Jet Aerated Loop Reactors

as Alternative to Stirred Tank Reactors

Dissertation

Zur Erlangung des

Doktorgrades der Ingenieurwissenschaften (Dr. Ing.)

der Naturwissenschaftlichen Fakultät I – Biowissenschaften

der Martin-Luther-Universität

Halle-Wittenberg,

vorgelegt von

Herrn Sebastian Weber (MSc)

geboren am 05. Juli 1986 in Heidelberg

Datum der Verteidigung: 23.04.2019

Erstgutachter: Prof. Dr. M. Pietzsch

Zweitgutachter: Prof. Dr. J. Büchs

Content

Motivation

From the perspective of chemical engineering the jet loop reactor is a well-known reactor type. In the field of bioprocess engineering jet loop reactors might help to improve the performance of highly aerobic processes that are normally carried out in stirred tank reactors.

Comparative studies on mass transfer, mixing and fermentation performance of jet loop reactors and stirred tank reactors are already available in the literature. However, as introduced in chapter 1 the results of this comparison are not self-evident. The mode of operation and reaction parameters that are common for chemical processes can differ a lot from those needed for highly aerobic fermentation processes. If the data in the literature is reduced to the relevant range of volumetric power inputs and superficial gas velocities, it turns out that the available knowledge is limited. Therefore, the motivation of this study was to evaluate the jet loop reactor as an alternative reactor type for industrial bioprocesses. It was aimed to characterize the jet loop reactor with respect to reactor design and operation. Furthermore, strategies for further process intensification should be evaluated.

Comprehensive overview

The main features of the jet loop reactor (JLR) are introduced in Chapter 1. First, the general applicability of the JLR concept was shown in lab scale. The JLR was benchmarked against a stirred tank reactor (STR) with an identical scale and geometry. The reactors were compared for an aerobic fed batch fermentation of *E.coli* (Chapter 2). The lab scale JLR was then available for further process development with industrial strains. Simultaneously, the physical performance of the respective JLR was evaluated in more detail. The utilized nozzles were characterized with respect their gas entrainment-, dispersion- and mass transfer performance (Chapter 3). It was shown that high local power inputs could contribute to an effective gas dispersion and high mass transfer rates. It was tested if the inhomogeneous power distribution in JLRs impacts the balance between micro- and macromixing in JLRs (Chapter 4). An optimized nozzle operation can contribute to process intensification. For further tests, a scalable pilot jet loop reactor for highly aerobic processes was designed. In the following, the gas entrainment and compression characteristics of the pilot reactor were determined. The mass transfer- and the energy efficiency were evaluated (Chapter 5). The obtained data were used to conduct an economic evaluation of a large-scale application (Chapter 6).

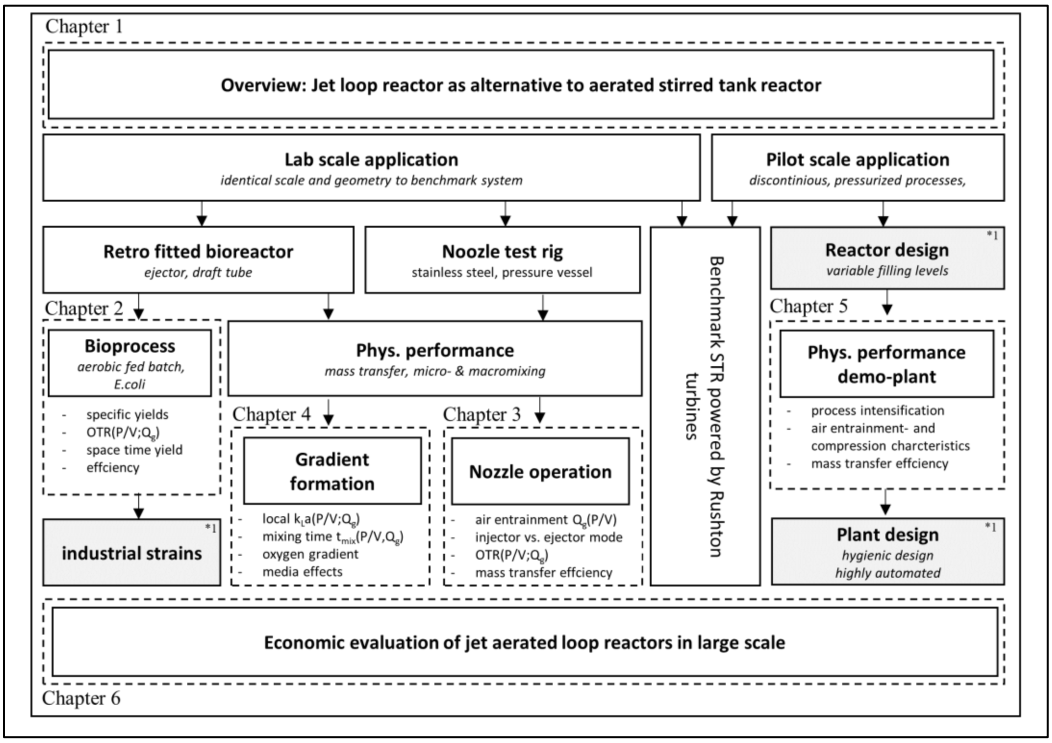

*Figure 1: Topics of thesis linked to experimental setup. Respective chapter given in superscript. (*1) intellectual property of BASF SE and therefore not presented within this thesis*

Chapter 1

Introduction - Jet aerated loop reactors as alternative to stirred tank reactors

Nomenclature

Abbreviations		**Symbols**		
OTR	oxygen transfer rate	A	surface	[m^2]
JLR	jet loop reactor	D	diameter	[m]
STR	stirred tank reactor	Dp	differential pressure	[bar]
k_La	oxygen transfer coefficient	E	mass transfer efficiency	[kgO_2 kW^{-1} h^{-1}]
		H	reactor height	[m]
Indices		L	length	[m]
D	draft tube	p	pressure	[Pa]
g	gas	P	power	[W]
j	jet	Q	volumetric flow	[m^3 h^{-1}]
L	lower	V	volume	[m^3]
L	liquid	X	area ratio	[-]
R	reactor			
u	upper	**Greek letters**		
		η	efficiency	[-]

1 Introduction

An important step towards a bio based economy is the integration of industrial bioprocesses into the value chains of the chemical industry. Bioprocesses promote cheap product synthesis via new routes and can help to replace fossil resources by renewable feedstocks. In order to compete against well optimized petrochemical processes also the demands for a sustainable and energy efficient production must be full filled [1]. Therefore, process intensification as the concept of ‘‘doing more with less’’ is an important aspect for the development of economic bioprocesses. The microbial performance itself can be increased by metabolic engineering and molecular biotechnology. However, to use the full potential of microbial reactions the conditions within the bioreactor must be controlled. Thereby improved reactor designs and optimized operation procedures can help to maximize the performance of bioprocesses [2] [3].

1.1 Challenges regarding aerobic bioprocesses

The aerobic cultivation of microorganisms allows fast growth and the generation of high turnover rates. For aerobic bioprocesses limited by oxygen mass transfer, the minimization of diffusional limitations can increase the achievable space time yields [2]. This is usually done by an enlargement of the gas liquid interface or an increase of the driving force for oxygen transport. Simultaneously to an enhanced molecular transport also an intensification of mixing is required [4]. Minimization of diffusional lengths scales and mixing volumes will lead to faster reactions. For a reliable and efficient operation, the processes of mixing and mass transfer should be well balanced, otherwise gradient formation might occur. Even micro environmental heterogeneities such as differences in substrate concentrations or partial oxygen pressure can potentially induce metabolic pathways leading to losses in selectivity and the formation of anaerobic- or overflow metabolites [5] [6].

1.2 Reactors for highly aerobic bioprocesses

Stirred tank reactors (STRs) are commonly used and highly valued for their benefits regarding easy operability. The demands for mass transfer and mixing can be addressed beforehand by the choice of the respective stirrer type. The rotational speed and the aeration rate can be adapted separately during operation [7]. In aerated bioreactors the intensification of mass transfer is usually achieved by increasing power input and aeration rate. However, for highly aerated processes the susceptibility of stirrers to high gas loads should be considered. In case of standard Rushton turbines, high amounts of dispersed gas phase lower the power that can be dissipated to the medium and therefore also the ability to transfer oxygen to the broth [11]. This problem can be avoided when gas tolerant stirrer types such as hydrofoil impellers and hollow blade turbines or a combination of stirrers is used [8-12]. In the unaerated case they provide lower power numbers but significant improvements regarding suspension and dispersion in highly aerated liquids can be achieved [13]. Due to their aforementioned flexibility to meet the time constants for mass transfer and mixing, aerated stirred tank reactors are preferred at small (10^{-1} m^3) and intermediate scales (10^1 m^3). However, the STR significantly loses its efficiency in larger scale [14] [15]. For highly aerobic bioprocesses the size of a stirred reactor is limited to around 200 m^3 [1]. If the cultivation volumes become even larger than 500 m^3, the traditionally used aerated stirred tank reactors become excessively expensive. Costs are increased due to mechanically limited volumetric power inputs (up to 5 kW m^{-3}) and low energy efficiencies for the required air compression [16]. Therefore, bubble

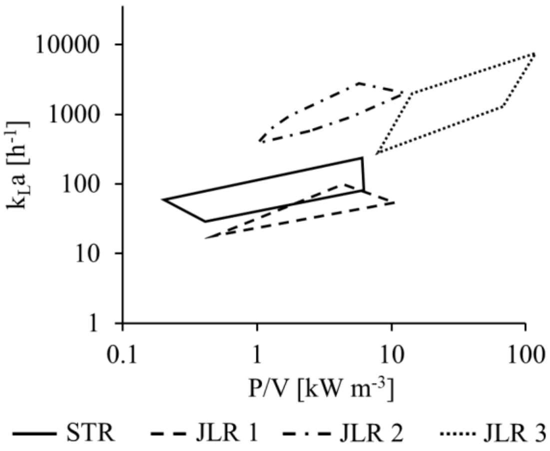

Figure 2: Comparison of $k_La(P/V)$ for STR and JLR. Reproduced and adapted from Warnecke et al.[15].

columns and airlift loop reactors are often used instead of stirred tank reactors [17]. However, volumetric power inputs and subsequently oxygen mass transfer rates (OTRs) of such apparatuses are limited [6]. In contrast to the previously mentioned reactor types the so called jet loop reactor (JLR) can economically provide high power inputs (> 5 kW m^{-3}) in large scale [7] [16].

STRs are aerated via a sparger at the reactor bottom. An intensive secondary dispersion is taking place at the respective stirrer blades. In case of the JLR, the gas phase is directly channeled through the nozzle that is working as the primary dispersion device. Within the nozzle the local power inputs are at least one order of magnitude higher than those expected for stirred tank reactors.

The simple design of the JLRs offers an easy scale up [8]. In chemical engineering they an efficient alternative to STRs for the intensification of mass transfer limited reactions [18-20]. As it can be referred from Figure 2, JLRs have the potential to achieve higher k_La values per power input compared to a STR (STR vs. JLR 2). The obtainable k_La values can even be further increased by higher power inputs (STR vs. STR 3). However, a general statement cannot be made. Due to their versatility STR can also compete against JLRs in terms of mass transfer (STR vs. JLR 1). If a JLR is considered as alternative for an STR, process specific parameters such as liquid phase properties as well as mass transfer- and mixing demands should be addressed beforehand by the respective reactor design.

1.3 Jet aerated loop reactors

In general jet loop reactors consist of a reaction vessel that is aerated via gas liquid nozzles. The nozzles are powered by a liquid pump integrated into an external loop. Within the nozzle a liquid jet is channeled through a suction chamber and a mixing tube to suck in, compress and disperse fresh or recycled gas [21]. Within the installed nozzle a fine gas liquid dispersion is created. Subsequently, the gas liquid dispersion is distributed across the reactor by the remaining impulse of the liquid jet. The achievable mass transfer is determined by power dissipation, the respective gas throughput and the residence time of gas [20]. The internal flow regime and the gas distribution is significantly affected by the geometry of the reaction vessel and the respective internals [22]. It can be summarized that the performance of the JLR is mainly determined by hydraulic power input and reactor geometry [23]. In comparison to STRs, JLRs can provide intensified mass transfer at higher energy efficiencies [24]. In the following the major design aspects are introduced.

1.3.1 Reactor geometry

The geometry of the reaction vessel and the internals of a JLR significantly affect the flow regime within the reactor (Figure 3A). Geometric ratios such as the aspect ratio (H:D), the relation of draft tube diameter to draft tube length (L_D/D_D) and the relation of draft tube diameter to reactor diameter (D_D/D_R) can be used to characterize a reactor design [3] [25]. For an optimization of the internal flow rates also the ratios of the deflection areas between the riser and the downcomer section (X_U, X_L) are of major importance. The ratio is determined by the draft tube- and the reactor diameter, the distance between the lower edge of the draft tube and the reactor bottom (A_L) as well as the distance between the upper edge of the draft tube and the liquid surface (A_U).

In jet loop reactors longitudinal mixing in each circulation and back mixing due to flow deflection can superimpose each other [25]. The minimization of flow losses leads to increased internal flow rates, faster circulation and intensified mixing [25]. On the other side an optimization towards maximal internal liquid circulation rates can lead to pipe flow and therefore regions with suboptimal back mixing.

The mass transfer in regions with pipe flow was found to be decreased by an order of magnitude compared to intensively mixed zones near the jet [26]. High aspect ratios lead to increased gas velocities within the reactor. In general, high superficial gas velocities are promoting gas liquid mass transfer. However, the gas load to the annuli of the reactor is limited. If the gas throughput is increased above a certain value, the homo- or heterogenous flow regime can be disturbed and slug bubbles will be formed [27] [28]. Therefore, it is important to consider the required gas- and liquid flow already in the design phase of the apparatus.

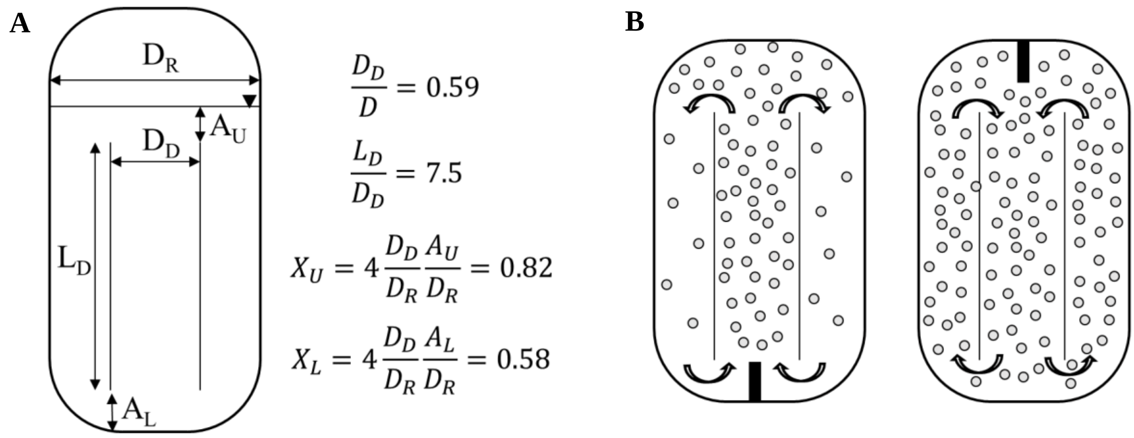

Figure 3: Geometry and assembly of JLRs (A) Optimal geometric ratios of reactor diameter (D_R), draft tube diameter (D_D), draft tube length (L_D) and upper and lower distance of draft tube (A_U, A_L) for calculation of deflection area ratios (X_U, X_L). (B) Nozzle position and gas distribution.

Optimal ratios for the design of JLRs were published by Blenke *et al* [25] [29-31]. For a reactor equipped with a draft tube it was investigated that a diameter ratio (D_D/D_R) of 0.59, a draft tube aspect ratio (L_D/D_D) of 7.5 and deflection zones with X_U:0.82 and X_L:0.58 yield maximal liquid circulation. In case a JLR is designed to achieve maximal mass transfer, a draft tube geometry with a D_D/D_R ratio of 0.44 should yield optimal results [32-37] (Figure 3).

1.3.2 Draft tube

A draft tube can significantly change the flow regime and the gas distribution in a JLR [38]. If a draft tube is not installed, a major fraction of the momentum provided by the liquid jet is lost by creating a zone with high turbulence directly behind the gas liquid nozzle. Within the draft tube an effective momentum transfer is generated. For a JLR with a nozzle in downflow configuration the flow from top to bottom is achieved in the downcomer (Figure 3B). If the minimal circulation velocity in the downcomer is reached, the gas liquid flow is deflected at a baffle plate and the separated gas phase enters the riser section of the apparatus [39] [40]. Consequently, the rising air bubbles are creating an internal loop flow by the airlift principle. Thereby higher gas holdups and gas residence times are achieved [21] [41] and the internal liquid flow rates can be increased by a factor of 5 [42].

1.3.3 Nozzle position

The aforementioned gas liquid nozzles can be installed in an upward or a downward orientation (Figure 3B). Nozzles in an upward orientation are installed near the reactor bottom. They offer the advantage for operation at low liquid flow rates. Due to the parallel orientation of the momentum of the liquid jet and the buoyancy forces of bubbles, the supplied gas phase passes the entire reactor already at low power inputs. Thereby the minimal power input is determined by the hydrostatic pressure at the reactor bottom.

If the gas liquid nozzle is installed in a downward orientation in the upper part of the reactor, the hydrostatic pressure at the reactor bottom is of minor interest. However, the buoyancy forces of the gas phase and the momentum of the liquid jet are in a countercurrent orientation. Installation of the nozzle in a downward position increases the gas residence time and gas holdup (Figure 3B). As a result higher mass transfer efficiencies can be achieved [43] [44]. The minimal power input to achieve sufficient aeration is determined by the impulse that is required for bubble transport from top to bottom [25]. If nozzles are plunged below the liquid surface, the slip between gas and liquid phase is reduced and a higher energy efficiency can be achieved. However, with increasing immersion depths lower gas holdups and k_La values are obtained [45].

1.3.4 Nozzle operation

The gas liquid nozzle of a JLR is powered by a liquid pump via an external loop. High local power inputs and shear rates create a fine gas liquid dispersion [17]. The power of the liquid jet is determined by the liquid flow (Q_L) and the pressure drop over the nozzle (Dp_L). If the respective gas phase is supplied by an external compressor, the nozzle is operated as injector. If the utilization of an external compressor is not intended, the gas liquid nozzle can be operated as an ejector. In the ejector mode the air entrainment is achieved by the Bernoulli's principle.

The pressure course across the nozzle determines its gas entrainment characteristics. For given operational parameters it is a result of the geometry of the ejector nozzle [46] (Figure 4A). The energy efficiency of a nozzle strongly depends on the mixing tube and the diffuser design [47]. Diffusors can recover pressure from kinetic energy and increase the energetic efficiency. However, in case of JLRs the available momentum is required for further gas dispersion and gas distribution [25]. Therefore a pressure recovery from kinetic energy by the application of diffusers and consequently also the maximal energy efficiency is limited [48].

Ejectors can be also considered as compression devices. The hydraulic power input is used to entrain and compress a gas stream (Q_G) from a pressure p_G at the gas inlet to a pressure p_R at the outlet of the ejector nozzle. In general, maximal gas entrainment is achieved for low pressure differences (Dpg= p_R-p_G). However, a modulation of pressure differences offers an additional parameter for an optimization of momentum exchange between gas and liquid phase. The mechanism of isothermal compression in the throat of an ejector is related to momentum transfer. The compression efficiency (η) can be increased when the compression ratio between gas- and liquid phase (Dp_G/Dp_L) is optimized (Figure 4 B). The pressure drop over the liquid nozzle (Dp_L) is determined by its geometry and the liquid flow supplied by the pump (Q_L). Therefore, the gas differential pressure (Dp_G) must be optimized.

Most important for an efficient air entrainment and compression by ejector nozzles is the breakup of the liquid jet in the suction chamber of the nozzle [21]. It was found that the ratio of the area of the nozzle throat and the surface of the expanding liquid jet can be optimized [49] [50] and a value of 1 yields optimal results [51]. In general, best results are achieved when the mixing zone is created in the cylindrical part of the throat. Higher backpressures in the throat force earlier jet break up and mixing. For lower pressures, the mixing zone moves downstream and the efficiency significantly decreases when the mixing zone is reaching the diffusor [52] [53]. The breakup and therefore the compression efficiency (Figure 4B) can be controlled by tuning the discharge pressure at the end of the mixing tube by throttling a valve in the offgas line of the respective apparatus. Consequently, the headspace pressure of the apparatus (p_R) is increased and a higher Dp_G is seen (Figure 4A).

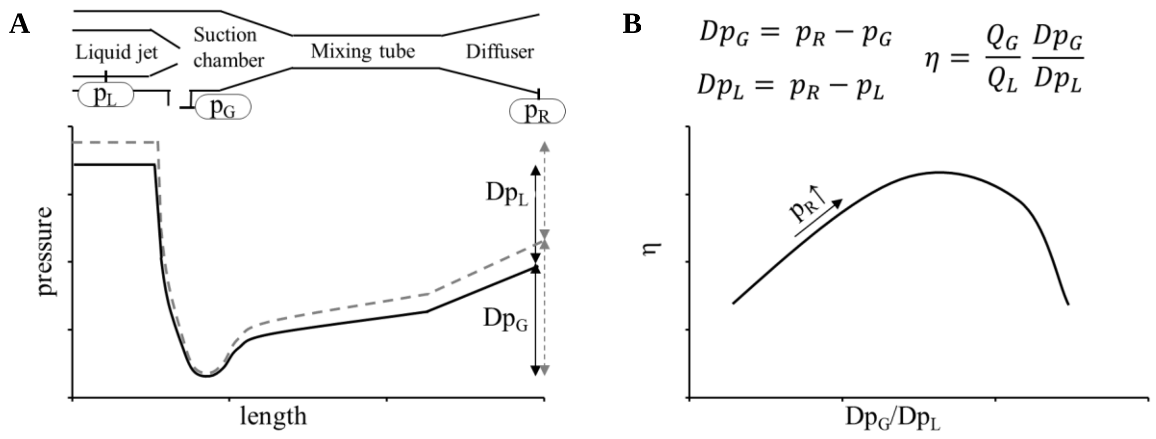

Figure 4: Pressure and compression characteristics of ejector nozzle. Characterized by pressure at liquid inlet (p_L), gas inlet (p_G) and nozzle outlet (p_R)and pressure difference of gas and liquid phase (Dp_L Dp_G). (A) Development of pressure within ejector nozzle. Standard operation (solid black line), operation at increased backpressure at optimal compression ratio (grey dashed line). (B) Development of compression efficiency (η) for changing compression ratio (Dp_G/Dp_L) with increasing backpressure p_R.

1.3.5 Microbial cultivation in JLR

Although JLRs are known for their efficient mass transfer performance, only limited data with respect to the cultivation of microorganisms is available. It was shown that JLRs can be used for the cultivation of yeast. Promising results were achieved for the fermentation of *Kluyveromyces fragilis*, *Endomycopsis lipolytica*, *C. utilis* and *Trichosporon cutaneum* [3] [27] [54] [55]. Also shear sensitive filamentous bacteria such as *Thermornonospora sp.* and *Strepromyces tendae* [56] [57] can be cultivated successfully in JLR. Surprisingly not much attention was paid to single cell bacterial production systems. Single- and small cells should be more robust with respect to the occurring shear forces and therefore ideal for JLR applications. Ughetti *et al.* recently published a first study focusing on a JLR as an alternative reactor system for the cultivation *E.coli* [58]. A STR was compared to a JLR for batch cultivations on a glycerin substrate. The JLR achieved higher mass transfer rates and consequently higher dissolved oxygen levels were maintained by the JLR compared to the STR [58].

Within this study (Chapter 2) more focus was given to the maximal mass transfer rates and the related space time yields. First test with respect to the mass transfer performance of the JLR were made using an oxygen depleting sulfite system with a validated transferability to microbial cultivations [3] [59] [60]. Subsequently, fed batch cultivations of *E.coli* on glucose were performed. The oxygen consumption was controlled by an exponentially increasing feed profile. Then the achievable oxygen transfer rates at a maximal driving force (pO_2~0) were determined. Biomass growth and the formation of overflow metabolites were monitored. In the following, yield coefficients, space time yields and the energy efficiency of mass transfer for a strictly aerobic cultivation were determined. The achieved results were compared to data obtained with a STR powered by Rushton turbines. To yield comparable results, STR and JLR shared the same scale and geometry. The cultivations in JLR and STR were performed at the same volumetric power inputs and most importantly at identical gas throughputs.

1.3.6 Mass transfer performance

The yield of reactions limited by gas liquid mass transfer is determined by gas throughput and power dissipation [61]. As the JLR should be evaluated as a potential alternative for the STR, it is obvious to perform the comparative studies at identical volumetric power inputs and aeration rates. In case of the STR, the stirrer speed and the aeration rate can be chosen freely within the boundary conditions given by the respective setup.

The operation range of the JLR is more restricted with respect to volumetric power input and aeration rate. In the self-entraining ejector mode the specific aeration rate is linked to the flow and the pressure drop over the liquid nozzle and consequently hydraulic power input (chapter 1.4.5). If higher aeration rates are needed additional gas can be provided by an external compressor. The nozzle is then operated in injector mode. The choice of operation mode can influence the achievable mass transfer, the mixing performance as well as the energy efficiency of the reactor. Consequently, a differentiation between the operation modes is needed when the JLR should be compared to the STR (Chapter 3).

If the nozzle is operated in the self-entraining ejector mode, the respective aeration rates and therefore the expected mass transfer rates are considerably lower. On the other hand, an additional air compressor can be dispensed or a less powerful aggregate can be chosen. An aspect that especially becomes important in technical- and large-scale applications. However, as the nozzle is then also working as a gas compressor it becomes susceptible to backpressure caused by hydrostatic height or pressure losses in the vent line. In consequence the achievable aeration rates can be further reduced.

The advantage to save an additional compressor is often quoted in the literature [41] [55] [62] [63]. However, with respect to industrial biotechnology the attributed consequences were so far not addressed in detail. In chapter 3 the gas entrainment characteristics for the utilized ejector were determined. The reduction of air entrainment with increasing backpressures in the vent line was measured. Subsequently, the achievable k_La values for the self-entraining ejector mode and the injector mode with pressurized air supply were determined. The obtained k_La values were benchmarked against a STR operated at volumetric power inputs and aeration rates comparable to those achieved for the self-entraining ejector mode.

In a second scenario, JLR and STR were evaluated for a broader range of aeration- and agitation rates. The hydraulic power input in the unaerated case was set constant and the aeration rate was varied. The energetic efficiencies of mass transfer were calculated and compared to the performance of reactors described in the literature.

1.3.7 Gradient formation, Micro- and Macromixing

JLR and STR are known for fast mixing in aqueous and coalescence inhibited systems [64] [65]. For JLRs the achieved mass transfer coefficients are 5-10 times higher than those obtainable in water air systems [21]. High power inputs contribute to gas liquid mixing and the intensification of mass transfer limited reactions. However, high differences in local power input can cause an imbalance in macro- and micromixing. If the reaction rates are increased, also faster mixing is required. Otherwise the maximal turnover rates of the reactor must be reduced to avoid the development of inhomogeneities. At high local reaction rates the formation of gradients becomes more likely. Local limitations or an accumulation of substrates (e.g. carbon source or oxygen) can lead to a loss in selectivity and the formation of anaerobic byproducts or overflow metabolites. With respect to an efficient mixing and homogenization of aerobic and carbon limited fed batch processes, multiple aspects become important. Gas liquid dispersion, the distribution of gas and the rate limiting substrates as well as oxygen- and substrate depletion with residence time must be considered.

Fermentation experiments (Chapter 2) implied a susceptibility for gradient formation at high turnover rates. Therefore, the development of dissolved oxygen gradients in jet aerated reactors was further evaluated (Chapter 4). The development of k_La and mixing time with increasing power input was monitored. The steady sodium sulfite feeding technique was applied to visualize the development of oxygen gradients within the JLR and the benchmark STR. Also the effect of a draft tube on the mixing performance was evaluated. The obtained results were compared to data generated with a STR powered by Rushton turbines

Also medium specific changes can alter the mass transfer and mixing performance of JLR. High cell densities, the degradation or built up of polymeric substrates and products can alter the viscosity of the fermentation broth. Viscosity induced alterations of flow dynamics and mass transfer can restrict the applicability of JLRs for fermentation processes [25] [35] [66]. Therefore this potential drawbacks were further evaluated (Chapter 4). The effect of an increased viscosity in the context of mass transfer, mixing and oxygen gradient formation was determined.

1.3.8 Process intensification for JLRs

The operation of a JLR with a self-aspirating ejector nozzle can be a major advantage. If the nozzle is optimized for air entrainment, an additional air compressor is not required. For large scale STRs, the energy costs of air compressors can exceed the costs for hydraulic power input [3]. Therefore JLRs might help to decrease investment. and operational costs.

Furthermore, ejector nozzles can be used for headspace pressurization of the reactor. An increase of the driving force for oxygen transfer allows process intensification. It was reported that a higher gas density leads to the formation of smaller bubbles and consequently increased volumetric mass transfer coefficients (k_La) [48]. Simultaneously the volumetric gas flow in the reactor can be decreased and a delayed formation of slug flow is proposed [27].

Headspace pressurization can be achieved by throttling a valve in the offgas line of the JLR (Chapter 5). Significant pressure levels were only achievable in pilot scale. The compression efficiency (η) (Figure 4B) was thereby used as an optimization parameter. Subsequently, the achievable gas holdups and oxygen transfer rates for an operation at maximal gas entrainment and pressurized operation were determined. The energy efficiency and the expectable turnover rates were calculated. The achieved results were benchmarked against data obtained for a STR powered by Rushton turbines.

1.4 Evaluation of jet loop bioreactors for large scale applications

In large scale application the JLR design offers significant advantages. Due to their simple and robust design as well the high mass transfer efficiency they are attractive reactors for the treatment of wastewater [45] [67] [68] . In industrial biotechnology the JLR was applied for the fermentative cracking of hydrocarbon molecules in the 10^3 m^3 scale [69]. In contrast to other reactor types the power input is not restricted by mechanical limitations. Available standard equipment can be used. The required power input and aeration rates as well as the needed surface for heat removal can be achieved by numbering up the external loops, heat exchangers and liquid pumps. High energetic oxygen transfer efficiencies (E) of 2 to 3 kgO_2 kW^{-1} m^{-3} can be achieved. As variable energy costs are a main cost driver in industrial biotechnology, the potential impact of the JLR technology on the production costs was evaluated (Chapter 6). Fixed and variable cost for JLR and STR are compared to identify the pros and cons of the respective reactor technology.

Literature

[1] Woodley, J.M., Breuer, M., Mink, D., A future perspective on the role of industrial biotechnology for chemicals production. *Chem. Eng. Res. Des.* 2013, *91*, 2029–2036.

[2] Jenck, J.F., Agterberg, F., Droescher, M.J., Products and processes for a sustainable chemical industry: a review of achievements and prospects. *Green Chem.* 2004, *6*, 544–556.

[3] Seipenbusch, R., Blenke, H., The loop reactor for cultivating yeast on n-paraffin substrate, in: *Advances in Biochemical Engineering, Volume 15*, Springer Berlin Heidelberg, 1980, pp. 1–40.

[4] Stitt, E.., Alternative multiphase reactors for fine chemicals. *Chem. Eng. J.* 2002, *90*, 47–60.

[5] Takors, R., Scale-up of microbial processes: impacts, tools and open questions. *J. Biotechnol.* 2012, *160*, 3–9.

[6] Sandoval-Basurto, E.A., Gosset, G., Bolívar, F., Ramírez, O.T., Culture of Escherichia coli under dissolved oxygen gradients simulated in a two-compartment scale-down system: Metabolic response and production of recombinant protein. *Biotechnol. Bioeng.* 2005, *89*, 453–463.

[7] Nienow, A.W., Aeration, Biotechnology, in: *Kirk-Othmer Encyclopedia of Chemical Technology*, John Wiley & Sons, Inc., 2000.

[8] Schaepe, S., Kuprijanov, A., Sieblist, C., Jenzsch, M., et al., kLa of stirred tank bioreactors revisited. *J. Biotechnol.* 2013, *168*, 576–583.

[9] Karimi, A., Golbabaei, F., Mehrnia, M.R., Neghab, M., et al., Oxygen mass transfer in a stirred tank bioreactor using different impeller configurations for environmental purposes. *Iran. J. Environ. Health Sci. Eng.* 2013, *10*, 6.

[10] McFarlane, C.M., Nienow, A.W., Studies of High Solidity Ratio Hydrofoil Impellers for Aerated Bioreactors. 4. Comparison of Impeller Types. *Biotechnol. Prog.* n.d., *12*, 9–15.

[11] Warmoeskerken, M., Smith, J.M., Hollow blade agitator for dispersion and mass transfer. *Chem. Eng. Res. Des.* 1989, *67*, 193–8.

[12] Moucha, T., Linek, V., Prokopová, E., Gas hold-up, mixing time and gas–liquid volumetric mass transfer coefficient of various multiple-impeller configurations: Rushton turbine, pitched blade and techmix impeller and their combinations. *Chem. Eng. Sci.* 2003, *58*, 1839–1846.

[13] Linek, V., Benes, P., Sinkule, J., Hollow blade agitator for mass transfer in gas-liquid bioreactors. *Food Bioprod. Process.* 1991, *69*, 145–148.

[14] Stitt, E.., Alternative multiphase reactors for fine chemicals. *Chem. Eng. J.* 2002, *90*, 47–60.

[15] Warnecke, H.-J., Geisendörfer, M., Hempel, D.C., Mass transfer behaviour of gas-liquid jet loop reactors. *Chem. Eng. Technol.* 1988, *11*, 306–311.

[16] Nordkvist, M., Grotkjær, T., S. Hummer, J., Villadsen, J., Applying rotary jet heads for mixing and mass transfer in a forced recirculation tank reactor system. *Chem. Eng. Sci.* 2003, *58*, 3877–3890.

[17] Nagel, O., Kürten, H., Sinn, R., Strahldüsenreaktoren, Teil I: Die Anwendung des Ejektorprinzips zur Verbesserung der Gasabsorption in Blasensäulen. *Chem. Ing. Tech.* 1970, *42*, 474–479.

[18] Jamshidi, A.M., Sohrabi, M., Vahabzadeh, F., Bonakdarpour, B., Studies on the hydrodynamic behavior and mass transfer in a down-flow jet loop reactor with a coaxial draft tube. *J. Chem. Technol. Biotechnol.* 2001, *76*, 39–46.

[19] Cramers, P.H.M.R., Beenackers, A.A.C.M., van Dierendonck, L.L., Hydrodynamics and mass transfer characteristics of a loop-venturi reactor with a downflow liquid jet ejector. *Chem. Eng. Sci.* 1992, *47*, 3557–3564.

[20] Behr, A., Becker, M., Dostal, J., Kohlmann, D., Hydrodynamik und Verweilzeitverhalten eines Düsenumlaufreaktors für den Einsatz in der Mehrphasenkatalyse. *Chem. Ing. Tech.* 2008, *80*, 1501–1508.

[21] Zehner, P., Kraume, M., Bubble Columns, in: Wiley-VCH Verlag GmbH & Co. KGaA (Ed.), *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany 2000.

[22] Behr, A., Becker, M., Dostal, J., Kohlmann, D., Hydrodynamik und Verweilzeitverhalten eines Düsenumlaufreaktors für den Einsatz in der Mehrphasenkatalyse. *Chem. Ing. Tech.* 2008, *80*, 1501–1508.

[23] Fuchs, S., Hahn, T., Construction and application of a jet-stirred loop reactor: Aufbau und Anwendung eines Kreislaufreaktors mit Gasstrahlpumpe. *Chem. Eng. Process. Process Intensif.* 1993, *32*, 225–231.

[24] Warmeling, H., Behr, A., Vorholt, A.J., Jet loop reactors as a versatile reactor set up-Intensifying catalytic reactions: A review. *Chem. Eng. Sci.* 2016, *149*, 229–248.
[25] Blenke, H., Loop reactors, in: *Advances in Biochemical Engineering, Volume 13*, Springer, 1979, pp. 121–214.
[26] Evans, G.., Biń, A.., Machniewski, P.., Performance of confined plunging liquid jet bubble column as a gas–liquid reactor. *Chem. Eng. Sci.* 2001, *56*, 1151–1157.
[27] Flores-Cotera, L.B., García-Salas, S., Gas holdup, foaming and oxygen transfer in a jet loop bioreactor with artificial foaming media and yeast culture. *J. Biotechnol.* 2005, *116*, 387–396.
[28] Wu, B., Firouzi, M., Mitchell, T., Rufford, T., et al., A critical review of flow maps for gas-liquid flows in vertical pipes and annuli. *Chem. Eng. J.* 2017, *326*.
[29] Blenke, H., Bohner, K., Hirner, W., Druckverlust bei der Strömungsumlenkung um 180° im Schlaufenreaktor. *Chem. Ing. Tech.* 1970, *42*, 479–480.
[30] Blenke, H., Bohner, K., Pfeiffer, W., Hydrodynamische Berechnung von Schlaufenreaktoren für Einphasensysteme. *Chem. Ing. Tech.* 1971, *43*, 10–17.
[31] Blenke, H., Bohner, K., Schuster, S., Beitrag zur optimalen Gestaltung chemischer Reaktoren. *Chem. Ing. Tech.* 1965, *37*, 289–294.
[32] Prasad, K.Y., Ramanujam, T.K., Overall volumetric mass transfer coefficient in a modified reversed flow jet loop bioreactor with low density particles. *Bioprocess Eng.* 1995, *12*, 209–214.
[33] Velan, M., Ramanujam, T.K., Hydrodynamics and mixing in down flow jet loop bioreactor with a non-Newtonian fluid. *Bioprocess Biosyst. Eng.* 1992, *7*, 193–197.
[34] Velan, M., Ramanujam, T.K., Gas-liquid mass transfer in a down flow jet loop reactor. *Chem. Eng. Sci.* 1992, *47*, 2871–2876.
[35] Selvi, P., Devi, U.A., Mass transfer studies and optimization of geometrical variables for a down flow jet loop reactor. Int. J. Chem. Sci. 2010, 77-83
[36] Prasad, K.Y., Ramanujam, T.K., Gas holdup and overall volumetric mass transfer coefficient in a modified reversed flow jet loop reactor. *Can. J. Chem. Eng.* 1995, *73*, 190–195.
[37] Prasad, K.Y., Ramanujam, T.K., Liquid circulation velocity and overall gas holdup in a modified jet loop bioreactor with low density particles. *Bioprocess Eng.* 1994, *10*, 131–137.
[38] Ludwig, W., Szafran, R.G., Kmiec, A., Dziak, J., Measurements of Flow Hydrodynamics in a Jet-Loop Reactor Using Piv Method. *Procedia Eng.* 2012, *42*, 1157–1168.
[39] Wagh, S.M., Koranne, K.V., Mankar, R.B., Sonolikar, R.L., Flow regimes in a two phase reversed flow jet loop bioreactor. *Biotechnol Bioproc E* 2010, *15*, 497–504.
[40] Tebel, K.H., Zehner, P., Fluid dynamic description of jet-loop reactors in multiphase operation. *Chem. Eng. Technol.* 1989, *12*, 274–280.
[41] Bhutada, S.R., Pangarkar, V.G., Gas induction and hold-up characteristics of liquid jet loop reactors. *Chem. Eng. Commun.* 1987, *61*, 239–258.
[42] Blasey, G., Steiff, A., Weinspach, P.-M., Zum Vermischungsverhalten der Gas- und Flüssigkeitsphase in Freistrahl- und Strahldüsenreaktoren. *Chem. Ing. Tech.* 1987, *59*, 434–435.
[43] Tojo, K., Miyanami, K., Oxygen transfer in jet mixers. *Chem. Eng. J.* 1982, *24*, 89–97.
[44] Ma, X., Hong, D., Huang, R., Xu, T., Gas holdup and volumetric liquid phase mass transfer coefficients in a downjet loop reactor. *Chem. Eng. J.* 1992, *49*, 49–54.
[45] Fakeeha, A.H., Effect of Design Parameters on Oxygen Mass Transfer Coefficient in a Free Jet Bioreactor. *Eng. Life Sci.* 2002, *2*, 19–22.
[46] Yadav, R.L., Patwardhan, A.W., Design aspects of ejectors: Effects of suction chamber geometry. *Chem. Eng. Sci.* 2008, *63*, 3886–3897.
[47] Rylek, M., Zahradník, J., Design of Venturi-tube gas distributors for bubble-type reactors. *Collect. Czechoslov. Chem. Commun.* 1984, *49*, 1939–1948.
[48] Cramers, P.H.M.., Beenackers, A.A.C.., Influence of the ejector configuration, scale and the gas density on the mass transfer characteristics of gas–liquid ejectors. *Chem. Eng. J.* 2001, *82*, 131–141.
[49] Kandakure, M.T., Gaikar, V.G., Patwardhan, A.W., Hydrodynamic aspects of ejectors. *Chem. Eng. Sci.* 2005, *60*, 6391–6402.
[50] Balamurugan, S., Gaikar, V.G., Patwardhan, A.W., Effect of ejector configuration on hydrodynamic characteristics of gas–liquid ejectors. *Chem. Eng. Sci.* 2008, *63*, 721–731.
[51] Lohrengel, B., Vogelpohl, A., Auslegung einer im Ejektorbetrieb arbeitenden Zweistoffdüse. *Chem. Ing. Tech.* 1990, *62*, 338–339.

[52] Bonnington, S.T., Water driven air ejectors, British Hydromechanics Research Association, 1960.
[53] Bonnington, S.T., King, A.L., Jet Pumps and Ejectors-A State of the Art Review and Bibliography, British Hydromechanics Research Association, Fluid Engineering, 1972.
[54] Jaramillo, A., Fluid dynamics and oxygen transfer during the cultivation of Trichosporon cutaneum in jet loop bioreactors, PhD Thesis, Diss. Naturwiss. ETH Zürich, Nr. 7899, 0000. Ref.: Fiechter, A.; Korref.: Hamer, G., 1985.
[55] Moresi, M., Bartolo Gianturco, G., Sebastiani, E., The ejector-loop fermenter: Description and performance of the apparatus. *Biotechnol. Bioeng.* 1983, *25*, 2889–2904.
[56] Sternad, W., Trick, I., Trösch, W., Henkel, H.J., et al., Characterization of bioreactors with three biological systems. *Bioprocess Eng. Vol 4 Part B Downstr. Process. Recovery Bioprod. Saf. Biotechnol. Regul. Biotechnol.* 1990, *2*, 737–740.
[57] Meyer, H., Charles, M., Cultivation of a filamentous bacterium in a deep jet fermentor. *Biotechnol. Bioeng.* 1982, *24*, 1905–1909.
[58] Ughetti, M., Jussen, D., Riedlberger, P., The ejector loop reactor: Application for microbial fermentation and comparison with a stirred-tank bioreactor. *Eng. Life Sci.* n.d.
[59] Yang, J.D., Wang, N.S., Oxygen mass transfer enhancement via fermentor headspace pressurization. *Biotechnol. Prog.* 1992, *8*, 244–251.
[60] Wiedemann, M., Räbiger, N., Schlüter, M., Eisenlauer, J., et al., Scale-down des Strahlzonen-Schlaufenreaktors: Entwicklung eines Screening-Tools für transportlimitierte chemische Reaktionen. *Chem. Ing. Tech.* 2011, *83*, 349–357.
[61] Nagel, O., Hegner, B., Kürten, H., Kriterien für die Auswahl und die Auslegung von Gas/Flüssigkeits-Reaktoren. *Chem. Ing. Tech.* 2004, *50*, 934–944.
[62] Wagh, S.M., Koranne, K.V., Sonolikar, R.L., Operating and hydrodynamic characteristics of a reversed flow jet loop bioreactor (RFJLB) with ejector. *Bioresour. Technol.* 2012, *110*, 417–422.
[63] Havelka, P., Linek, V., Sinkule, J., Zahradník, J., et al., Effect of the ejector configuration on the gas suction rate and gas hold-up in ejector loop reactors. *Chem. Eng. Sci.* 1997, *52*, 1701–1713.
[64] Havelka, P., Linek, V., Sinkule, J., Zahradník, J., et al., Hydrodynamic and mass transfer characteristics of ejector loop reactors. *Chem. Eng. Sci.* 2000, *55*, 535–549.
[65] Jamshidi, A.M., Sohrabi, M., Vahabzadeh, F., Bonakdarpour, B., Hydrodynamic and mass transfer characterization of a down flow jet loop bioreactor. *Biochem. Eng. J.* 2001, *8*, 241–250.
[66] Jianping, W., Ping, N., Lin, H., Yunlin, C., Local overall volumetric gas–liquid mass transfer coefficients in gas–liquid–solid reversed flow jet loop bioreactor with a non-Newtonian fluid. *Biochem. Eng. J.* 2000, *5*, 225–229.
[67] Farizoglu, B., Keskinler, B., Influence of draft tube cross-sectional geometry on KLa and ε in jet loop bioreactors (JLB). *Chem. Eng. J.* 2007, *133*, 293–299.
[68] Farizoglu, B., Keskinler, B., Yildiz, E., Nuhoglu, A., Cheese whey treatment performance of an aerobic jet loop membrane bioreactor. *Process Biochem.* 2004, *39*, 2283–2291.
[69] Langhans, G., Verfahrens- und Strömungstechnische Untersuchungen zum Einsatz der Tauschstrahlbeluftung in der Abwasserbehandlung, Ingenieurhochschule Koethen, 1980.

Chapter 2

Jet aeration as alternative to overcome mass transfer limitation of stirred bioreactors

Abstract

In industrial biotechnology increasing reactor volumes have the potential to reduce production costs. Whenever the achievable space time yield is determined by the mass transfer performance of the reactor, energy efficiency plays an important role to meet the requirements regarding low investment- and operating costs. Based on theoretical calculations, compared to bubble column, airlift reactor and aerated stirred tank, the jet loop reactor shows the potential for an enhanced energetic efficiency at high mass transfer rates. Interestingly, its technical application in standard biotechnological production processes has not yet been realized. Compared to a stirred tank reactor powered by Rushton turbines, maximum oxygen transfer rates about 200 % higher were achieved in a jet loop reactor at identical power input in a fed batch fermentation process. Moreover, a model based analysis of yield coefficients and growth kinetics showed that *E. coli* can be cultivated in jet loop reactors without significant differences in biomass growth. Based on an aerobic fermentation process, the assessment of energetic oxygen transfer efficiency [kgO_2 kW^{-1} h^{-1}] for a jet loop reactor yielded an improvement of almost 100 %. The jet loop reactor could be operated at mass transfer rates 67 % higher compared to a stirred tank. Thus, an increase of 40 % in maximum space time yield [kg m^{-3} h^{-1}] could be observed.

This chapter has been published in Engineering and Life Science

Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., Dietzsch, C, Jet aeration as alternative to overcome mass transfer limitation of stirred bioreactors. Eng. Life Sci. 2018, 18, 244-253

Chapter 3

Impact of nozzle operation on mass transfer in jet aerated loop reactors. Characterization and comparison to an aerated stirred tank reactor

Abstract

The impact of mass transfer on productivity can become a crucial aspect in the fermentative production of bulk chemicals. For highly aerobic bioprocesses the oxygen transfer rate (OTR) and productivity are coupled. The achievable space time yields can often be correlated to the mass transfer performance of the respective bioreactor. The oxygen mass transfer capability of a jet aerated loop reactor is discussed in terms of the volumetric oxygen mass transfer coefficient k_La [h^{-1}] and the energetic oxygen transfer efficiency E [$kgO_2\ kW^{-1}\ h^{-1}$]. The jet aerated loop reactor (JLR) is compared to the frequently deployed aerated stirred tank reactor. In jet aerated reactors high local power densities in the mixing zone allow higher mass transfer rates, compared to aerated stirred tank reactors. When both reactors are operated at identical volumetric power input and aeration rates, local k_La values up to 1.5 times higher are possible with the JLR. High dispersion efficiencies in the JLR can be maintained even if the nozzle is supplied with pressurized gas. For increased oxygen demands (above 120 mmol $L^{-1}\ h^{-1}$) improved energetic oxygen transfer efficiencies of up to 100 % were found for a JLR compared to an aerated stirred tank reactor operating with Rushton turbines.

This chapter has been published in Engineering and Life Science

Weber, S., Schaepe, S., Freyer, S., Kopf, M.H., Dietzsch, DC., Impact of Nozzle Operation on Mass Transfer in Jet Aerated Loop Reactors. Characterization and Comparison to an Aerated Stirred Tank Reactor. Eng. Life Sci. 2018, 18, 579-588

Chapter 4

Monitoring gradient formation in a jet aerated bioreactor

Abstract

Jet aerated loop reactors (JLRs) provide high mass transfer coefficients (k_La) and can be used for the intensification of mass transfer limited reactions. The jet loop reactor achieves higher k_La values than a stirred tank reactor (STR). The improvement relies on significantly higher local power inputs ($\sim 10^4$) than those obtainable with the STR. Operation at high local turnover rates requires efficient macromixing, otherwise reactor inhomogeneities might occur. If sufficient homogenization is not achieved, the selectivity of the reaction and the respective yields are decreased. Therefore, the balance between mixing and mass transfer in jet loop reactors is a critical design aspect. Monitoring the dissolved oxygen levels during the turnover of a steady sodium sulfite feed implied the abundance of gradients in the JLR. Prolonged mixing times at identical power input and aeration rates (~100%) were identified for the JLR in comparison to the STR. The insertion of a draft tube to the JLR led to a more homogenous dissolved oxygen distribution, but unfortunately a reduction of mixing time was not achieved. In case of increased medium viscosities as they may arise in high cell density cultivations, no gradient formation was detected. However, differences in medium viscosity significantly altered the mass transfer and mixing performance of the JLR.

This chapter has been published in Engineering and Life Science

Weber, S., Schaepe, S., Freyer, S., Kopf, M.H., Dietzsch, D. Monitoring Gradient Formation in a Jet Aerated Bioreactor, Eng. Life Sci. 2019, 19, 159-167

Chapter 5

Effect of ejector operation on the oxygen transfer in a pilot jet loop reactor

Abstract

Jet loop reactors (JLRs) are an alternative reactor type for the intensification of aerobic bioprocesses which are normally carried out in stirred tank reactors (STR). A JLR is capable to generate the same oxygen transfer rate (*OTR*) at a higher efficiency compared to a STR. If the ejector nozzle of a JLR is used for headspace pressurization, the oxygen mass transfer can be increased even further. However, intensified mass transfer usually requires increased power inputs while mass transfer efficiencies are decreased. In this respect, the energy efficiency of a JLR designed for intensification of an industrial bioprocess was evaluated. Compared to a STR, the JLR achieved a 70 % higher mass transfer rate at identical power input. Based on the results obtained for mass transfer performance, an increase in space time yield (STY) up to 100 % can be expected for the JLR in comparison to the STR.

This chapter has been published in Chemical Engineering & Processing: Process Intensification

Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., Dietzsch, C., Effect of ejector operation on the oxygen transfer in a pilot jet loop reactor. Chem. Eng. Process. - Process Intensif. 2018, 131, 43–50

Chapter 6

Economic evaluation of jet aerated loop reactors in large scale. Comparison to an aerated stirred tank reactor.

Abstract

In comparison to an STR the JLR concept provides an improved mass transfer performance. This feature allows either to obtain higher mass transfer rates or operation at high mass transfer efficiencies. An improved energy efficiency reduces the cost for reactor operation. Due to the increased productivity a production plant with a lower hold up and in theory less investment would be required. However, from the economical perspective the effective production costs as sum of fixed and variable costs are significant. For the evaluated example raw material, energy consumption and waste disposal were determined to be the main cost drivers. For operation at lower OTRs the JLR was more energy efficient than the STR. For operation at intensified mass transfer, the energy efficiency was decreased. Contrary to the expectations, the investment costs could not be decreased by process intensification. The minimal production costs calculated for the JLR were only reduced by 5.6 % in comparison to the STR. The variable energy costs as a major cost driver were dominated by the energy needed for cooling. The cooling demand itself was mainly determined by metabolic heat and was therefore not affected by the reactor technology.

Nomenclature

Abbreviations			**Indices**	
GBS	gravity base structures		air	aeration
JLR	jet loop reactor		cool	cooling
STR	stirred tank reactor		g	gas
			j	jet
Symbols			L	liquid
C	costs	[€]	max	maximum
m	mass	[kg]	met	metabolic
M	molar mass	[g mol^{-1}]	motor	Motor
$\dot{m}$	mass flow	[kg s^{-1}]	O_2	Oxygen
p	pressure	[Pa]	pump	Pump
P	power	[W]	s	
Q	volumetric flow	[m^3 h^{-1}]	S	Substrate
R	gas constant	[kg m^2 s^{-1} mol^{-1} K^{-1}]	sum	Total
T	temperature	[K]	X	Biomass
Y	yield	[-]		

Greek letters

α	start	η	efficiency
Δ	delta	ω	end

6 Economic evaluation

In the previous chapters the JLR was evaluated as an alternative to aerated STRs. It was shown that the JLR is able to generate higher oxygen transfer per power input. In general, an improved energy efficiency should be beneficial for a reduction of operational costs. An increased oxygen transfer rate allows operation at higher turnover rates and consequently higher space time yields can be achieved. Due to the increased productivity a production plant with a lower hold up and less investment would be required. However the production costs are determined by the sum of the fixed and the variable cost. As the energy efficiency decreases for intensified reactor operation the following scenarios were evaluated

- Determination of production costs for operation at the maximal energy efficiency. In scenario 1 (JLR 1) the impact of low variable energy costs was evaluated

- Determination of production costs for operation at the maximal mass transfer. High turnover rates allow to operate smaller reactors. In scenario 2 (JLR 2) the impact of process intensification on investment costs was evaluated.

The JLRs are compared to an aerated stirred tank reactor. An aerobic fed batch fermentation process was assumed as an exemplary process.

6.1 Exemplary process

The major percentage of bioprocesses are operated in batch or fed batch mode. To successfully operate a highly aerobic bioprocess, the required oxygen transfer rates must be generated via volumetric power input and aeration rates. To achieve high energetic mass transfer efficiencies over the entire range of operation, the power input must be controlled from low values at the beginning of a fermentation to maximum values in late phases of the process. In a fed batch process, the growth rate and therefore oxygen consumption can be controlled by the feed rate of the growth limiting substrate. An apparatus with an improved mass transfer capacity can achieve higher productivities and in consequence, space time yields.

A previous study in lab scale [1] showed that that a wildtype *Escherichia coli* K12 (ATCC 25404, NCIMB 11290) could be cultivated in STR and JLR without differences in microbial growth and biomass yield. In this evaluation the formed biomass is the aspired fermentation product. The obtained data for oxygen mass transfer and productivity were used to assess the JLR for a future application in industrial biotechnology. The energy demand for agitation and aeration was investigated in lab- and pilot scale [2] [3]. The metabolic heat arising from the aerobic conversion of glucose to biomass was assumed with 500 MJ $kmol^{-1}O_2$ [4]. The feed rate was assumed increase exponentially with a rate of 0.5 h^{-1}. When the maximum achievable OTR for the respective setup was reached a constant feed rate was maintained until a final product concentration of 60 g L^{-1} was achieved.

6.2 Determination of variable costs

Within this evaluation the variable costs are divided in three main blocks.

- energy costs
- raw material costs
- waste disposal costs / sterilization

An annual capacity of 10 kt product was assumed for the economic evaluation. At an identical capacity the raw material- and waste disposal costs will be more or less equal for JLR and STR. Focus is given to the variable energy costs.

6.2.1 Energy costs

The major amount of energy is consumed to fulfill the main tasks agitation, aeration and cooling. Apart from the effective power input, the unit efficiencies (η) of the used machinery are essential for the determination of the energy costs. For this evaluation the actual power consumption of the aggregates was scaled with unit efficiencies (JLR (η_{pump}:0.5), STR (η_{motor}:0.8, $\eta_{compressor}$:0.8)), (Figure 6). The energy demand for cooling was calculated from pneumatic- and hydraulic power input as well as exothermal heat generated by microbial conversion (equation (9), equation (4)). From the total energy consumption, the energy costs were calculated by assuming a price of 0.1 € kWh^{-1} for electrical power and 0.02 € kWh^{-1} for cooling water supply.

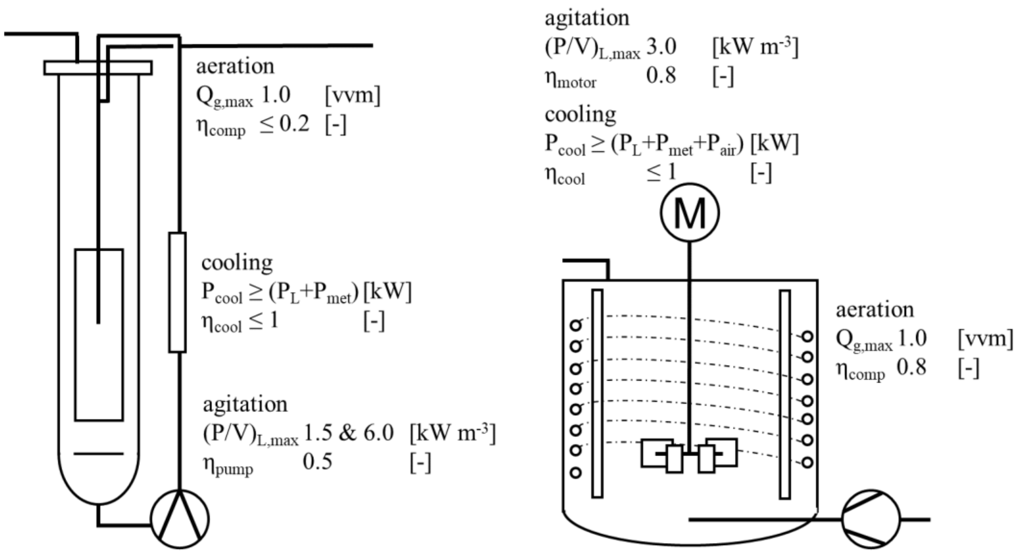

Figure 6: (A) Pilot JLR powered by centrifugal pump for agitation. Ejector for air entrainment. Plate heat exchanger for temperature control. (B) Pilot STR agitated by Rushton turbine and powered by motor. Aeration by compressor. Temperature control by coiled tubing. Operational range and efficiency (η) implied next to respective aggregate.

Jet loop reactor

The hydraulic power input by the liquid jet can be calculated by the liquid flow in the external loop and the liquid pressure difference up- and downstream the ejector nozzle (equation (1)).

$$\mathrm{P_{jet}} = \Delta \mathrm{p_{jet}}\, \mathrm{Q_L} \tag{1}$$

Power input by expansion of the entrained gas phase was accounted by equation (2).

$$P_{air} = \frac{\dot{m}_G\, R\, T}{M} \ln \frac{p^{\alpha}}{p^{\omega}} \tag{2}$$

The actual power demand of the process pump was then accounted by an efficiency η_{pump}.

$$P_{pump} = \frac{P_{jet}}{\eta_{pump}} \tag{3}$$

For calculation of the total power demand (P_{sum}) also the power demand for cooling (P_{cool}) must be considered. It was accounted as the sum of energy input by agitation, gas expansion and the metabolic reaction.

$$P_{cool,JLR} = P_{jet} + P_{air} + P_{met} \tag{4}$$

$$P_{sum,JLR} = P_{pump} + P_{cool,JLR} \tag{5}$$

Stirred tank reactor

In practice the effective power input to the liquid phase (P_s) can be determined via a torque measurement at the agitator shaft (equation (6)). The actual power consumption of the motor powering the stirrer can then be accounted by an efficiency η_{motor} (equation (7)).

$$P_s = M\ 2\pi\ n \tag{6}$$

$$P_{motor} = \frac{P_s}{\eta_{motor}} \tag{7}$$

As for the JLR, the pneumatic power input by air expansion was accounted by equation 2.

$$P_{comp} = \frac{P_{air}}{\eta_{comp}} \tag{8}$$

However, in contrast to the JLR the air must be supplied by an external compressor. For a given aeration rate the pressure at the reactor bottom determines the minimal power demand. The power demand for air compression (P_{comp}) was accounted with an efficiency for the compressor unit (η_{comp}). It was assumed that coiled tubing within the reactor allowed tempering of the liquid phase. As for the JLR, the power input by agitation (P_s), the expansion of gas (P_{air}) and the metabolic conversion (P_{met}) was accounted for calculation of the power demand for cooling (P_{cool}, equation(9)).

$$P_{cool,STR} = P_s + P_{air} + P_{met} \tag{9}$$

$$P_{sum,STR} = P_{motor} + P_{comp} + P_{cool,STR} \tag{10}$$

6.2.2 Raw material costs

The prices for the calculation of raw material costs are listed in Table 1. The given raw material prices were used to calculate the raw material costs per kg product according to equation (11). A detailed medium composition can be referred from chapter 2.

$$C_{raw\ material} = \sum C_{educt,i} \cdot \frac{\left(\frac{m_{educt,i}}{batch}\right)}{\left(\frac{m_{product}}{batch}\right)} \tag{11}$$

Table 1: Educt- and raw material costs in €/100kg used for economic evaluation

Substance	**price in €/100kg**
Magnesium sulfate heptahydrate	23
Monopotassium phosphate	210
Diammonium phosphate	128
Citric acid monohydrate	108
Glucose-syrup (100%)	52
Trace elements	**price in €/100kg**
Cobalt (II) chloride hexahydrate	3000
Manganese (II) chloride tetrahydrate	365
Copper (II) chloride tetrahydrate	227
Sodium perborate	3000
Sodium molybdate dihydrate	700
Zinc acetate dihydrat	2300
Iron (III) citrate	7000
EDTA	135
Thiamine hydrochloride	1960

6.2.3 Waste disposal and sterilization

The costs for sterilization and waste disposal were assumed with 2 € kg^{-1} product [15]. Based on the annual production capacity about 20 million € will be spent on waste disposal and sterilization.

6.3 Determination of fixed costs

Within this evaluation the fixed costs are divided in three main blocks

- capital costs
- staff costs

- maintenance costs

6.3.1 Capital costs

Capital cost arise from the investment into tangible assets. For a chemical production plant the respective costs can be structured according to the elements listed in Figure 7. Usually the capital costs are depreciated over a period of 10 years. In addition, an imputed interest rate of 8 % was considered for the annual depreciation. At an early conceptual stage the capital costs can be estimated with an accuracy of +/- 40 % [5]. In general, an accuracy of approximately +/-30 % is aspired at the end of the basic design phase. In the chemical industry the cost groups construction, machinery, measurement and control as well as planning make up 15 % to 20 % of the total capital costs. About 10 % of the capital costs are usually spend on piping work. Supplying the machinery with electrical power accounts for 6 % of the capital costs (Figure 7)

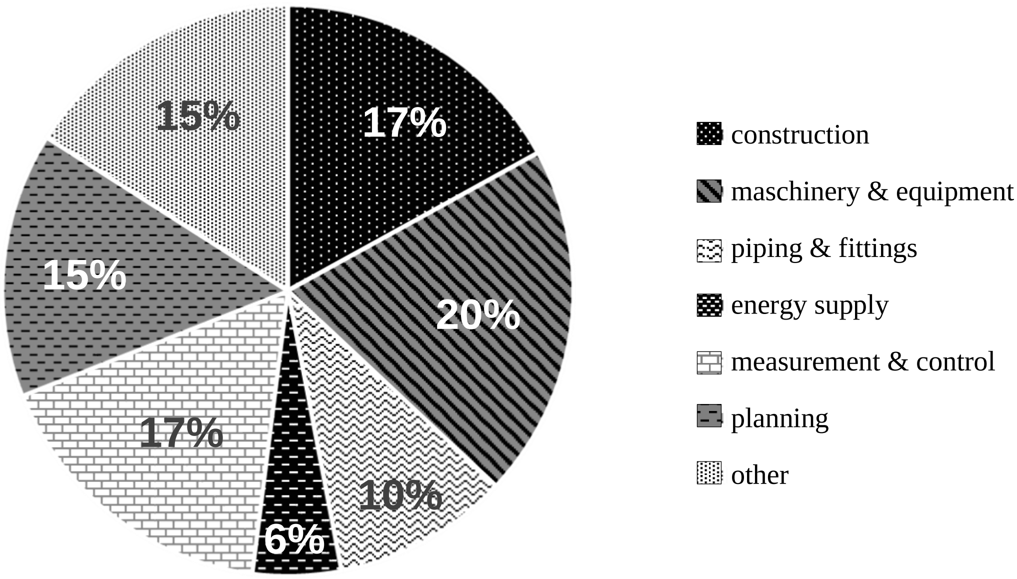

Figure 7: Typical structure of capital costs in the chemical industry [6].

6.3.2 Staff costs

Staff costs (C_{staff}) arising from wages, social spending and insurance were assumed by an average value of 120 k€ a^{-1}. The production plant was assumed to be operated with a three-shift system for 250 days a^{-1}. For operation and maintenance of the production facilities 0.6 man hours per ton product were assumed [6].

$$C_{staff,total} = C_{staff} * \frac{m_{product} * \frac{man\ hours}{ton\ product}}{\frac{hours}{shift} * \frac{operating\ days}{year}}$$

6.3.3 Maintenance costs

In the conducted evaluation the maintenance costs were derived directly from the capital costs. They were assumed by 6 % of the annual depreciation [7].

6.3.4 Determination of production costs

The production costs are determined by fixed- and variable costs. JLR and STR follow different design principles. They differ in mass transfer efficiency and the obtainable space time yield. Therefore, it was assumed that capital costs and variable energy costs would cause differences in production costs.

For quantification of that impact, the JLR was evaluated for two different scenarios. At an identical mass transfer rate, the JLR is twice as efficient than the STR (Chapter 5). In scenario 1 the JLR (JLR1) and the STR were considered to be operated at the same maximal oxygen transfer rate of 75 mmol L^{-1} h^{-1}. According to differences in the oxygen transfer efficiency the JLR could achieve the respective OTR at a volumetric power input of 1.5 kW m^{-3}. For the STR a volumetric power input of 3.0 kW m^{-3} would be required respectively. In scenario 1 the JLR is more energy efficient than the STR. In scenario 2 the JLR is operated at the maximal achievable oxygen transfer rate. As determined in chapter 5 it was assumed that the JLR could achieve an OTR increased by 100% in comparison to the STR. Thereby both reactors achieve the same energetic efficiency in kgO_2 kW h^{-1}. In scenario 2 the JLR is operated at an OTR of 150 mmol L^{-1} h^{-1} at a volumetric power input of 6 kW m^{-3}.

Prior the economical evaluation the basic design of the actual production plants had to be determined. The calculations were made based on the parameters defined in Table 2 and the process design described in section 6.1.

Table 2: Parameters for calculation of reactor size, heat exchange surface, energy consumption, batch time and space time yield. Scenario 1 (JLR 1 vs. STR). Scenario 2 (JLR 2 vs. STR)

Parameter	JLR 1	JLR 2	STR	Unit
Equipment				
Operating hours	8000	8000	8000	$h \cdot a^{-1}$
Setup time	12	12	12	h
Power input	1500	6000	3000	$W \cdot m^{-3}$
Aeration rate	1	1	1	vvm
ΔT_{ln}	9,9	9,9	9,9	K
c_p value	288	288	288	$W \cdot m^{-3} \cdot h^{-1}$
Aspect ratio	5	5	3	-
Process				
Maximal product concentration	60	60	60	$g \cdot L^{-1}$
Feed concentration	600	600	600	$g \cdot L^{-1}$
$Y_{X/S}$	0,35	0,35	0,35	$g \cdot g^{-1}$
$Y_{O/S}$	0,46	0,46	0,46	$g \cdot g^{-1}$
Metabolic heat coefficient	500	500	500	$J * mol^{-1}$
Maximal OTR	75	150	75	$mmol \cdot L^{-1} \cdot h^{-1}$
Production capacity	10	10	10	$kt \cdot a^{-1}$

Due to the identical turnover rates assumed for JLR 1 and the STR also the achieved space time yield and the required reactor volumes are equal. Due to an increased energetic efficiency, less heat is generated by JLR 1 in comparison to the STR. Consequently, less heat exchange surface for cooling would be needed. Differences in reactor geometry led to different numbers for filling levels and bottom pressures.

The increased oxygen transfer assumed for JLR 2 led to an increased space time yield. Consequently, the reactor could be built smaller. Despite the reactor is smaller, more heat would be generated by agitation and substrate turnover. Consequently, more surface for heat removal would be required.

Table 3: Calculated space time yield, batch time, reactor geometry and bottom pressure as basic input for economical evaluation.

Parameter	JLR 1	JLR 2	STR	Unit
Space time yield	0.96	1.5	0.96	kg m^{-3} h^{-1}
Batch time	44	35	44	h
Initial volume	960	550	960	m^3
Final volume	1300	830	1300	m^3
Reactor volume	1880	1200	1880	m^3
max. heat generated	20760	24645	20510	kW
Surface heat exchanger	7270	8647	7200	m^2
Gas flow	77520	49723	77520	m^3 h^{-1}
Reactor height	39	34	28	m
Filling level	27	23	19	m
Bottom pressure	382000	344000	303000	Pa

In the following the basic design data was used as an input for the estimation of investment costs. The cost estimation was made with an BASF internal planning tool.

With respect to aerobic fermentation processes STRs are limited to a maximal volume between 200 m^3 and 500 m^3 [8]. For calculation of investment and capital costs it was decided to process the liquid volume of 1300 m^3 in three stirred tank reactors. Consequently, the food print of the facility is increased, and more space would be required. Consequently, setting up the production facility for three STRs turned out to be more expensive than for the respective JLR. Also, the calculated costs for GBS installation, insulation and piping are higher for the STR. However, the hydraulic agitation of an JLR is usually scaled up by numbering up the external loops. For the JLRs this led to high costs for machinery and equipment. Altogether nearly identical investment costs were determined for the JLR 1 and the STR in the 1300 m^3 scale. In case of JLR 2 the process was intensified by high volumetric power inputs. Due to operation at higher turnover rates, it was possible to decrease the reactor size of JLR 2 by 35%. On the other hand, the installation of powerful aggregates led to higher hardware and engineering costs (Table 4). Consequently, the required investment for JLR 2 was calculated to be about 10 % higher than those calculated for the STR and JLR 1. The investment costs determined for the three scenarios are all within the claimed confidence interval of +/- 30%. Within this evaluation no significant advantage or disadvantage of JLR and STR could be determined

Table 4: Investment cost for JLR 1 (1300 m^3 scale), JLR 2 (830 m^3 scale) and STR (1300 m^3 scale).

Invest costs	JLR 1	JLR 2	STR	
Production facility	1.430.000	1.760.000	2.180.000	€
GBS-installation, insulation	830.000	910.000	2.290.000	€
Mobile equipment	320.000	310.000	240.000	€
Machinery, equipment, spare parts	21.100.000	20.690.000	16.130.000	€
Piping & fittings	2.440.000	3.440.000	2.540.000	€
Energy supply	210.000	350.000	550.000	€
Control systems	1.520.000	2.560.000	5.320.000	€
Installation	4.260.000	6.060.000	4.130.000	€
Engineering	10.860.000	12.210.000	11.300.000	€
Non-capitalised expenses	270.000	310.000	280.000	€
Tax and interest	1.300.000	1.470.000	1.360.000	€
Reserve for contingencies	9.780.000	10.990.000	10.170.000	€
Sum	54.320.000	61.060.000	56.490.000	€

The variable energy costs would mainly arise from the main tasks agitation, aeration and cooling. To ensure a good comparability, specific costs in € $kg_{product}^{-1}$ were calculated (Figure 8). In all cases cooling is dominating the variable energy costs. The major heat source is cell metabolism. As the formation of heat is more or less stoichiometric to oxygen and substrate consumption the identical cooling costs per kg product has to be accounted. It was assumed that JLR 1 is operated at the highest energy efficiency. Consequently, also the lowest energy costs for agitation and cooling were obtained for JLR 1. In case of the STR aeration must be ensured by an additional compressor. If the respective costs for agitation and aeration are summed up the highest energy costs per kg product are obtained.

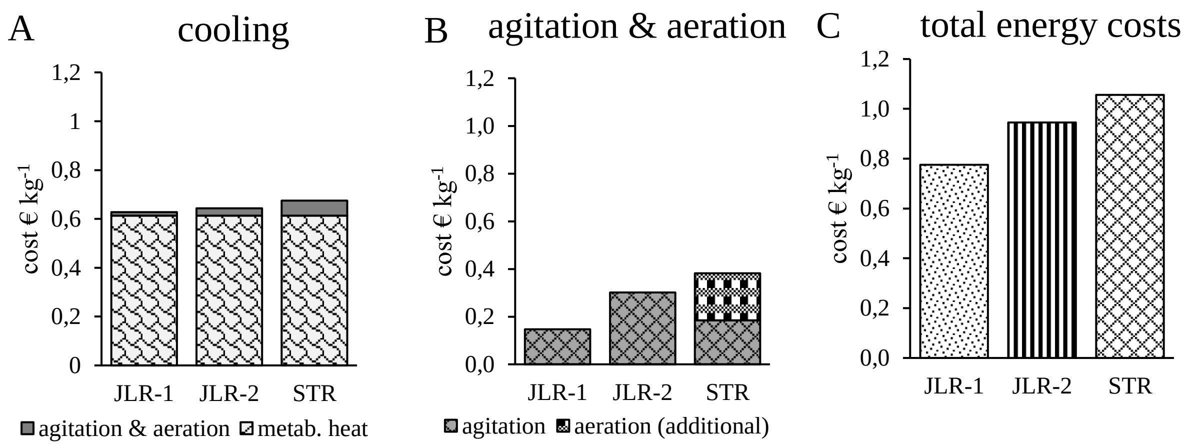

Figure 8: Variable energy costs for (A) cooling, (B) aeration & agitation and (C) total numbers for JLR 1 (1300 m^3 scale), JLR 2 (830 m^3 scale) and STR (1300 m^3 scale).

In the following the production costs were calculated. In Table 5 the production costs are split into the six main blocks for fixed and variable costs defined in chapter 6.2. and chapter 6.3. The absolute costs in € $kg_{product}^{-1}$ as well as the relative costs in % of the total production costs are given. As it can be referred from the relative numbers, raw material, energy consumption and waste disposal are the main cost drivers for the exemplary process.The energy efficient JLR 1 achieved the lowest production costs. For JLR 2 energy- and capital costs are increased. The obtained production costs are increased by 4.6 %. For the STR the highest production costs were calculated. The synthesis of one kg product in JLR 1 is about 5.6 % cheaper than in the STR.

Table 5: Production costs for JLR 1 (1300 m^3 scale), JLR 2 (830 m^3 scale) and STR (1300 m^3 scale). Specific numbers given in € $kg_{product}^{-1}$ and % of the total production costs.

	production costs			
	JLR 1 abs. / rel.	JLR 2 abs. / rel.	STR abs. / rel.	
Raw material	2.0 / 37	2.0 / 35	2.0 / 35	$€ \cdot kg_{product}{}^{-1}$ / %
Energy	0.78 / 14	0.95 / 17	1.06 / 18	$€ \cdot kg_{product}{}^{-1}$/ %
Waste disposal	2.0 / 37	2.0 / 35	2.0 / 35	$€ \cdot kg_{product}{}^{-1}$/ %
Capital	0.58 / 11	0.66 / 12	0.61 / 11	$€ \cdot kg_{product}{}^{-1}$ / %
Maintenance	0.01 / < 1	0.01 / < 1	0.02 / < 1	$€ \cdot kg_{product}{}^{-1}$/ %
Staff	0.04 / < 1	0.04 / < 1	0.04 / < 1	$€ \cdot kg_{product}{}^{-1}$/ %
Sum	5.41 / 100	5.66 / 100	5.73 / 100	$€ \cdot kg_{product}{}^{-1}$/ %

Conclusion

In comparison to an STR, the JLR concept can provide an improved mass transfer performance. This feature allows either to obtain higher mass transfer rates or operation at high mass transfer efficiencies. Energy consumption is one of the major cost drivers for production costs. Operation at high mass transfer efficiencies and at moderate volumetric power inputs is most promising. However, in the evaluated case the production costs obtained with the JLR are only reduced by 5.6 % in comparison to the STR. Therefore, the calculated cost advantage is rated to be non-sufficient for an investment decision. With respect to the performance for the assumed exemplary process the evaluated technologies yield comparable results.

Literature

[1] Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., et al., Jet aeration as alternative to overcome mass transfer limitation of stirred bioreactors. *Eng. Life Sci.* 2018, *18*, 244–253.
[2] Weber, S., Schaepe, S., Freyer, S., Kopf, M.H., et al., Impact of Nozzle Operation on Mass Transfer in Jet Aerated Loop Reactors. Characterization and Comparison to an Aerated Stirred Tank Reactor. *Eng. Life Sci.* n.d.
[3] Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., et al., Effect of ejector operation on the oxygen transfer in a pilot jet loop reactor. *Chem. Eng. Process. Process Intensif.* n.d.
[4] Bailey, J.E., Biochemical Engineering Fundamentals. *Chem. Eng. Educ.* 1976.
[5] Prinzing, P., Rödl, R., Aichert, D., Investitionskosten-Schätzung für Chemieanlagen. *Chem. Ing. Tech.* n.d., *57*, 8–14.
[6] Koch, A., Betrachtung der Wirtschaftlichkeit von Biostrahlschlaufenreaktoren unter Berücksichtigung eines optimierten Betriebs von Injektorstrahldüsen, Masterthesis, BASF SE & HS Kaiserslautern, 2016.
[7] Storhas, W., Bioverfahrensentwicklung, John Wiley & Sons, 2012.
[8] Woodley, J.M., Breuer, M., Mink, D., A future perspective on the role of industrial biotechnology for chemicals production. *Chem. Eng. Res. Des.* 2013, *91*, 2029–2036.

Summary

In chemical engineering the jet loop reactor (JLR) is known as an efficient reactor type for multiphase processes. Compared to other reactor types the JLR generates a large gas liquid interface and achieves high mass transfer rates. Therefore, the jet loop reactor is an interesting reactor type for aerobic bioprocesses. Within the field of highly aerobic production processes the JLR competes against the commonly used aerated stirred tank reactor (STR). The advantageous performance of JLRs is originated by the integrated gas liquid nozzles. They can be operated as self-aspirating ejector. Especially in large scale, when the costs for external air compression can exceed the costs for hydraulic power input, a self-aspirating reactor technology can become a significant advantage

In the past, jet loop reactors were successfully applied for the cultivation of yeast and filamentous bacteria. For large and shear sensitive microorganisms high local power inputs within the nozzle had an adverse effect on the obtained results. In contrast to already existing studies, more focus was given to the single cell Gram-negative and facultatively anaerobic model organism *E.coli* K12. The performance of the JLR was compared to a STR powered by Rushton turbines. The reactors shared the same scale and geometry. Studies that compared the performance at different operational parameters were supplemented with data obtained at identical power inputs and superficial gas velocities. *E.coli* K12 was cultivated at according to fed batch fermentation scheme. For both reactor types the volumetric power input was varied between 1.6 and 4.6 kW m^{-3}. For shear rates of $2.7*10^5$ s^{-1} and local power inputs up to $1.6*10^7$ kW m^{-3} no adverse effects on growth and metabolism could be observed. Maximal oxygen transfer rates (OTRs) of 230 mmol L^{-1} h^{-1} and 78 mmol L^{-1} h^{-1} were obtained for the JLR and the STR respectively. For fermentations with controlled dissolved oxygen levels no differences in substrate and oxygen utilization were observed between JLR and STR. The advantageous mass transfer performance of the JLR allowed an aerobic cultivation at higher feed rates. As a result, the JLR achieved space time yields up to 100 % higher than those obtained with the STR.

For a STR agitation and aeration and therefore pneumatic- and hydraulic power input can be adapted separately. For an ejector driven JLR air entrainment and therefore the aeration rate is directly correlated to hydraulic power input. It is defined by the liquid flow and the pressure drop over the

nozzle. Furthermore, the amount of gas entrainment is determined by the differential pressure between the gas in- and outlet of the nozzle. In lab scale, entrainment rates from 2 L min^{-1} to 4 L min^{-1} were achieved for power inputs from 6.4 W to 17.5 W. The entrainment rates were decreased with increasing gas differential pressures. It was also shown that the decrease in $k_La(Q_g,Q_L)$ can be restored and even improved when the nozzle was supplied with pressurized gas and operated in injector mode. At identical volumetric power inputs and aeration rates the k_La obtained with the JLR in ejector mode were increased by 30 to 50 % in comparison to the STR. Based on the obtained results it can be concluded that the JLR and the STR can provide efficient mass transfer above 2 kgO_2 kW^{-1} h^{-1}. The STR is most efficient for moderate OTRs around 100 mmol L^{-1} h^{-1}. For an increased oxygen demand above 150 mmol L^{-1} h^{-1} the JLR in injector mode was more energy efficient.

For substrate limited cultivation of the facultatively anaerobic *E.coli* at dissolved oxygen concentrations close to zero, up to 1.5 g L^{-1} of the anaerobic metabolite acetate were found in samples taken from the JLR. In comparison to the STR the mass transfer limitation was overcome, but there was a higher risk for a decreased selectivity due insufficient mixing at high mass transfer rates. The intensification of mass transfer by jet loop reactors is based on high local power inputs at the site of air dispersion. High local mass transfer goes along with high local turnover rates and consequently a faster homogenization is required. It was found that medium viscosities can change local turnover rates. Processes such as the bubble coalescence in macro scale and oxygen diffusion on the molecular scale can be affected. Experiments on micro- and macromixing performance showed that in contrast to the STR, where k_La and mixing time were correlated with $P/V^{0.4}$ and $P/V^{-0.4}$ respectively, a rather imbalanced correlation of $k_La(P/V^{0.7})$ and mixing time $(P/V^{-0.3})$ was found for the JLR. Monitoring dissolved oxygen levels during the turnover of a sodium sulfate feed implied uncontrolled gradient formation in the JLR when it was operated in a free jet configuration. To a certain extend the undefined gradient formation was controllable by the insertion of a draft tube. However, as no significant reduction in mixing time was achieved, maintaining selectivity at high differences in local turnover remains a critical aspect.

For the characterization of JLR and STR in lab scale the comparability of geometric and operational parameters was prioritized. For further evaluation a pilot jet loop reactor with an optimized reactor geometry and transferability to larger scales was built. To achieve high mass transfer rates the nozzle was designed to entrain high amount of gas and to generate elevated gas differential pressures. For the JLR with a nozzle installed in a downward orientation, the inserted draft tube determined the minimal power input. For bubble transport from top to bottom a power input 1.5 kW m^{-3} was required.
For free gas entrainment maximal a gas holdup of 36 % was obtained. A maximal k_La of 2140 h^{-1} and a OTR of 440 mmol L^{-1} h^{-1} were achieved. Operation at an optimized compression efficiency allowed a further intensification of mass transfer by 40 %. A maximal OTR of 660 mmol L^{-1} h^{-1} was achieved. The advantageous performance seen in lab scale was also confirmed for the scalable pilot reactor. In comparison to the reference STR, the obtainable OTR was increased by 100 %. At increased OTRs the JLR was more efficient than the STR.

Especially in large scale the obtainable oxygen transfer in STRs is limited. JLRs can provide efficient mass transfer even in the largest scales. Based on an exemplary large scale process it the possibility to intensify mass transfer up to 100 % leads to a 35 % smaller reactor volume. However, the required investment costs could not be decreased significantly. The energy demand was found to be a major cost driver. For the JLR an improvement in production costs of 5.6 % was calculated in comparison to STR. The relatively low reduction is originated in the fact that the major part of the energy would be needed for the removal of metabolic heat. Metabolic heat is correlated to microbial turnover and its specific value is independent from the reactor technology.

It can be concluded that the outstanding mass transfer performance of JLRs helps to increase turnover rates and to save energy for agitation and aeration. However, mass transfer efficiency is only one parameter among multiple aspects with relevance for production costs. Even though OTRs could be increased by 100 % and the mass transfer was generated at an increased energy efficiency, the calculated cost advantage of 5.6 % is rated to be non-sufficient for an investment decision. With respect to the performance for the assumed exemplary process the evaluated technologies yield equivalent results.

Nevertheless, the JLR is a potential alternative to a standard STR. The JLR showed advantageous performance for coalescence inhibited systems and processes limited by oxygen mass transfer.

Publications

Peer Reviewed International Journal Articles

1. Weber S., Schaepe S., Freyer S., Kopf M.- H., Dietzsch C., **Jet aeration as alternative to overcome mass transfer limitation of stirred bioreactors**. *Engineering in Life Sciences* 2018, *18*, 244–253.

2. Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., Dietzsch C., **Impact of nozzle operation on mass transfer in jet aerated loop reactors. Characterization and comparison to an aerated stirred tank reactor**. *Engineering in Life Sciences 2018, 18, 579-588*

3. Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., Dietzsch C., **Monitoring Gradient Formation in a Jet Aerated Bioreactor**, *Engineering in Life Sciences. 2019, 19, 159-167*

4. Weber, S., Schaepe, S., Freyer, S., Kopf, M.-H., Dietzsch C., **Effect of ejector operation on the oxygen transfer in a pilot jet loop reactor**. Chemical Engineering & Processing: Process Intensification 2018, 131, 43–50

5. Knapp, R., Rabe, J.-H., Kirchgaessner, S., Storhas, W., Wolf, M.J., **A Laboratory Experiment for Teaching Bioprocess Control Part 2: Bioprocess Design, Modelling, Simulation, and Fermentation Execution**. IFAC Proceedings Volumes 2012, 45, 384–389.

Presentations on Scientific Conferences

1. **Alternative Reactor Systems for Industrial Biotech Processes.** 2016, 11th European Symposium on Biochemical Engineering Science (ESBES), Dublin, Ireland.

Curriculum Vitae

Name:	Sebastian Weber geb. Kirchgäßner
Date of Birth:	05.07.1986
Place of Birth:	Heidelberg
Citizenship:	German
Residence	Carl-Benz-Straße 98, 68167 Mannheim

School Education

09/2003 - 07/2006	Secondary School Bertha-von-Suttner-Schule, Ettlingen

University Education

10/2006 - 02/2007	Molecular Biotechnology - Bachelor Programme Ruprecht-Karls-Universität Heidelberg
03/2007 - 08/2010	Biotechnology - Bachelor Programme Mannheim University of Applied Science
09/2010 - 03/2013	Biotechnology Bioprocess Development - Master Programme Mannheim University of Applied Science
03/2013 - today	Doctoral Candidate Center of Engineering Sciences/ Faculty I of Natural Science Martin-Luther-Universität Halle-Wittenberg

Employment in industry

05/2018 - today	Teamleader, Environmental Monitoring BASF SE, Ludwigshafen
03/2013 – 03/2018	Research Engineer, Chemical and Process Engineering BASF SE, Ludwigshafen

Erklärung

Hiermit erkläre ich an Eides statt, dass ich die vorliegende Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen als solche kenntlich gemacht habe. Hiermit erkläre ich weiterhin, dass ich mich mit der vorliegenden Arbeit erstmals um die Erlangung des Doktorgrades bewerbe. Die Arbeit wurde noch keinem anderen Promotionsausschuss vorgelegt.

Ludwigshafen (Rhein), 09.09.2018 Sebastian Weber