Engineering in Life Sciences

Eng. Life Sci. **2017**, *17*, 500–511 www.els-journal.com

Stephan C. Kaiser[1]
Sören Werner[2]
Valentin Jossen[2]
Matthias Kraume[3]
Dieter Eibl[2]

[1] Finesse Solutions Inc., Santa Clara, USA

[2] Institute of Chemistry and Biotechnology, Zurich University of Applied Sciences, Wädenswil, Switzerland

[3] Technische Universität Berlin, Fachgebiet Verfahrenstechnik, Berlin, Germany

Research Article

Development of a method for reliable power input measurements in conventional and single-use stirred bioreactors at laboratory scale

Power input is an important engineering and scale-up/down criterion in stirred bioreactors. However, reliably measuring power input in laboratory-scale systems is still challenging. Even though torque measurements have proven to be suitable in pilot scale systems, sensor accuracy, resolution, and errors from relatively high levels of friction inside bearings can become limiting factors at smaller scales. An experimental setup for power input measurements was developed in this study by focusing on stainless steel and single-use bioreactors in the single-digit volume range. The friction losses inside the air bearings were effectively reduced to less than 0.5% of the measurement range of the torque meter. A comparison of dimensionless power numbers determined for a reference Rushton turbine stirrer ($N_P = 4.17 \pm 0.14$ for fully turbulent conditions) revealed good agreement with literature data. Hence, the power numbers of several reusable and single-use bioreactors could be determined over a wide range of Reynolds numbers between 100 and $>10^4$. Power numbers of between 0.3 and 4.5 (for $Re = 10^4$) were determined for the different systems. The rigid plastic vessels showed similar power characteristics to their reusable counterparts. Thus, it was demonstrated that the torque-based technique can be used to reliably measure power input in stirred reusable and single-use bioreactors at the laboratory scale.

Keywords: Measurement / Power input / Single-use bioreactors / Stirrers / Torque

Received: April 8, 2016; *revised:* October 8, 2016; *accepted:* October 20, 2016

DOI: 10.1002/elsc.201600096

1 Introduction

Power input (or volumetric power input) is one of the most important engineering and scale-up criteria for bioreactors, since it is related to most unit operations, such as mixing, gas dispersion, gas–liquid mass transfer, heat transfer, and solid suspension [1–3]. Furthermore, power input is associated with hydrodynamic stress, which may affect cell growth and/or productivity of shear-sensitive production organisms [4–6]. However, unlike pilot and production scale agitators, only limited data on power input in laboratory-scale bioreactors are available, in particular for single-use bioreactors. In contrast to their reusable counterparts, these systems are delivered by the manufacturers that are preassembled, sterilized, and ready to use [7, 8]. Furthermore, most single-use bioreactors are agitated by specially designed impellers making it difficult to compare them with their reusable counterparts.

As described in the review by Ascanio et al. [9], temperature- and torque-based measurement techniques prevail over others, something which is also confirmed by Table 1 that summarizes some studies on power measurements described in the literature [10–37]. Even though this overview is far from complete, it is obvious that the majority of these studies focused on standard stirrers, such as Rushton turbines [10–24], pitched blade impellers [10, 15, 20, 23, 25–27], curved blade impellers [12, 21, 24], or more modern stirrers, such as SCABA [14, 28] and Lightnin [16, 19, 27, 29–31] impellers. These are commonly used for agitation in baffled, flat-bottomed tanks. In fact, only one experimental study on power input investigations in single-use benchtop bioreactors was found [32], where the Mobius CellReady 3L, the UniVessel 2L SU, and the BioBLU 5L (formerly known as CelliGen BLU) were investigated for a few operational conditions that only examined water-like viscosities with Reynolds numbers in excess of 3.5×10^3 [32]. This means that most

Correspondence: Dr. Stephan C. Kaiser (skaiser@finesse.com), Finesse Solutions Inc., 3501 Leonard Court, Santa Clara, CA 95054, USA

Abbreviations: CFD, computational fluid dynamics

Table 1. Examples of power input measurements described in the literature

	System/stirrer	Geometrical details V_L (L)	D (m)	d/D (−)	Flow regime (Re)	Ref.
Load cell	Rushton turbine and curved blade impellers in baffled, flat-bottomed, cylindrical vessel	50	0.40	0.33	Turbulent (8.86×10^4–2.72×10^5)	[24]
Electrical power	Minibioreactor with triple Rushton turbine	0.007	0.016	0.44	Transition–turbulent (1×10^3–6×10^3)	[33]
	Four-bladed 45° pitched-blade and flat-blade impellers in a flat-bottomed, baffled mixing tank	570	0.90	0.34	Turbulent (2.5×10^5–7×10^5)	[26]
	Rushton turbine, Prochem Maxflo T, and Lightnin A-315 in fermentor tank	600	0.82	0.37–0.50	Transition–turbulent (300–10^6)	[19]
Strain gauge	Rushton turbine, Smith turbine, pitched blade impellers in baffled vessel	2.5	0.147	0.33	Transition–turbulent (100–8×10^4)	[15]
	Two-stage four flat-blade turbines in unbaffled, flat-bottomed cylindrical vessel	8	0.21	0.40	Transition–turbulent (300–9×10^4)	[34]
	Lightnin A-315 impeller in flat-bottomed cylindrical vessel with baffles	72	0.45	0.49	Laminar–low turbulent (1–10^3)	[29]
	Xanthan fermentation with Rushton turbines, Prochem Maxflo T or SCABA 6SRGT impellers	130	0.49	0.33–0.54	Turbulent[a)] (1.63×10^6–5.72×10^6)	[28]
	Prochem Maxflo T and Lightnin A315 in baffled, cylindrical, flat-bottomed vessel	135	0.56	0.40–0.51	Turbulent[b)] (10^5–6.4×10^6)	[30]
	Rushton turbine, Smith turbine, pitched blade turbine, and propeller in baffled, cylindrical flat-bottomed vessel	170	0.60	0.33	Turbulent (3×10^4–2×10^5)	[20]
	Rushton turbine, 45° pitched blade impellers in baffled vessel	175	0.61	0.33	Turbulent[b)] (9.6×10^4–3.15×10^6)	[25]
	Four-blade and six-blade Scaba SRGT impellers and Rushton turbine in flat-bottomed, baffled, cylindrical vessel	175	0.61	0.33	Transition–turbulent (10^3–0^6)	[14]
	Rushton turbine, Smith turbine, Lightnin A315 in flat-bottomed, baffled, cylindrical vessel	200	0.634	0.33	Turbulent (9.5×10^4–2.52×10^5)	[31]
	One or two 6-bladed disc turbines in baffled, cylindrical vessel under aeration	280–560	0.72	0.33	Turbulent	[22]
Dynamometer	Baffled minibioreactor with Rushton turbine	0.1	0.06	0.33	Transition–turbulent (2×10^3—1.3×10^4)	[35]
	6-blade disk turbines, 2-blade flat paddles, and 4-bladed 45° pitch turbines in baffled, flat-bottomed, cylindrical vessels	2.5 / 20	0.15–0.30	0.25–0.75	Low-to-medium turbulent (6×10^3–10^5)	[10]
	Rushton turbine in flat-bottomed, cylindrical vessel with baffles	6.5	0.205	0.52	Transition–turbulent (2×10^3–10^5)	[17]
	Rushton turbine, six-bladed pitched turbine, EKATO Intermig, Lightnin A-310, and Chemineer HE-3 in baffled cylindrical vessel	19	0.29	0.33–0.60	Laminar–turbulent (40–10^5)	[16]

(*Continued*)

Table 1. Continued.

	System/stirrer	Geometrical details V_L (L)	D (m)	d/D (−)	Flow regime (Re)	Ref.
	Rushton turbine, pitched-blade turbine, MIXEL-TT propeller, MIXEL-TTP propeller, two-stage EKATO INTERMIG in baffled cylindrical vessel with conical-shaped bottom	20	0.288	0.33–0.73	Turbulent	[36]
Torque meter	Minibioreactor with hollow-shaft gas inducing blade impeller[c)]	0.012		0.7	Laminar–turbulent (10^3–1.1×10^4)	[37]
	Rushton turbine in flat-bottomed cylindrical vessels	0.6–18.7	0.09–0.288	0.5	Laminar–transition (1–400)	[13]
	Mobius CellReady 3L, UniVessel SU 2L and 5L CelliGen BLU disposable and 2L glass bioreactor	1.5–3.5	0.13–0.17	0.42–0.59	Transition–turbulent (3.5×10^3–3.3×10^4)	[32]
	Rushton turbine & concave blade impellers in flat-bottom cylindrical vessel with baffles	5.4	0.19	0.33	Turbulent (2.67×10^4–4×10^4)	[21]
	Rushton turbine and pitched blade impellers in baffled, flat-bottomed, cylindrical vessel	10.8	0.24	0.33–0.50	Transition–turbulent (300–1.5×10^5)	[23]
	Blade impellers in baffled vessels	18.5–348	0.287–0.762	0.20–0.32	Transition–turbulent[d)] (1.4×10^3–1.59×10^5)	[11]
	Dual-stage Rushton turbine in baffled, flat-bottomed, cylindrical vessel	20	0.294	0.33	Turbulent (4×10^4)	[18]
	Rushton turbine, curved and pitched blade impellers in a hemispherical-bottomed cylindrical, and fully baffled mixing tank	40	0.40	0.325–0.45	Transition–turbulent (200–2×10^5)	[12]
	Two-stage radial disc, pitched blade, and Lightnin A315 impellers in baffled, flat-bottomed, cylindrical vessel	45	0.39	0.41	Turbulent[d)] (1×10^5–1.25×10^5)	[27]

a) Related to water-like media.
b) Reynolds numbers were calculated from the provided data.
c) The torque sensor was mounted to the bioreactor vessel rather than to the impeller.
d) Reynolds numbers were calculated from the provided data.

available data are for moderate or fully turbulent conditions, but there is still a lack of available data for lower Reynolds numbers, which are relevant for shear sensitive production organisms and highly viscous, non-Newtonian culture broths. The latter applies, for example, to fungi-based or plant cell based cultures [38–40].

Particularly at laboratory scales, most measurement techniques suffer from a low degree of measurement accuracy. In temperature-based measurements, this lack of accuracy is related to low heat generation and losses to the surroundings. However, in torque-based setups it may be caused by low resolution of the sensors being used and/or high losses from agitator bearings and mountings.

Hence, the objective of the present study was to develop a measurement setup that is suitable for power input measurements in reusable and single-use bioreactors with working volumes in the one-digit liter range and to determine power input over a wide range of turbulence conditions. The system was designed to be flexible, easy to use, and reproducible, and should offer the possibility for automation. The DECHEMA single-use technology working group recommends estimating power input in single-use bioreactors by determining the impeller torque with torque meters [41, 42], but there is a lack of experimental data to validate this approach. Hence, a further aim of the present study is to generate experimental data that provides additional evidence for the DECHEMA recommendation. In order to encourage standardization of future work, the experimental method is described here in detail.

2 Materials and methods

2.1 Tested stirrers and bioreactors

If not mentioned otherwise, the power input in all bioreactors was determined with 2 L working volumes. Initially, the power input of a standard Rushton turbine with a diameter d of 53 mm (geometrical details provided in Table 2) was measured

Table 2. Summary of the geometrical details of the stirrers investigated

Configuration	Vessel diameter D (mm)	Impeller diameter d/D (−)	Off-bottom clearance z_M/d (−)	Impeller distance z_R/d (−)	Blade angle α (°)	Blade height b/d (−)	Blade thickness s/d (−)	Baffle width B_S/D (−)	Baffle thickness H_S/D (−)	Baffle thickness a_S/D (−)
Glass vessel with Rushton turbine	130	0.41	1.00	n.a.	90	0.198	0.026	0.092	1.17	0.046
SmartGlass 3L	130	0.43	0.87	1.19	90/45[a]	0.20/0.741[a]	0.028	0.092	1.17	0.046
SmartVessel 3L	130	0.43	0.87	1.19	90/45[a]	0.20/0.741[a]	0.037	n.a.	n.a.	n.a.
Mobius CellReady 3L	130	0.55	0.44	n.a.	25	0.181	0.024	n.a.	n.a.	n.a.
UniVessel 2L SU	128	0.41	1.02	1.21	30	0.566	0.038	n.a.	n.a.	n.a.

[a] Values are given for the lower/upper impellers.
n.a. = not available.

in order to validate the measurement technique. The turbine was mounted into a torospherical bottomed glass vessel (DIN 28011 [43]) with an off-bottom clearance (z_M) equal to d. The vessel diameter D was 130 mm and it was fitted with three baffles (width $B_S/D = 0.092$, length $H_S/D = 1.17$, thickness $a_S/D = 0.046$) installed through the preconfigured ports in the head plate of the SmartGlass bioreactor at 120° from each other and with an offset of 3 mm from the vessel wall. In addition, the impellers used in the SmartGlass 3L bioreactor and the SmartVessel 3L bioreactor (Finesse Solutions Inc., CA, USA) were also tested. In this case, the disc blade and segment impellers, both with diameters of 56 mm, were mounted at a distance of 64 mm from each other with an off-bottom clearance of 49 mm ($z_M/d = 0.72$). This impeller configuration was tested with and without baffles in the glass tank.

Finally, the power inputs in the UniVessel 2L SU and the Mobius CellReady 3L bioreactors were determined. These bioreactors are described in detail elsewhere [32].The main geometrical parameters for all the bioreactors examined in this study are also summarized in Table 2.

2.2 Measurement setup

The experimental setup is schematically shown in Fig. 1. The bioreactor vessels of interest were placed into a vessel holder and covered by a specially designed stainless steel head plate, which required the removal of the original head plates from the single-use bioreactors. An air bearing with an inner diameter of 13 mm and length of 50 mm (IBS precision engineering, Netherlands) was integrated into the head plate, in order to minimize the load free torque. The porous media bushing, which was supported with 5.5 bar pressurized air, provided an almost frictionless radial bearing (see also discussion below).

The dynamic torques were measured using a T20WN torque meter with a nominal torque of 0.2 Nm (HBM Hottinger Baldwin Messtechnik GmbH, Germany). The torque meter was held axially and centrically by a plate that was perpendicularly fixed to the head plate. According to the manufacturer, the sensor provides a measurement accuracy and RSD of reproducibility of ±0.2% and <0.05% of the nominal torque, respectively [44]. Two metal bellow-type couplings (Uiker AG, Switzerland) were used to install the torque meter between the brushless AC servo motor (AKM2, Kollmorgen, Germany) and the impeller shaft with a diameter of 13 mm (tolerance: −0.0076 mm) and length of 325 mm that was provided by Bioengineering AG (Switzerland). The bellow-type couplings compensated for parallel and angular misalignments as well as imbalances of the impeller shafts.

A PC-based RPDPmini control unit (kindly provided by Finesse Solutions Inc.) was used to control agitation, gas flow, and vessel temperature using μTruBio PC control software (v. 3.1). For data acquisition with Catman easy software (HBM, Germany), the torque sensor was connected to a Spider-8 AD converter (HBM, Germany).

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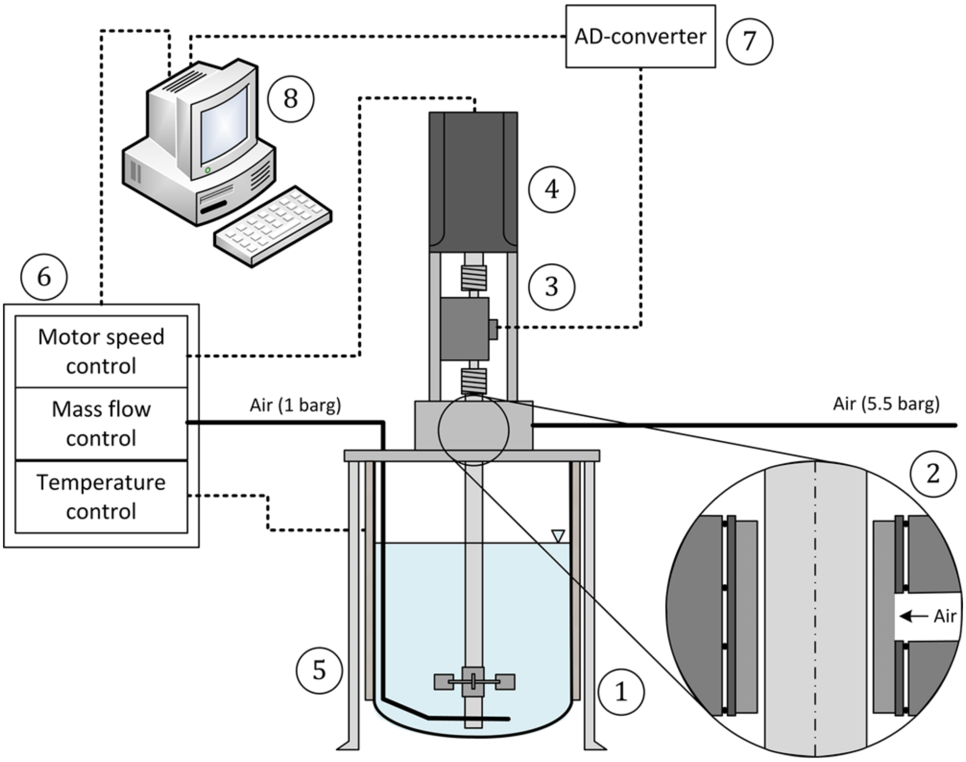

Figure 1. Schematic of the experimental setup. (1) Vessel holder, (2) air bushing, (3) torque meter, (4) agitator motor, (5) heating blanket, (6) controller for motor speed and gas mass flow, (7) AD converter, and (8) PC.

2.3 Measurement procedure

The power input in the liquid P_L was calculated directly from the effective torque (M_{eff}) and the rotational impeller speed (N) using Eq. (1):

$$P_L = 2 \cdot \pi \cdot M_{eff} \cdot N = 2 \cdot \pi \cdot (M_L - M_D) \cdot N \tag{1}$$

where M_{eff} was obtained from the difference between the torque measured in liquid M_L and the dead torque M_D (torque without liquid inside the vessel). The dimensionless power number N_P (also known as Newton number) was calculated using Eq. (2), where ρ_L is the liquid density:

$$N_P = \frac{P_L}{\rho_L \cdot N^3 \cdot d^5} = \frac{2 \cdot \pi \cdot M_{eff}}{\rho_L \cdot N^2 \cdot d^5} \tag{2}$$

Even though the dead torque is very low, due to the air bearing, it was determined for each bioreactor for rotational speeds of between 50 and 900 rpm. However, the effective measurement range was limited to 300 rpm for all unbaffled examples due to vortex formation, which was limited to vortex depths of approximately 20 mm based on visual inspection. For each experiment, the vessels were filled with 2 L pure water or sucrose solution (20–60% w/w). The density and viscosity of the solutions were calculated based on data from [45]. Some reference measurements were also conducted using a DCAT 11 tensiometer (Dataphysics, Germany) and a MCR 302 Modular Compact Rheometer (Anton Paar Switzerland AG). All samples showed good agreement (relative deviation ≤5%) with the literature data. The impeller Reynolds numbers (Re) were then calculated using Eq. (3):

$$\mathrm{Re} = \frac{N \cdot d^2 \cdot \rho_L}{\eta_L} \tag{3}$$

Using the recipe tool integrated in the μTruBio PC software, up to 110 individual measurements could be conducted in a single experiment. A typical measurement profile is shown in Fig. 2, where the impeller speed of the Rushton turbine was increased stepwise over time. After each adjustment of the impeller speed, peak values in the torque signal were observed. The peak torque signal values are related to the PID-based impeller speed controller and the initial acceleration of the liquid. In order to obtain a stable torque signal for each measurement point, the impeller speed was kept constant for 3 min and the peak torque after each speed adjustment was ignored. The measured torques (M_L) represent the average value obtained from a minimum of 240 data points with a measurement frequency of 2 Hz, as shown in Fig. 2. For the majority of measurement points, the RSDs of these mean values were lower than 3%, which indicates stable measurement signals.

3 Results and discussion

3.1 Determination of dead torque

Based on our experience, reducing the dead torque (i.e. torque during agitation without liquid) is one of the most important

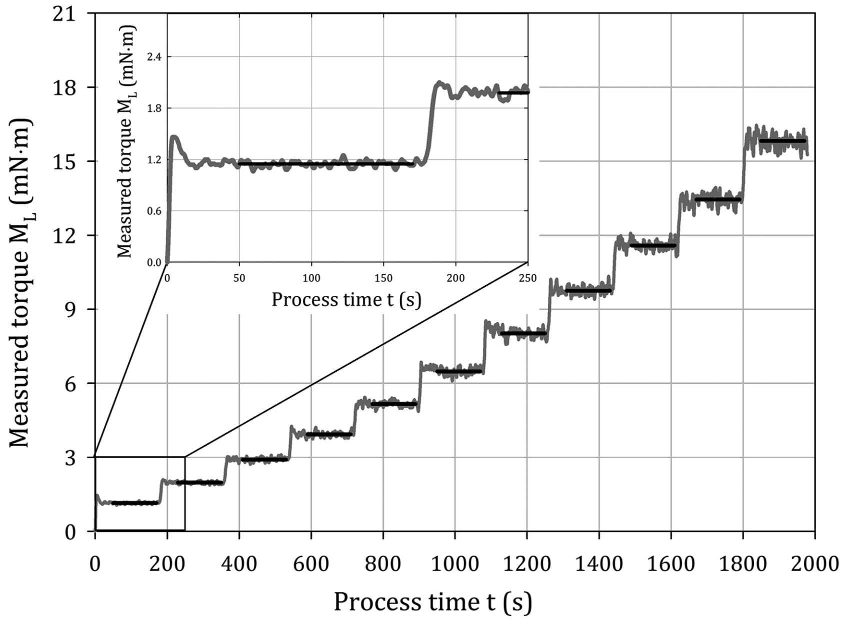

Figure 2. Example measurement in the 2 L baffled glass bioreactor with a Ruston turbine. The impeller speed was increased every 3 min from 150 to 450 rpm in steps of 30 rpm. The black lines indicate the averaged torque values of the individual measurement steps.

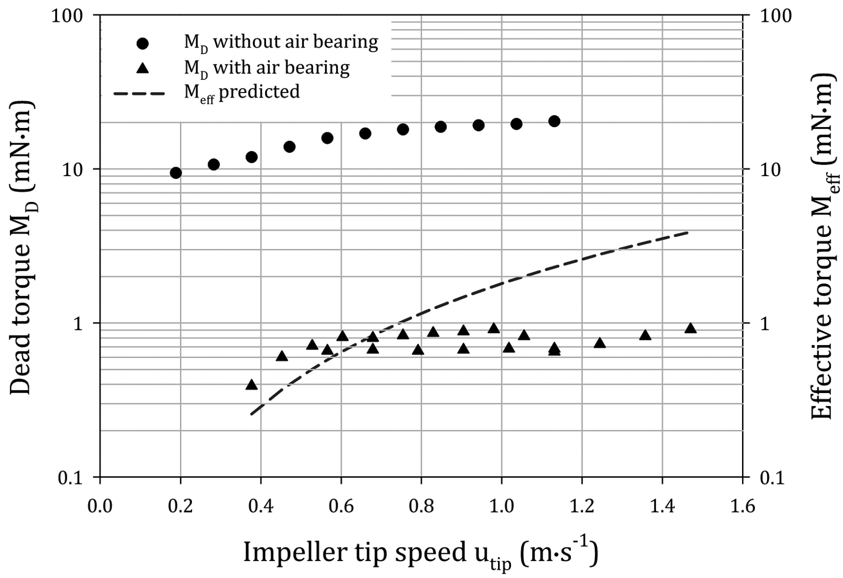

Figure 3. Dead torque as a function of the impeller tip speed in the CellReady 3L bioreactor. The dashed line indicates the expected effective torque based on experimental data [32] and CFD models [46].

factors for accurate power input measurements, particularly in laboratory-scale bioreactors, whereas often it does not need to be taken into account in larger vessels, as proposed by [19, 26, 34]. As can be seen from Fig. 3, the dead torque in the CellReady 3L bioreactor with the built-in bearing was between 9.4 and 20 mN·m depending on the rotational speed, i.e. tip speed defined as:

$$u_{\text{tip}} = \pi \cdot N \cdot d \tag{4}$$

This is up to two orders of magnitude higher than the expected effective torque based on experimental data [32] and computational fluid dynamics (CFD) models [46]. For the Uni-Vessel SU, dead torque values of approximately 3 mN·m at a rotational speed of 150 rpm have been reported [32]. Considering the measurement accuracy of the sensors used, it is difficult to resolve such small effective torque values, i.e. differences in torque in liquid versus air. This is particularly true for low impeller speeds.

Using the zero-friction air bearing, the dead torque was effectively reduced to values between 0.4 and 0.9 mN·m. Thus, the ratio $M_{\text{eff}}/M_{\text{D}}$ (based on the predicted effective torque) was only between 0.2 and 1.5. It should be emphasized that the residual dead torque in the CellReady 3L bioreactor was still the highest of all the tested bioreactors, which can be explained by the built-in impeller shaft fixing on the vessel bottom. During rotation, the impeller shaft collided with this fixing, a fact that can also be observed during cultivation experiments.

For the other agitators that were tested, residual dead torque values in the order of 0.1–0.5 mN·m were observed, which may be caused by minor radial misalignments of the impeller shaft.

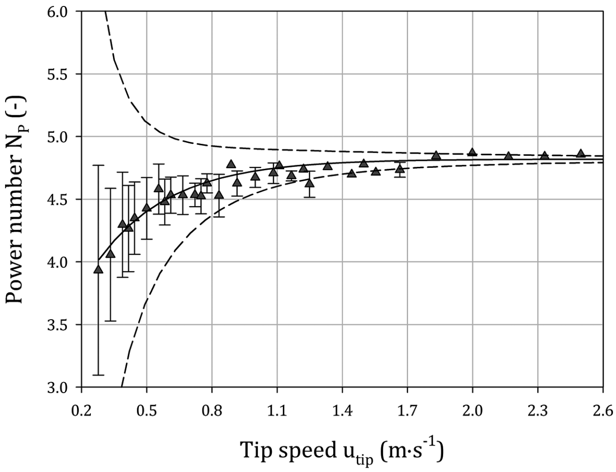

Figure 4. Determined power numbers of the Rushton turbine as a function of the impeller tip speed. The error bars represent the simple SDs of four individual experiments. The dashed lines indicate the confidence interval based on the sensor accuracy (i.e. ±0.2% of the nominal torque equal to ±0.4 mN·m).

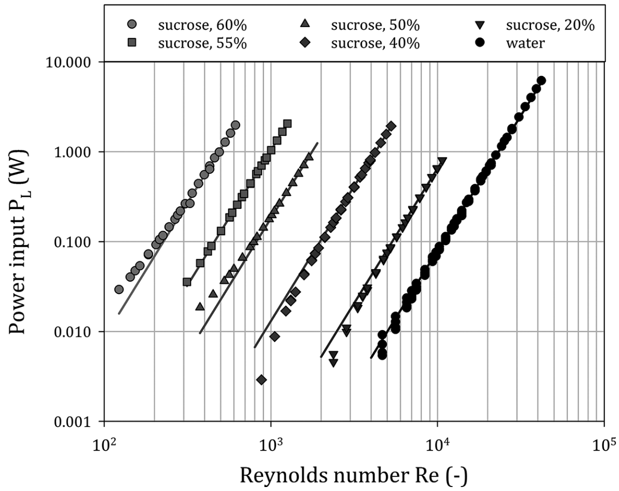

Figure 5. Power input of the Rushton turbine as a function of the Reynolds number. Increasing the sucrose mass fraction resulted in the Reynolds number varying by two orders of magnitude (between 1×10^2 and 3×10^4). The solid lines represent regression models assuming $P \propto Re^3$ for constant power numbers.

Furthermore, none of the tested agitators had a bearing near the vessel bottom. Consequently, even very small bends in or imbalances of the impeller shaft could result in significant oscillations during rotation, particularly in the single-use bioreactors, due to the fact that their shafts are made out of plastics and are, as a result, more flexible.

3.2 Measurement reproducibility

Measurement reproducibility was evaluated using a Rushton turbine operated at impeller speeds of between 100 rpm and 900 rpm (corresponding to tip speeds of 0.27 and 2.45 $m{\cdot}s^{-1}$). As can be seen in Fig. 4, the SDs of the four replicates decrease as tip speed increases (from 21–<1%). This agreed with expectations due to the lower relative importance of the dead torque and the higher absolute torque at elevated impeller speeds. Qualitatively similar scattering has also been reported after comparisons between nine different laboratories (Members of the German GVC-VDI working group on mixing) that have measured power inputs for Rushton turbines and pitched blade impellers in 0.4 m diameter vessels, i.e. 50 L scale [47]. Using different measurement systems, including strain gauges, shaft-mounted torque meters, and turntables, system intrinsic deviations have been reported for measured values equal to 10% or less of the nominal torque. In the present study, the effective torque values obtained with the air bearing were between 0.5 and 16 mN·m, which corresponded to 0.25 and 8% of the nominal torque of the sensor that was used. Thus, reliable measurements were obtained for very low torque values related to the nominal measurement range.

It should be emphasized that most measurement points were within the confidence interval around the mean values based on the sensor accuracy provided by the manufacturer (i.e. ±0.2% of the nominal torque equal to ±0.4 mN·m [44]), which is presented as a dashed line in Fig. 4. Nevertheless, in order to ensure reliable results, only those measurements for which the RSD of replicates was <5% and the effective torque was ≥2 mN·m, corresponding to 1% of the nominal torque, were considered in further experiments.

3.3 Power input of standard and single-use agitators under nonaerated conditions

3.3.1 Rushton turbine

In Fig. 5, the determined power input of the Rushton turbine in a 2 L working volume is shown for Reynolds numbers between $1{\cdot}10^2$ and $3{\cdot}10^4$. Using impeller speeds between 150 and 450 rpm, the Reynolds numbers were also influenced by the liquid density (998.2–1286.5 $kg{\cdot}m^{-3}$) and viscosity (0.89–58.5 mPa·s) of water and the sucrose solutions, with mass fractions of up to 60% w/w. As expected, individual profiles were obtained for each of the liquids, which showed that the power input increased as the Reynolds number increased. In the range investigated, it is well-known that the power number of the Rushton turbine is almost constant, as reported in several studies [10,12,16]. Hence, as can be seen from Eqs. (2) to (3), the power input P follows the relationship $P_L \propto Re^3$ for a constant impeller diameter. The experimental data agreed well with this correlation (with $R^2 = 0.9992$, see Fig. 5).

The power characteristic of the Rushton turbine is shown in Fig. 6. In agreement with expectations, the power number N_P decreased at low Reynolds numbers ($100 < Re < \approx 500$) before it increased again above $Re \approx 2000$. Under fully turbulent conditions ($Re > 10^4$), an almost constant power number of $N_P = 4.17 \pm 0.14$ was obtained. These observations showed good qualitative agreement with data reported by Shiue and Wong [12] and Ibrahim and Nienow [16] for the Re range investigated (see Fig. 6). These authors have determined the power input of a single Rushton turbine in 20 and 40 L working volumes, respectively.

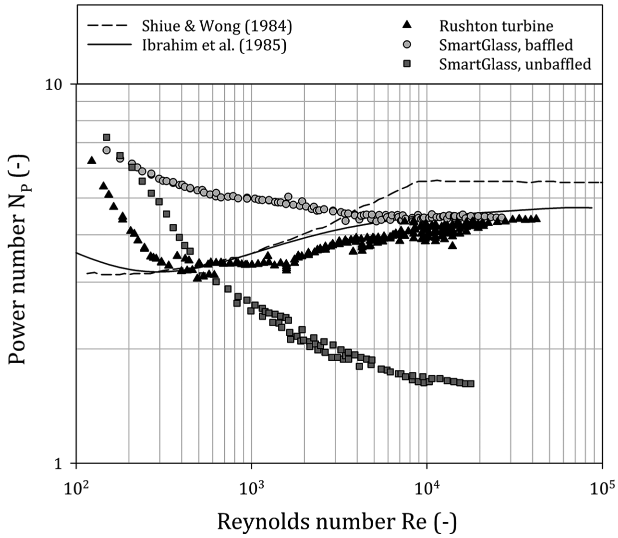

Figure 6. The power number as a function of the Reynolds number for the stainless steel agitators investigated.

However, some discrepancies were found in a more quantitative comparison. The power numbers for Re < 300 seem to be overestimated by up to a factor of 2. Although such low Reynolds numbers are unlikely in animal cell cultures (even at very low impeller speeds) they may be relevant in plant cell cultivations, where increases in the broth viscosity by up to a factor of 400 have been reported [40], resulting in a considerably lower Re according to Eq. (3).

Furthermore, the power number for fully turbulent conditions is up to 25% lower than that provided by reference data of $N_P \approx 4.7$ [16] and $N_P \approx 5.5$ [12]. As can be seen from Table 3, other researchers found N_P values for Rushton turbines in baffled vessels in a range of 3.6–5.9 [10,14–17,20,27,35,36,48], depending on the stirrer and vessel geometry used. Furthermore, an even lower N_P value of 3.36 has been reported for an unbaffled Rushton turbine agitated minibioreactor [35].

However, it should be emphasized that direct comparison is difficult because of the differences in the geometrical details. The majority of data that has been published is for flat-bottomed tanks with four baffles, whereas in the present study, only three baffles were installed in a vessel with a torospherical bottom. The number and position of the baffles was given by the preconfigured ports in the head plate of the SmartGlass bioreactor. Furthermore, it has been demonstrated that the power number depends on the diameter ratio (d/D) [10, 49] and the blade thickness [10, 50], with a relationship of $N_P \propto (s/d)^{-0.22}$ being reported [50]. This was confirmed by our own measurements in a 10 L scale vessel, where $N_P \propto (s/d)^{-0.32}$ was determined (data not shown). Finally, it has been stated that the disc thickness also has a notable influence on the power number [10], but not all references from Table 3 provide the blade thickness used in their studies.

3.3.2 SmartGlass bioreactor

Figure 6 also shows the power characteristic of the SmartGlass bioreactor, which is agitated by a combination of a top-mounted axial flow segment blade impeller (also known as an elephant ear impeller) and a modified disc blade turbine with tapered blades (i.e. a modified Rushton turbine), where the latter exhibits a predominantly radial flow in CFD simulations (data not shown). In the baffled vessel, the total power number continuously decreased from $N_P \approx 6.5$ for Re $\approx 10^2$ to $N_P \approx 4.46$ for Re $> 10^4$. This indicates that the reduced drag at the disc blade, compared to a classic Rushton turbine, is equalized by the second impeller.

In contrast, the power number in the unbaffled SmartGlass bioreactor decreased over the complete Re range investigated. Because this behavior has also been described for various other unbaffled agitators [1, 49], it agreed with expectations and can be explained by centrifugal forces that result in fluid rotation and finally the formation of a vortex.

3.3.3 SmartVessel bioreactor

Not entirely surprisingly, a very similar power characteristic for the SmartVessel bioreactor (Finesse Solutions, Inc.), the

Table 3. Summary of determined power numbers N_P for Rushton turbines under fully turbulent conditions for different geometries reported in the literature

d/D (−)	z_M/D (−)	s/d (−)	t/d (−)	a/d (−)	b/d (−)	Baffles (−)	N_P (−)	Ref.
0.43	0.41	0.027	0.026	0.29	0.20	3	4.17 ± 0.14	This work
0.25–0.75	0.16–0.75	n.a.	0.013–0.11	0.25	0.20	4	3.6–5.9[b)]	[10]
0.31	0.31	0.016	0.024	0.25	0.20	4	4.6 ± 0.4[a)]	[48]
0.33	0.33	0.075	n.a.	0.25	0.20	0	3.36 ± 0.09[a)]	[35]
0.33	0.33	n.a.	n.a.	0.25	0.20	4	5.10 ± 0.06[a)]	[20]
0.33	0.33	0.031	n.a.	0.25	0.20	4	5.1[a)]	[15]
0.33	0.25	0.008	n.a.	0.25	0.20	4	5.27 ± 0.05[a)]	[14]
0.41	0.33	0.009–0.076	n.a.	0.25	0.20	4	5.58[b)]	[27]
0.52	0.25	n.a.	0.013	0.25	0.20	4	4.6 ± 0.28[a)]	[17]
0.33	0.20	n.a.	n.a.	n.a.	n.a.	4	5.5[b)]	[36]
0.50	0.25	n.a.	0.05	0.25	0.20	4	5.0[b)]	[16]

In all literature studies, flat-bottomed vessels were examined, whereas the bottom was torospherical in the present work.
a) These data were determined from (logarithmically scaled) graphs in the references given.
b) No information is provided about the relationship between impeller thickness and the power number.
n.a. = not available.

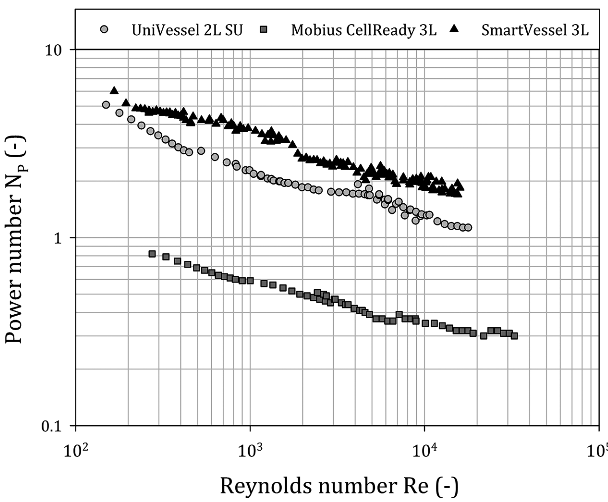

Figure 7. The power number as a function of the Reynolds number for the unbaffled single-use bioreactors investigated.

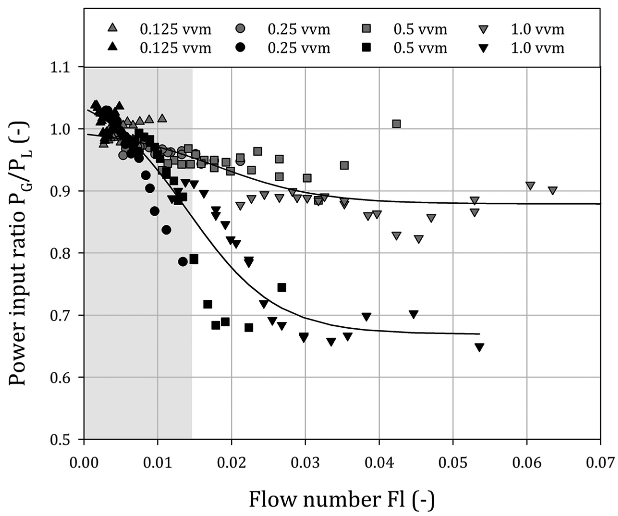

Figure 8. Power input ratio under aeration in the Mobius CellReady 3L (black symbols) and the SmartGlass 3L (gray symbols) bioreactors. The gray marked square indicates typical operating ranges for cell culture applications used in our laboratory.

single-use counterpart of the SmartGlass 3L bioreactor, was also determined (see Fig. 7). In the unbaffled vessel, a power number of $N_P = 2$ was determined for $Re = 10^4$. Small deviations (with relative values in the range of −25 and +40%, depending on the Reynolds number) between the single-use and multiuse vessel can be explained by differences in the impeller designs. Even though the shape of the impellers and their main geometric parameters (d, z_M, z_R, b, α in Table 2) were identical for both the stainless steel and the plastic impellers, small modifications resulting from the manufacturing process could not be avoided. The blades of the plastic impellers were thicker (2 vs. 1.5 mm) and their edges were rounded compared to the sharp-edged steel blades. The bottom-mounted shaft holder in the SmartVessel bioreactor may also have an impact on the flow structure below the impellers.

Measurements with lower filling volume, where only the lower impeller was covered, revealed a power number of 1.3 for $Re = 10^4$ (data not shown). Assuming negligible interactions between the impellers, something that has been found for systems with $z_R/d > 1.2$ [49–51], the power number of the upper impeller would be 0.65. This value is comparable to reported data for a similarly shaped elephant ear impeller [51] and also to data from the two-stage segment blade impellers in the UniVessel 2L SU bioreactor (see discussion below).

3.3.4 UniVessel 2L SU bioreactor

For the UniVessel 2L SU bioreactor, power numbers of between 5.08 and 1.13 were determined, depending on the Reynolds numbers ($1.5 \times 10^2 < Re < 1.78 \times 10^4$). These N_P values are somewhat lower than experimental data reported by van Eikenhorst et al. [32], e.g. $N_P = 1.9$ for $Re = 1.4 \times 10^4$. Interestingly, their data showed the same relationship of $N_P \propto Re^{-0.336}$ as found in the present study for comparable Reynolds number ranges. The different absolute values may be explained by the different measurement techniques. While the dead torque in the present study was considerably lower than the effective torque, it was higher for the two experiments presented in the reference study [32], which presumably caused higher experimental errors. However, the overall agreement between the two studies was satisfactory.

3.3.5 Mobius CellReady 3L bioreactor

Finally, the power input of the Mobius CellReady 3L bioreactor was determined for Reynolds numbers between 2.75×10^2 and 3.06×10^4. Due to the low blade angle of the marine impeller, the power numbers obtained were only between 0.82 and 0.31. Again comparable experimental values have been reported [32] and were also obtained from numerical CFD models [46].

3.4 Power input for standard and single-use agitators under aerated conditions

The influence of aeration on the power input was studied for the single-use Mobius CellReady 3L and the reusable SmartGlass 3L bioreactors over a wide range of aeration rates (0.125–1 vvm). In Fig. 8, the ratio of gassed power input to ungassed power input (P_G/P_L) that was obtained from the torque measurements is shown as a function of the gas flow number Fl, which was defined as:

$$Fl = \frac{F_G}{N \cdot d^3} \quad (5)$$

where F_G is the volumetric gas flow rate. As expected, the gassed power input in both bioreactors decreased as gas flow rates increased. At flow numbers of $Fl \approx 0.04$, the P_G/P_L ratio became constant, which has also been reported for traditional impellers, such as Rushton turbines [14, 31] and curved blade impellers [21]. Surprisingly, the Mobius CellReady marine impeller showed a higher dependency on the flow rate ($P_G/P_L \propto \mathrm{Fl}^{-0.15}$) than the SmartGlass bioreactor impellers ($P_G/P_L \propto \mathrm{Fl}^{-0.04}$), which may be explained by the lower gas dispersion efficiency of the marine impeller. Furthermore, P_G/P_L ratios slightly above one were determined for low gas flow numbers in the Mobius CellReady bioreactor, which has also been demonstrated for hydrofoil impellers [30]. It has been stated that the rising gas–liquid plume opposes the impeller pumping action at low impeller speeds and, therefore, the power numbers under aeration become higher than those under nonaerated conditions at the same speed.

Finally, it should be emphasized that the results only consider the measured power input based on the torque, whereas the power input from the gas, which can be calculated from Eq. (6), assuming isothermal gas expansion, was not considered.

$$P_{G,b} = F_G \cdot (\rho_L - \rho_G) \cdot g \cdot H_{GL} \quad (6)$$

In fact, the power input released from gas expansion exceeded the measured power input under certain operation conditions (typically high aeration rates and low impeller speeds). Nevertheless, it should be noted that aeration rates and gas flow numbers above 0.25 vvm and 0.015 are typically not used for cell culture applications based on protocols developed in our laboratory. Therefore, it can be concluded that the influence of aeration on power input in the investigated systems is negligible.

4 Concluding remarks

Even though the (specific) power input is an important parameter for engineering characterization and scaling-up/down of bioreactors, only limited experimental data for benchtop scale systems is available in the literature. In particular, little data on power input for laboratory-scale single-use bioreactors, which come ready to use from the manufacturers, has been published to date. This study has closed some gaps for commercially available single-use systems at benchtop scale, namely the UniVessel 2L SU, the Mobius CellReady 3L, and the SmartVessel 3L bioreactors. The determined power numbers cover a wide range of Reynolds numbers between very low and moderate turbulence and are regarded as useful for defining suitable operating conditions for most cell culture applications (or even microbial processes with moderate agitation requirements). Finally, this study has also demonstrated that the power input in the bioreactors investigated is only slightly influenced by typical cell culture aeration rates.

Based on the current results, it can be concluded that the recommendations provided by the DECHEMA working group guidelines [42] are also applicable for bioreactors at the benchtop scale. During the development of the test setup, special attention was given to reducing the dead torque that usually limits the measurement range and accuracy, particularly for small agitators. By using an air bearing, as has already been described in previous works [10, 52], it was possible to minimize the dead torque to values of below 1 mN·m, irrespective of the impeller speed and bioreactor used. Good agreement was found with available literature data for the standard Rushton turbine used. The typical power characteristic was also determined, which demonstrated the suitability of the measurement setup.

Nevertheless, laminar flow conditions with Re < 100 were still not achievable. For such conditions, either a further increase in the liquid viscosity or a decrease in the impeller speed would be required. Using sucrose solution as a cheap Newtonian model medium, a maximum dynamic viscosity of ≈ 60 mPa·s was established with mass fractions of 60% w/w, which is close to the solubility limit at room temperature (66.7% w/w [53]). Alternatively, glycerol or silicone oils with viscosities > 1000 mPa·s could be used. The lowest possible impeller speeds were restricted by the resolution of the torque meter (to ≈100 rpm in most cases). To the best of the author's knowledge, there are only a few commercially available sensors with lower measurement ranges (e.g. with a nominal torque of 0.1 Nm [44]). However, none of these were used because of the additional investment costs.

This may also limit the use of the current experimental setup for smaller bioreactors with volumes of below one liter (and geometrically similar agitators). For instance, a 10% smaller impeller diameter results in an approximately 40% lower impeller torque for a given impeller speed and shape (i.e. power number), because of the $M \propto d^5$ relationship between torque and impeller diameter. Consequently, the torque meter and the experimental set up must be carefully considered. Further work is planned to establish an experimental set up for measuring torque in vessels with volumes of 1 L and less.

Practical application

Measuring power input in small-scale bioreactors is still challenging because of the limited accuracy and resolution of common measurement techniques. The torque-based methods that currently dominate are often limited by the relatively high friction losses of the bearings that are usually used. Consequently, there is still a lack of data on power inputs in benchtop scale bioreactors, in particular for single-use bioreactors, which are preassembled, sterilized, and delivered ready to use from the manufacturers. The present study shows that air bearings can be used to effectively reduce the friction losses and, thus, enable accurate measurements for a wide range of operational conditions. Based on reference measurements with a conventional Rushton turbine, which agreed well with literature data, the power inputs in different multiuse and single-use bioreactors were determined for low-to-moderate turbulence, which is often found in cell culture based processes with low agitation.

The authors would like to thank Dieter Häussler and Beat Gautschi for their assistance during the experimental set up. We are also grateful to Darren Mace for English proof reading.

The authors have declared no conflicts of interest.

Nomenclature

a	[m]	Impeller blade width
a_S	[m]	Baffle thickness
b	[m]	Impeller blade height
B_S	[m]	Baffle width
d	[m]	Impeller diameter
D	[m]	Vessel diameter
g	$[m \cdot s^{-2}]$	Gravitational acceleration
F_G	$[m^3 \cdot s^{-1}]$	Gas flow rate
Fl	[−]	Flow number
H_{GL}	[m]	Gas bubble rising height in liquid
H_S	[m]	Baffle height
M_D	[N·m]	Dead torque (measured in air)
M_{eff}	[N·m]	Effective torque
M_L	[N·m]	Torque measured in liquid
N	$[s^{-1}]$	Impeller rotational speed
N_P	[−]	Power number (Newton number)
P_L	[W]	Power input, ungassed
P_G	[W]	Power input, gassed
$P_{G,b}$	[W]	Power input by gas expansion
Re	[−]	Reynolds number
s	[m]	Impeller blade thickness
t	[m]	Impeller disc thickness
u_{tip}	$[m \cdot s^{-1}]$	Impeller tip speed
V_L	$[m^3]$	Liquid volume
x	[−]	Sucrose mass fraction
z_M	[m]	Off-bottom clearance
z_R	[m]	Distance between impellers

Greek symbols

α	[°]	Impeller blade angle
η_L	[Pa·s]	Liquid dynamic viscosity
π	[−]	Mathematical constant
ρ_G	$[kg \cdot m^{-3}]$	Gas density
ρ_L	$[kg \cdot m^{-3}]$	Liquid density

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