in microstructured devices: a review, *Chem. Comm.*, DOI: 10.1039/C4CC07849G

Schoenitz, M., 2015a, Kontinuierliche Kristallisation von Lipidnanopartikeln in mikrostrukturierten Apparaten, Diss., Technische Universität Braunschweig.

Schoenitz, M., Finke, J.H., Hohlen, A., Warmeling, N., Müller-Goymann, C.C., Augustin, W., Scholl, S., 2015b, Fouling in a Micro Heat Exchanger during Continuous Crystallization of Solid Lipid Nanoparticles, *Heat Transfer Eng.* vol. 36, pp. 731-740.

Wilson, I., 2009, Preface, Proc. of 8th HXFC, Schladming, Austria.

Zhang, X., Jones, P., Haswell, S.J., 2008, Attachment and detachment of living cells on modified microchannel surfaces in a microfluidic-based lab-on-a-chip system, *Chem. Eng. J.*, vol. 135, pp. 82-88.