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ORIGINAL PAPER

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Scale-up of stirring as foam disruption (SAFD) to industrial scale

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Abstract Foam disruption by agitation–the stirring as foam disruption (SAFD) technique–was scaled up to pilot and production scale using Rushton turbines and an up-pumping hydrofoil impeller, the Scaba 3SHP1. The dominating mechanism behind SAFD–foam entrainment–was also demonstrated at production scale. The mechanistic model for SAFD defines a fictitious liquid velocity generated by the (upper) impeller near the dispersion surface, which is correlated with complete foam disruption. This model proved to be scalable, thus enabling the model to be used for the design of SAFD applications. Axial upward pumping impellers appeared to be more effective with respect to SAFD than Rushton turbines, as demonstrated by retrofitting a 12,000 l bioreactor, i.e. the triple Rushton configuration was compared with a mixed impeller configuration from Scaba with a 20% lower ungassed power draw. The retrofitted impeller configuration allowed 10% more broth without risking excessive foaming. In this way a substantial increase in the volumetric productivity of the bioreactor was achieved. Design recommendations for the application of SAFD are given in this paper. Using these recommendations for the design of a 30,000 l scale bioreactor, almost foamless *Escherichia coli* fermentations were realised.

Keywords Foam · Scale-up · Mechanical foam control · Gas/foam entrainment · Multiple impellers

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Introduction

A novel method for reducing the foam layer on broth by agitation was presented by Hoeks et al. [6]. This new approach was called "stirring as foam disruption" (SAFD) and was developed at a laboratory scale with a small variety of commercially available impellers. The aim of SAFD is to use agitation–specifically with the upper impeller of a set of impellers–in bioreactors to enhance foam disruption. Less foam enables the broth mass in the tank to be increased and, therefore, bioreactor output to be improved. In general, the formation of foam is an undesired phenomenon in gassed reactors as it reduces productive volume. Even worse, foam may lead to loss of product or to discarding a production batch.

The industrial application of the novel SAFD technique has the following advantages over other methods of foam reduction:

1. Foam is being disrupted mechanically using agitation, which is already a feature of a stirred tank.
2. Anti-foam agents are added in smaller amounts or are not required at all when applying SAFD. The addition of large amounts of anti-foam is undesirable because it reduces gas hold-up and oxygen transfer [10,18] and may have negative effects on subsequent purification steps. Our industrial experience is that anti-foam may also have a potentially negative effect on the bioprocess. Furthermore, less anti-foam also means lower production costs.
3. No major mechanical modifications have to be carried out on existing bioreactors when applying SAFD, as would be required when installing either a mechanical foam breaker [10] or a draft tube with a conical shape into the bioreactor [15].

Implementing SAFD merely implies altering the stirrer configuration of the bioreactor. This would be easiest by moving the upper impeller closer to the dispersion level of the broth. However, some impellers–particularly hydrofoil impellers–are more effective than others in foam disruption with respect to power draw [3,6,12]. The standard Rushton turbine (ratio of impeller diameter over tank diameter (D/T) = 0.33) shows a rather poor performance with regard to SAFD [2]. Therefore, retrofitting is an attractive alternative when applying the SAFD technique to an existing bioreactor. Recent work has shown that up-pumping hydrofoil impellers may be the best retrofit to achieve SAFD [3,12]. However, guidelines for design have not yet been presented. For this purpose, adequate scale-up of SAFD, including design parameters, has to be demonstrated. A mechanistic model for SAFD, relating the foam height to a hypothetical horizontal liquid velocity near the dispersion surface as an adequate design parameter, was previously developed [6]. Underlying the SAFD model are the discharge flow of the upper impeller under gassed conditions, $Q_{L,g}$ (see Appendix for definitions and nomenclature used in this paper), and an imaginary cylinder extending from the middle of the upper impeller to the gas-liquid dispersion surface, with a diameter of half the tank diameter (see Fig. 1). A parameter representing the liquid flow velocity $v_{L,dl}$ at the position of the imaginary cylinder wall is obtained by dividing the impeller discharge flow by the vertical cylinder surface A_c (Fig. 1). Thus:

$$v_{L,dl} = \frac{Q_{L,g}}{A_c} \qquad (1)$$

Hoeks et al. [6] demonstrated that for values of $v_{L,dl}$ above a certain critical value, $v_{L,dl,0}$, foam is virtually absent and thus foam disruption is complete. Furthermore, it was demonstrated that the SAFD technique works equally well with both artificial media and real fermentation broth and that $v_{L,dl,0}$ does not depend on the medium [6].

The purpose of this paper is to present the results on the scale-up of SAFD to pilot and production scale, to demonstrate that the critical value for complete foam disruption, $v_{L,dl,0}$, is scale-independent, to provide guidelines for design, and to show that retrofitting a large scale bioreactor with an up-pumping upper impeller–the most effective design with respect to SAFD–has substantial economic benefits.

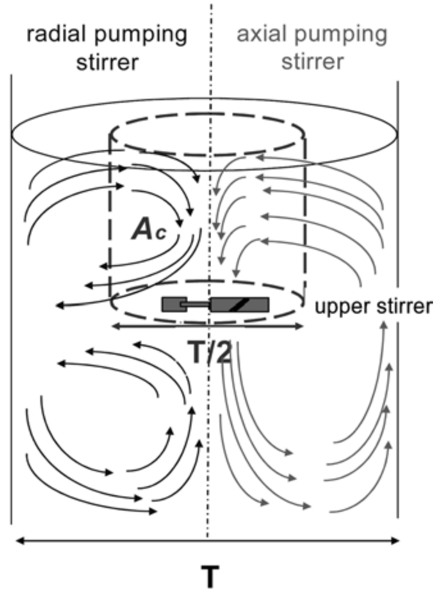

Fig. 1 Schematic representation of the upper impeller with the model cylinder and flow patterns of axial and radial pumping impellers. V_t Filling volume in the bioreactor at the level of the middle of the upper impeller, V_d filling volume in the bioreactor at the dispersion level. For radial pumping impellers, it was assumed that half the total liquid flow generated by the upper impeller flows in an upward loop. Furthermore, it was assumed that the flow from wall to axis above the radial impeller exists only in the upper half of the model cylinder. Therefore, Eq. 1 is also valid for radial pumping impellers as both $Q_{L,g}$ and A_c are divided by 2

Materials and methods

Experimental set-up

The scale-up experiments were carried out in four stirred tanks, of which three were stainless steel bioreactors with a total volume of 140 l, 450 l and 12,000 l with inner diameters (T) of 390, 636 and 1,876 mm (Applikon, Schiedam, Netherlands, Giovanola Frères, Monthey, Switzerland and Braun, Melsungen, Germany, respectively). A fourth tank was made of Perspex (T = 720 mm, 750 l volume) and was available at the University of Birmingham. Reference experiments were carried out on the 20 l scale (T = 195 mm) as described previously [6]. The Perspex tank had a flat bottom and a top-driven stirrer shaft, whereas the bioreactors had a dished bottom and were either bottom – (140 l, 450 l) or top – (12,000 l) driven. The Perspex tank was encased in a square section Perspex tank, which was filled with water to minimise light refraction and optical distortion at the curved surface of the inner vessel. Each tank had four equally spaced baffles with a width of approximately one-tenth of the tank diameter. The bioreactors were equipped with either two or three impellers. A ring sparger below the bottom stirrer was used for air supply. In Table 1, the geometries of the Rushton turbines used in the highest position are given (Fig. 2). Table 2 gives the configurations with the hydrofoil type impeller, the Scaba 3SHP1 (3 blades) pumping up (ABS Pump Production, Täby, Sweden) as upper impeller (Fig. 3). As bottom impellers,

Table 1 Dimensions and hydrodynamic data of the upper Rushton turbines with six blades on the laboratory ($T=195$), pilot ($T=390$, 636 and 720 mm) and production scale ($T=1{,}876$ mm). *T* Diameterof bioreactor, *D* impeller diameter, *W* blade width, *L* blade length, *x* material thickness of impeller, *RT* Rushton turbine (6 blades), *HB* hollow blade (type Chemineer CD-6, six blades), *6SRGT* hollow blade type Scaba 6SRGT six blades

Nominal volume (l)	*T* (mm)	*D* (swept) (mm)	*W* (mm)	*L* (mm)	*x* (mm)	Bottom impeller(s)	Lower rotational speed (rpm)	Tip speed at lower rotational speed (m/s)	Higher rotational speed (rpm)	Tip speed at higher rotational speed (m/s)
20	195	95	19	23.8	2	2 RT_{95}[a]	500	2.5	800	4.0
20	195	120	24	30	4.5	RT_{120}	500	3.1	800	5.0
140	390	130	26	32.5	4	RT_{130}–RT_{174}	350	2.4	500	3.4
140	390	195	39	49	3.9	RT_{174}	350	3.6	500	5.1
450	636	241	57	56	8	RT_{241}	235	3.0	300	3.8
750	720	240	48	60	6	$6SRGT_{296}$	200	2.5	275	3.5
750	720	357	72	90	7.2	HB_{290}	200	3.7	275	5.1
12,000	1,876	746	148	190	9.5	2 RT_{746}	77	3.0	102	4.0

[a]Subscript indicates diameter of impeller

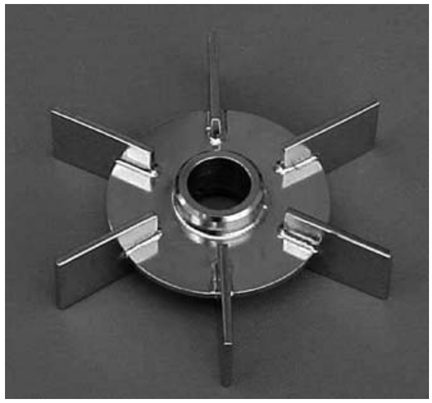

Fig. 2 A Rushton turbine

Fig. 3 An upward pumping hydrofoil Scaba 3SHP1 impeller, to be turned clockwise

either a Rushton turbine or a hollow blade agitator, the Chemineer CD-6 or the Scaba 6SRGT (6 blades) were used (Table 2, Fig. 4). It has been demonstrated that these types of bottom impeller do not influence the results of SAFD experiments as long as the bottom impeller fully disperses gas and does not interfere with the flow pattern generated by the upper impeller [1,6].

For a given broth mass, the level of dispersion in the tank and the height of the foam layer were measured for each of four parameter sets of superficial gas velocity and stirrer speed. Small quantities of broth, i.e. 1–3% of the broth mass, were taken out of (or added to) the tank and the above measurements were repeated to study the effect of the distance of the upper impeller to the dispersion level leading to a series of experiments (Fig. 5).

On the pilot and laboratory scale, each series of experiments was carried out in duplicate, i.e. each stirrer configuration was tested using two separate preparations of model medium for each series of experiments. On the large scale, the medium was prepared only once for each stirrer configuration.

Studying the SAFD technique mainly consists of measuring the dispersion level of the broth in the bioreactor and the level of the foam covering the broth. The foam level was determined by measuring the distance from the top of the tank to the foam layer.

When using the Perspex tank of 750 l for the SAFD experiments, the top of the dispersion level was read from a scale fixed on the wall. For the experiments in the large-scale non-transparent stainless steel vessels, another technique was developed based on the bubble-pipe used for measuring liquid heights in tanks [14]. An airflow of approximately 10 l/h was blown through a vertically mounted thin pipe (Fig. 6). The pressure in the bubble-pipe depends on how deep the pipe end is inserted into the foam or the broth. This pressure was measured using a water gauge. The position of the bubble-pipe outlet in the tank was measured as the distance between pipe outlet and a fixed point at the top of the tank

Table 2 Dimensions andhydrodynamic data of the Scaba configurations on the laboratory (T=195), pilot (T=720 mm) and production scale (T=1,876 mm). The Scaba 6SRGT impellers are hollow blade type impellers with 6 blades. The Scaba 3SHP1 hydrofoil impellers with 3 blades are up-pumping. C Bottom clearance of bottom impeller, ΔC impeller clearance

Tank		Bottom impeller					Middle and upper impeller								
Nominal volume (l)	T (mm)	D (swept) (mm)	D/T	Type	C (mm)	C/T	D (swept) (mm)	D/T	Type	ΔC (mm)	$\Delta C/T$	Lower rotational speed (rpm)	Tip speed at lower rotational speed (m/s)	Higher rotational speed (rpm)	Tip speed at higher rotational speed (m/s)
20	195	120	0.62	6SRGT	145	0.74	120	0.62	3SHP1	108	0.55	500	3.1	800	5.0
750	720	296	0.42	6SRGT	190	0.27	360	0.50	3SHP1	340	0.45	200	3.8	275	5.2
12,000	1,876	950	0.51	6SRGT	590	0.31	1,050	0.56	3SHP1	840/880	0.45/0.47	77	4.2	102	5.6

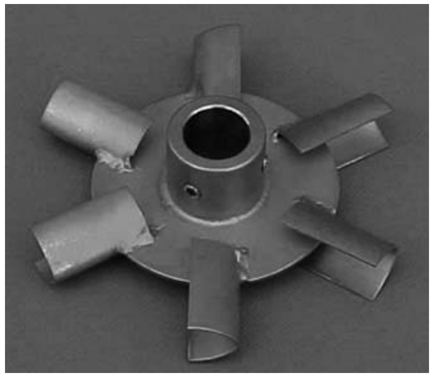

Fig. 4 A hollow blade agitator, the Scaba 6SRGT, to be turned clockwise

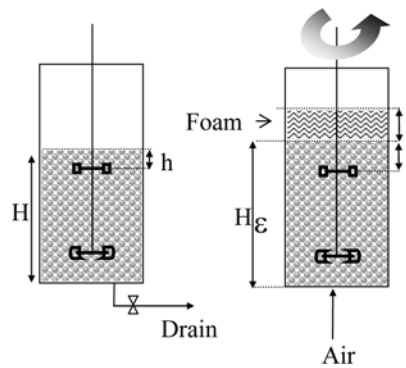

Fig. 5 Schematic representation of a vessel used for foam disruption experiments with the relevant heights measured. *Left* Unaerated, with H proportional to the broth mass; *right* regions of dispersion and foam when aerated and stirred

determined by markings on the pipe. Due to the differences in density between foam and broth, the differential of the pressure as a function of the height in the tank changes at the interface between broth and foam. Consequently, the plot of the pressure in the bubble-pipe as a function of the height in the tank consists in principle of two lines. The intersection of these lines was defined as the height of the dispersion level. On the 20 l and 750 l scale, the dispersion level measurement with the bubble-pipe was compared with the reading from a scale fixed to the transparent tank wall. The two dispersion level measurements were in good agreement (data not shown).

The foam level and the broth or dispersion level were determined midway between two baffles. On pilot and production scale, the fluctuations in both levels were approximately $\pm$25 mm.

On the 750 l scale, the stirrer shaft was fitted with two sets of strain gauges for separate measurements of the torque caused by the bottom impeller and by the full stirrer set as described by Otomo et al. [13]. The power draw was measured continuously using strain gauges and telemetry equipment as described by Kuboi et al. [9]. The power draw was measured both under SAFD conditions and under standard conditions with the unaerated liquid height equal to twice the tank diameter. The ungassed power numbers of the impellers have been reported previously [3].

On the 12,000 l scale, the electrical power taken up by the stirrer motor was continuously measured with a Fluke 41B Power Harmonics Analyser (The Fluke Corporation, Everett, Wash.) according to the method described by Hjorth et al. [5]. The gas hold-up was determined as described previously [6].

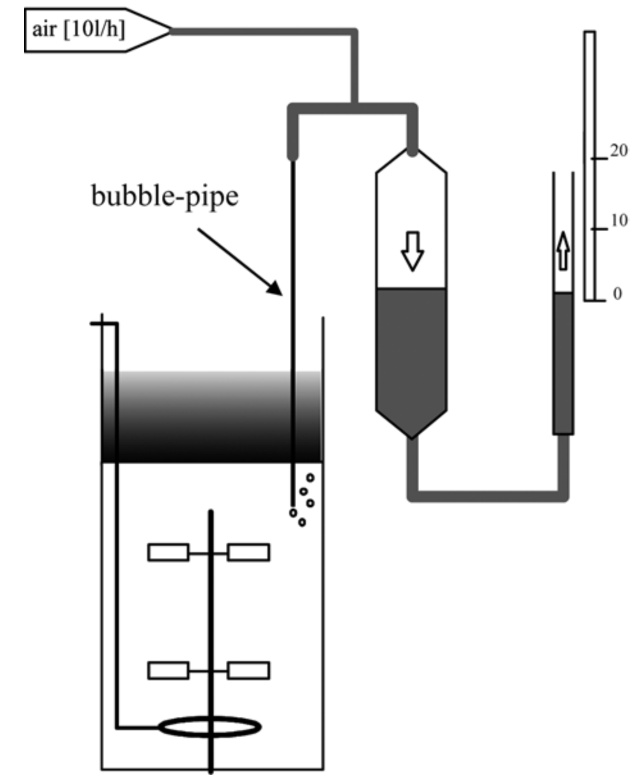

Fig. 6 Schematic representation of a bioreactor with the bubble-pipe level measurement used in the stirring as foam disruption (SAFD) experiments

Medium

The scale-up of SAFD to pilot and production scale was studied with a newly developed artificial medium, which resembles low viscosity fermentation broth. Using this model medium as described below is less labour intensive than running a bioprocess. Hoeks et al. [6] demonstrated that artificial media gave similar results to those obtained with a foaming, low viscosity fermentation broth.

The model medium used is a combination of two surfactants [0.2 g/l Tween 40 (polyoxyethylene-sorbitan-monopalmitate) and 0.4 g/l polypropylene glycol P 2000 (PPG)] and 7.5 g/l salt (NaCl) in deionised water. The preparation of this medium has been described previously [2]. The temperature of the medium during the experiments was controlled at 25±0.5°C.

Parameter choice for the scale-up experiments and the SAFD model

Hoeks et al. [6] started using eight parameter sets of superficial gas velocity and stirrer speed, but then reduced it to four when it became clear that eight parameter sets did not give more significant information than four. Therefore, for each of the above tanks, four parameter sets of superficial gas velocity and stirrer speed were chosen as follows.

A strong dependency of the foam height on the superficial gas velocity was found in previous work [6], which is consistent with the findings of Lee et al. [10], who related the equilibrium foam height to the superficial gas velocity. As a rule, the superficial gas velocity increases when scaling up but in order to obtain data relevant for large scale, all experiments were carried out at equal superficial gas velocities in the headspace that can also be found on large scale, i.e. 0.0065 and 0.013 m/s as tested previously [6].

In order to choose the stirrer speed, considerations with respect to scale-up and to large-scale bioreactor lay-out were again taken into account. Hoeks et al. [6] argued that the parameter to keep constant when scaling up SAFD is the tip speed of the impeller. In previous work, the tip speed ranged from 2.5 to 5 m/s, as occurs on a large scale [6]. Boon et al. [2] suggested that the D/T ratio was fairly high, i.e. up to 0.6, for the laboratory experiments on SAFD by Hoeks et al. [6]. Therefore, for each of the vessels used in the experiments, the lowest rotational speed was calculated from the tip speed of 2.5 m/s and an impeller diameter given by a D/T ratio of 0.33, which is "standard" for the Rushton turbine [2]. This rotational speed is referred to as the "lower rotational speed". Similarly, the highest rotational speed was calculated from the tip speed of 5 m/s and an impeller diameter given by a D/T ratio of 0.5, which is not unusual for low power number impellers [12]. This rotational speed is referred to as the "higher rotational speed". The rotational speeds and the corresponding tip speeds for the experiments in the five tanks are given in Tables 1 and 2. For each tank, the combination of the two rotational speeds and the two superficial gas velocities resulted in four parameter sets.

The ratio of gassed over ungassed power draw of the upper impeller, P_g/P_u as used in the SAFD model to calculate $v_{L,dl}$ [6], was estimated for the 20 l and the 140 l scale with the correlation from Hughmark for Rushton turbines [6,8]. The ratio of gassed to ungassed power draw for the up-pumping Scaba 3SHP1 on the 20 l scale was taken from graphs of P_g/P_u against gas flow number (Fl_G) found in the literature for pitched blade impellers pumping up [4]. P_g/P_u was determined during the SAFD experiments on the 750 l and on the 12,000 l scale.

P_g/P_u was measured for the triple Rushton combination on the 12,000 l scale and it was assumed that there was full gas recirculation. It was therefore assumed that the loss on power draw due to gassing was similar for each Rushton turbine. Using the flow map from Smith et al. [16] for multiple Rushton configurations, these appear to be reasonable assumptions for the applied low Fl_G (<0.07) and high Froude numbers (>7).

The ratio of gassed over ungassed power draw of the Scaba 3SHP1 impellers on 12,000 l scale was derived from P_g/P_u measured for the full set of Scaba stirrers in a similar way to Hjorth et al. [5].

For the Rushton turbine on the 450 l scale, P_g/P_u was determined by the BHR Group, Cranfield, UK as a function of Fl_G when operated as a single impeller (data not shown). BHR estimated that P_g/P_u for this Rushton turbine used as upper impeller at 300 rpm would be similar to the data of the single impeller at this stirrer speed. This is consistent with reports by Hudcova et al. [7] and Smith et al. [16], who have shown that P_g/P_u correlations for single impeller systems are also valid for upper impellers in multi-impeller systems at low values of Fl_G (<0.1) and high stirrer speeds, i.e. Froude numbers higher than 1, which is the case in the studies presented here.

For Rushton turbines, the flow number Fl has a value of 0.72. For a single Scaba 3SHP1, Fl has a value of 0.67 as given by the manufacturer ABS Pump Production (Täby, Sweden). This value may be reduced due to the small impeller clearance. The ungassed power draw in the Scaba stirrer configuration studied is reduced by 30% in comparison to the ungassed power draw of a single impeller [5]. By analogy to previous work [6], Fl is reduced by a factor of ($1–0.7^{0.34}$) resulting in a value for Fl of 0.59 for the Scaba 3SHP1, due to the impeller configuration.

The liquid velocity $v_{L,dl,0}$ above which all formed foam is virtually entrained, was estimated as described previously [6].

Results and discussion

Foam measurements and scale-up of SAFD

For each stirrer configuration and for each scale, the experiments generated the equilibrium foam height as a function of the amount of broth, the superficial gas

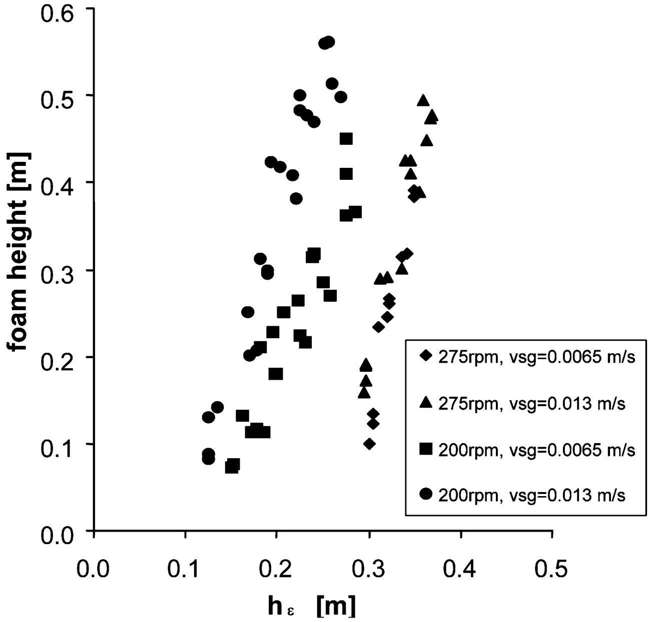

Fig. 7 Foam height as a function of the distance between the upper impeller and the dispersion level, the stirrer speed and the superficial gas velocity for the up-pumping hydrofoil Scaba 3SHP1 impeller on the pilot scale ($T = 720$ mm)

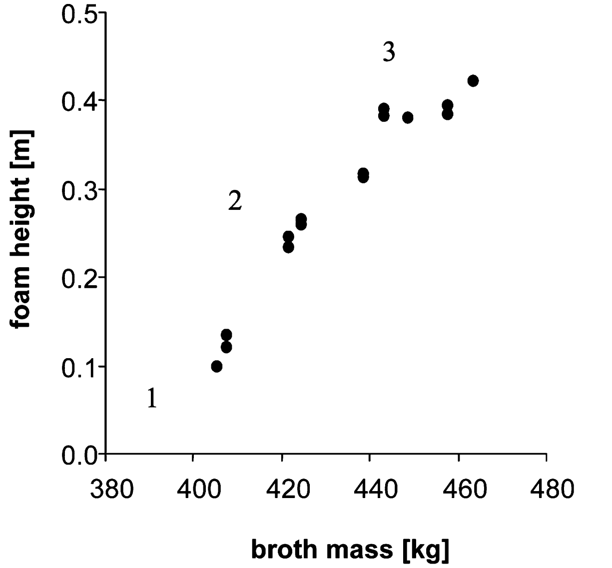

Fig. 8 Foam height as a function of the broth mass for a stirrer speed of 275 rpm and a superficial gas velocity of 0.0065 m/s for the up-pumping hydrofoil 3SHP1 impeller on the 750 l scale ($T = 720$ mm) indicating the foam regimes 1, 2 and 3

velocity and the stirrer speed. An example of the pilot scale results is given in Fig. 7 for the Scaba 3SHP1 up-pumping impeller on the 750 l scale. The foam height increased with increasing filling level of the stirred tank, i.e. the distance from the upper impeller to the dispersion level. Increasing the stirrer speed resulted in a decrease in foam height. Doubling the superficial gas velocity gave roughly a doubling of the height of the foam layer, similar to the laboratory scale results reported previously [6].

The foam regimes as defined within the context of SAFD by Hoeks et al. [6] for laboratory scale appeared also on the larger scales. An example of the foam regimes is given in Fig. 8:

Foam regime 1. A certain maximum broth mass below which hardly any foam was present. Foam disruption by stirring is virtually complete.

Foam regime 2. Foam height was almost linearly dependent on the broth mass for a given superficial gas velocity and stirrer speed. With increasing distance between foam layer and (upper) impeller, foam disruption by stirring is less effective.

Foam regime 3. Foam height was no longer linked to stirring.

For foam regime 2, an example of the foam height as a function of both the broth mass and of the distance from the upper impeller to the dispersion level is given in Fig. 9 for the production scale experiments with the up-pumping Scaba 3SHP1 impeller. Here too, increasing the stirrer speed resulted in a decrease in foam height,

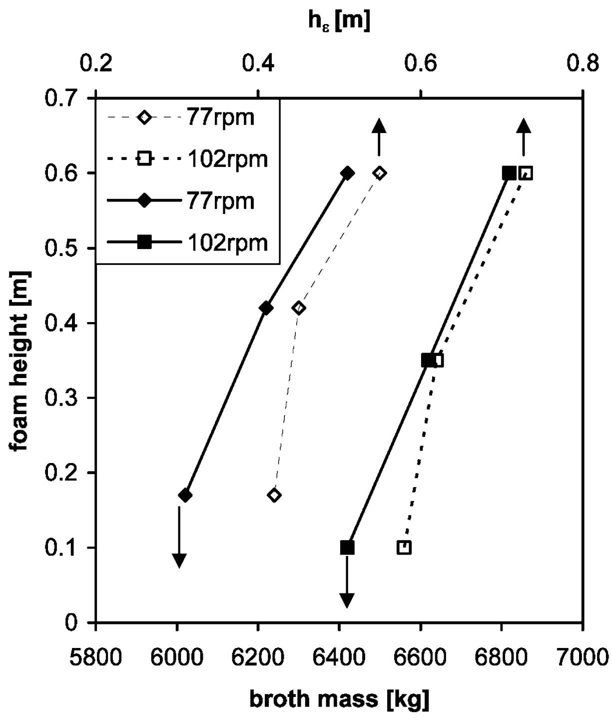

Fig. 9 Foam height as a function of the stirrer speed and either the distance between the upper impeller and the dispersion level, or the broth mass for a superficial gas velocity of 0.0065 m/s on the production scale ($T = 1{,}876$ mm) with a 1,050 mm Scaba 3SHP1 pumping upward as upper impeller

which means that SAFD also functions on a large scale. When reducing broth mass to achieve a zero foam height (regime 1), it was observed that the dispersion level tended to stay constant (Fig. 9), indicating an increase in gas hold-up as a consequence of gas and foam entrainment as discussed below.

These results demonstrate that foam disruption by stirring also occurs on large scale but the scalability of SAFD would be proven if complete foam disruption had a common parameter on all scales. Therefore, the parameter of the SAFD model for complete foam disruption, $v_{L,dl,0}$ was compared for one type of impeller for various scales and geometries. Table 3 shows that the value of $v_{L,dl,0}$ was 0.25 ± 0.03 m/s for the Rushton turbine over a range of scales. A similar value was obtained for Rushton turbines when working with a real bioprocess and with artificial media on a laboratory scale [6]. For the upward pumping hydrofoil impeller Scaba 3SHP1, for which no model parameter has been reported previously, $v_{L,dl,0}$ was 0.67 ± 0.03 m/s for laboratory, pilot and production scales. Furthermore, it was found that $v_{L,dl,0}$ is independent of the position of the upper impeller in the tank (data not shown), implying that raising the upper impeller is an effective way of applying the SAFD technique. Thus, the value of $v_{L,dl,0}$ depends on the type of impeller only, irrespective of scale, medium or geometry. Consequently, the scalability of complete foam disruption has been demonstrated for the impellers studied.

Retrofitting experiments

Because the output of a bioreactor is related to the broth mass, this parameter is to be optimised by applying SAFD. Fig. 10 shows that the broth mass could be increased on the pilot scale by 40% without risking overfoaming when a standard Rushton turbine ($D/T = 0.33$) was replaced by a larger Rushton turbine ($D/T = 0.5$), albeit at the cost of a substantially higher power draw. However, the Scaba 3SHP1 configuration on the pilot scale–with an ungassed power draw similar to the standard Rushton turbine–allowed a broth mass substantially higher than the standard Rushton turbine

Table 3 The parameter of the stirring as foam disruption (SAFD) model for complete foam disruption, $v_{L,dl,0}$, for Rushton turbines and the up-pumping hydrofoil impeller Scaba 3SHP1 for various scales and geometries

T (mm)	D (swept) (mm)	$v_{L,dl,0}$ (m/s)
Rushton turbines		
195	95	0.25
195	120	0.24
390	130	0.23
390	195	0.25
636	241	0.24
720	240	0.27
720	357	0.22
1,876	746	0.28
Scaba hydrofoil 3SHP1		
195	120	0.64
720	360	0.69
1,876	1,050	0.64

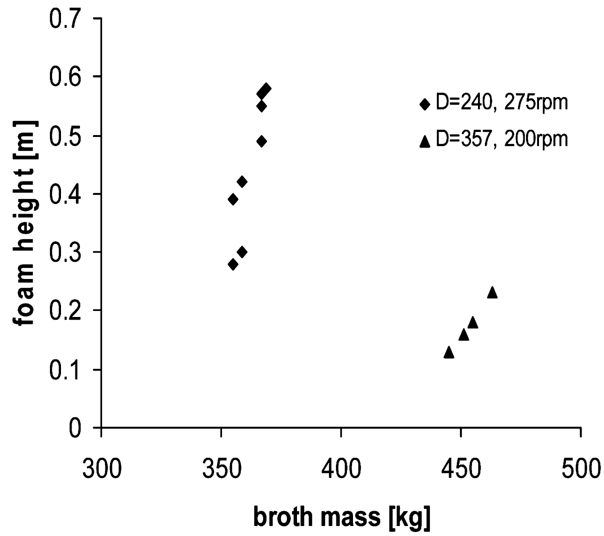

Fig. 10 Foam height as a function of broth mass for two Rushton turbines, RT_{240} and RT_{357}, as upper stirrers on the 750 l scale ($T = 720$ mm) at 275 and 200 rpm, respectively, and a superficial gas velocity of 0.013 m/s. For these stirrer speeds, the ungassed power draw of the RT_{357} was 2.4 times the ungassed power draw of the RT_{240}

(compare Figs. 8 and 10). Therefore, on the production scale, a comparison was made between the existing triple Rushton configuration and the retrofitted Scaba configuration. In Fig. 11, the foam height is depicted as a function of the broth mass for the experiments on the 12,000 l scale using the up-pumping 1,050 mm Scaba 3SHP1 and the 746 mm Rushton turbine as upper impellers. Replacing the existing triple Rushton configuration by the Scaba one at the production scale enabled the broth mass to be increased by 10% without risking excessive foaming. Clearly, this result of retrofitting represents an economical benefit in terms of a higher bioreactor output.

It is important to note that the range of broth mass in which foam regime 2 occurs should be as wide as possible in order to give maximum flexibility while still ensuring safe operating conditions for the process. Fig. 11 shows that the Scaba configuration gives a much wider span of operation on the 12,000 l scale, i.e. approximately 6,000–6,800 kg broth mass, than the triple Rushton configuration at 5,800–6,100 kg broth mass.

Power draw during SAFD

Applying SAFD means using impellers close to the dispersion surface. For the design of large-scale bioreactors, power data are required for this novel regime of impeller application. Therefore, the values of the ratio of the gassed over the ungassed power draw, P_g/P_u, of the (upper) impellers were determined on the 750 l and the 12,000 l scale (see Table 4). The general observation is that P_g/P_u for the up-pumping Scaba 3SHP1 is higher than for the Rushton turbine with values of 0.6–0.8, and

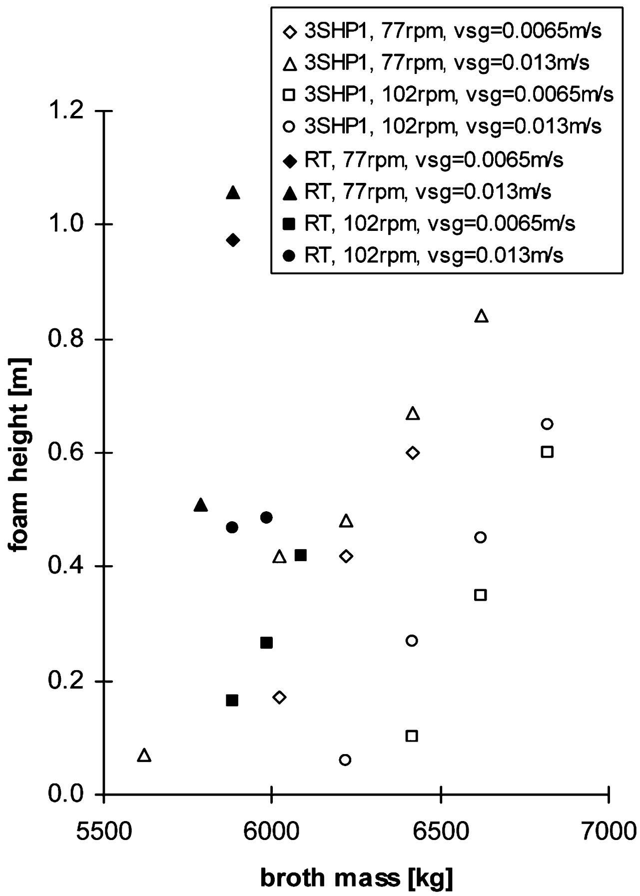

Fig. 11 Foam height as a function of broth mass, stirrer speed, superficial gas velocity and impeller type on production scale ($T = 1{,}876$ mm). A 1,050 mm Scaba 3SHP1 pumping upward (*open symbols*) and a 756 mm Rushton turbine (RT, *closed symbols*) are used as upper impellers

0.2–0.6, respectively. This general observation is consistent with other comparisons between these two types of impellers [12]. Secondly, P_g/P_u is lower for smaller impellers, which may be expected for this particular experimental set-up of fixed rotational speed and gas flow and, thus, higher Fl_G for smaller impellers. However, P_g/P_u values of 0.2 are low for upper Rushton turbines as they are normally in the range of 0.5 and higher [16]. These very low values are probably due to increased gas entrainment when applying SAFD with the standard Rushton turbine ($D/T = 0.33$) [2].

The observed range of P_g/P_u (see Table 4) related well to the measured range in gas hold-up (see Table 6 and below), i.e. the more gas entrained, the lower the value of P_g/P_u, as was demonstrated by Boon et al. [3].

In Table 5, a comparison is made for P_g/P_u values measured under standard and SAFD conditions and calculated by the Hughmark correlation [8]. On the pilot scale, the upper Rushton turbine with $D/T = 0.5$ has 15–30% lower P_g/P_u values under SAFD conditions as compared to standard conditions. However, the Hughmark correlation – derived for directly gassed impellers – gives P_g/P_u estimates that are within 10% of the values obtained under SAFD conditions, indicating that the Hughmark correlation is useful for SAFD evaluations.

For the 3SHP1 impellers, Hjorth et al. [5] found values of P_g/P_u close to unity for low values of Fl_G, i.e. < 0.05. When operated under the conditions of SAFD at Fl_G values of 0.01–0.025, the values of P_g/P_u for the 3SHP1 impellers were estimated to be considerably lower (0.68–0.83) probably also as a result of the enhanced gas and foam entrainment. As the ungassed power draw of the Scaba configuration on the 12,000 l scale was 20% lower than the ungassed power draw of the triple Rushton combination [5], the gassed power draw of both impeller configurations was approximately the same for each parameter set of stirrer speed and superficial gas velocity during the SAFD experiments.

Gas hold-up during SAFD

When SAFD occurs, gas/foam entrainment leads to an increase in gas hold-up, as shown in Fig. 12 for the Scaba 3SHP1 impeller on the production scale. Similar observations were made on the laboratory and pilot

Table 4 Ratio of gassed over ungassed power draw (P_g/P_u) on 750 l and 12,000 l scale forthe various upper impellers and for the four parameter sets of supercial gas velocities and rotational speeds given in Tables 1 and 2. Data for 12,000 l scale are derived from Hjorth et al. [5]. v_{sg} Superficial gas velocity

Upper impeller	Tank diameter (mm)	P_g/P_u (–)			
		$v_{sg} = 0.0065$ m/s lower rotational speed	$v_{sg} = 0.0065$ m/s higher rotational speed	$v_{sg} = 0.013$ m/s lower rotational speed	$v_{sg} = 0.013$ m/s higher rotational speed
RT_{240}	720	0.45–0.66	0.50–0.70[a]	0.23–0.36	0.4
RT_{357}	720	0.53	0.53[b]	0.45	0.44[c]
RT_{746}	1,876	0.60	0.65	0.50	0.55
$3SHP1_{360}$	720	0.67–0.77	0.65–0.75	0.58–0.67	0.58–0.67
$3SHP1_{1,050}$	1,876	0.83	0.77	0.75	0.68

[a]For foam regime 2. During foam regime 2a, P_g/P_u dropped to approximately 0.2 [2]
[b]Rotational speed = 242 rpm, lower than the setpoint of 275 rpm due to restricted motor power
[c]Rotational speed = 265 rpm, lower than the setpoint of 275 rpm due to restricted motor power

Table 5 Ratio of gassed over ungassed power draw on 750 l scale for the 357 mm Rushton turbine and the four parameter sets of superficial gas velocities and rotational speeds measured under standard ($H=2T$) and foam disruption conditions and calculated with the Hughmark correlation [6, 8]. N Stirrer speed

N (rpm)	v_{sg} (m/s)	P_g/P_u (–)		
		Standard conditions	During SAFD	Hughmark correlation
200	0.0065	0.74	0.53	0.59
200	0.013	0.55	0.45	0.49
242	0.0065	0.69	0.53	0.58
265	0.013	0.85	0.44	0.48

scale when moving from foam regime 3 to regime 2 to regime 1 [3,6]. The increased gas hold-up may be undesirable, as the productive volume of the bioreactor is, in this case, not taken up by the foam but by the entrained gas. Consequently, the performance of an impeller with respect to SAFD is determined not only by its ability to disrupt foam at a low power draw and high broth mass but also at a low gas hold-up.

For the stirrer configurations on the 750 and the 12,000 l scale, Table 6 gives the increase in the gas hold-up from minimal SAFD, i.e. the transition from foam regime 3 to foam regime 2, until more or less all the foam has disappeared, i.e. the transition from foam regime 2 to foam regime 1. Table 6 shows that a Rushton turbine with the "standard" D/T ratio of 0.33 generates a higher gas hold-up under SAFD conditions than a larger Rushton turbine with D/T of 0.5. In other words, the small Rushton turbine entrains more gas/foam under these circumstances, but the SAFD performance is considerably poorer as compared to the larger Rushton turbine (Fig. 10). Furthermore, Table 6 demonstrates that the up-pumping Scaba 3SHP1 is superior to the Rushton turbine if foam disruption at low gas hold-up is the criterion for performance. This is particularly true for the retrofit of the production scale bioreactor, because the Scaba configuration generates a substantially lower (0.03–0.10 lower) gas fraction than the triple Rushton configuration during SAFD operation.

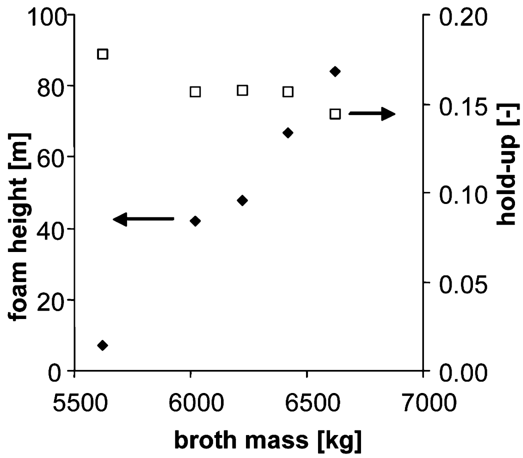

Fig. 12 Gas hold-up and foam height as a function of broth mass for a stirrer speed of 77 rpm and a superficial gas velocity of 0.013 m/s for the 1,050 mm Scaba 3SHP1 pumping upward on production scale (T = 1,876 mm)

In connection with the design of SAFD applications it has to be noted that, traditionally, gas hold-up and mass transfer have been considered to be directly related. However, recent work by Martin et al. [11] showed that with certain surface-active agents and impeller configurations, higher gas hold-up does not lead to higher mass transfer rates, i.e. at the same specific power input and superficial gas velocity, constant mass transfer rates were found. The earlier data in this project (data not shown) suggest that the foregoing reduction in gas hold-up for the retrofit did not lead to a fall in mass transfer.

Guidelines for design

The recommendations from this and previous work [1,2,3,6] for reducing the height of the foam layer on production scale for an increased reactor output of foaming processes are:

Table 6 Increase in the gas hold-up from minimal SAFD, i.e. the transition from foam regime 3 to foam regime 2, until more or less all the foam has been disrupted,i.e. the transition from foam regime 2 to foam regime 1. Data for the 750 l and the 12,000 l scale for the various upperimpellers and for the four parameter sets of supercial gas velocities androtational speeds given in Tables 1 and 2

Upper impeller	Tank diameter (mm)	Increase in gas hold-up (–)			
		$v_{sg}=0.0065$ m/s lower rotational speed	$v_{sg}=0.0065$ m/s higher rotational speed	$v_{sg}=0.013$ m/s lower rotational speed	$v_{sg}=0.013$ m/s higher rotational speed
RT_{240}	720	0.07–0.15[a]	0.09–0.18[a]	0.12–0.19[a]	0.16–0.20[a]
RT_{357}	720	0.13–0.14	0.14[b]	0.14–0.16	0.16–0.17[c]
RT_{746}	1,876	0.19	0.23–0.25	0.24	0.25–0.26
$3SHP1_{360}$	720	0.09–0.14	0.14	0.11–0.19	0.13–0.16
$3SHP1_{1,050}$	1,876	0.14–0.16	0.14–0.15	0.14–0.18	0.15–0.18

[a]For transition from foam regime 2a [2] to foam regime 1
[b]Rotational speed = 242 rpm, lower than the setpoint of 275 rpm due to restricted motor power
[c]Rotational speed = 265 rpm, lower than the setpoint of 275 rpm due to restricted motor power

1. Reduce the superficial gas velocity (consistent with Lee et al. [10]) by raising the head pressure and/or by reducing the air flow rate. The reduced mass transfer may be compensated by raising the backpressure, increasing the stirrer speed (see 3) and/or by oxygen enrichment of the airflow.
2. Bring the upper impeller closer to the dispersion level.
3. For a given stirrer configuration, stir faster, although this may lead to a high gas hold-up when applying SAFD with small impellers.
4. For a given size of the stirrer motor, and thus power draw, reduce the stirrer speed and increase the (upper) impeller diameter. This is often an option for Rushton turbines with adjustable blades.
5. Retrofit the bioreactor with another stirrer configuration. A stirrer may be added if the motor power is sufficient. Alternatively, the upper impeller may be replaced by a stirrer with a higher pumping efficiency, i.e. at constant power draw a larger impeller with a lower P_o can be installed.

An estimate of the optimal position of the upper impeller may be made by assuming or determining the value of $v_{L,dl,0}$ for the impeller in question and using the model equations provided by Hoeks et al. [6]. Furthermore, an estimate is required for the relation between clear liquid height and dispersion level using a correlation from literature or in-house data on gas hold-up. In operation, broth mass, stirrer speed and gas flow rate may be adjusted to achieve optimal performance. As a rule of thumb, the design value for the distance between the upper impeller and the dispersion level is advised to be 0.2 T.

From this and previous work [1,2,3,6], an impeller diameter with a D/T ratio of 0.5 or more is recommended. Smaller impellers lead to a higher gas hold-up and a narrow range of operation, i.e. a narrow range of broth mass in which SAFD occurs. Exceptions seem to be upward pumping hydrofoil impellers, because it was demonstrated that such an impeller with a D/T ratio of 0.41 disrupts foam really well [3]. Therefore, the recommendation for upward pumping hydrofoil impellers is a D/T ratio of at least 0.4.

A 30,000 l bioreactor with four Rushton turbines was retrofitted in accordance with the above guidelines [5] and operated with an *Escherichia coli* fermentation process as described in [17]. With the four Rushton turbines, foam heights of 1 m and more were obtained. However, using the mixed impeller Scaba configuration resulted in almost foamless *E. coli* fermentations.

Conclusions

Recommendations for the optimal design of a bioreactor with respect to SAFD are presented in this paper. Using the SAFD technique, disruption of the foam layer on low viscosity broths on industrial scale can be achieved through stirring. A simple mechanistic model, which has been presented previously [6], provides an adequate parameter to describe and predict complete foam disruption that can be used for scaling up a particular impeller with respect to SAFD. Retrofitting bioreactors with an upper impeller that is superior for SAFD may increase the bioreactor output by 10% as was demonstrated on the 12,000 l scale. On the 30,000 l scale, almost foamless *E. coli* fermentations were obtained after retrofitting.

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Appendix

Nomenclature

A_c Vertical surface area of cylinder with diameter $T/2$ above upper impeller (m^2)

$$A_c = \pi 0.5T \frac{(V_d - V_t)}{(\pi/4)T^2} \quad (2)$$

C Bottom clearance of bottom impeller (m)
D Impeller diameter (m)
Fl Impeller flow number (−)
Fl_G Gas flow number, Q_G/ND^3
g Acceleration due to gravity (by definition 9.81 m/s^2)
h_ε Height from the middle of the upper impeller to the dispersion level (m)
h_f Equilibrium foam height (m)
h Height from the middle of the upper impeller to the unaerated liquid level (m)
H_ε Dispersion height, measured from the base of the vessel (m)
H_f Foam level, measured from the base of the vessel (m)
H Unaerated liquid height, measured from the base of the vessel (m)
L Blade length (m)
N Stirrer speed (s^{-1})
P Power draw of an impeller (W)
P_o Power number (−)
Q_G Gas flow (m^3/s)
Q_L Discharge flow induced by impeller (m^3/s)

$$Q_{L,g} = \left(\frac{P_g}{P_u}\right)^{0.34} \mathrm{FlND}^3 \quad (3)$$

T Diameter of bioreactor (m)
$v_{L,dl}$ Horizontal radial liquid velocity near the dispersion level above upper impeller at distance T/2 from axis calculated from the discharge flow of the upper impeller (m/s)
v_{sg} Superficial gas velocity (m/s)

V Volume of liquid (m^3)
V_d Dispersion volume (m^3)
V_t Bioreactor volume from bottom to the top of the upper impeller (m^3)
W Blade width (m)
x Material thickness of impeller (m)
ΔC Impeller clearance (m)

Subscripts and superscripts

$_0$ Minimum velocity above which value $h_f = 0$
$_{95}$ Diameter of impeller: e.g. 95 mm
$_g$ Gassed conditions
$_u$ Ungassed conditions

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