ZETA INNOVATION PARTNER

ZETA
EVOLUTION OF TECHNOLOGY

BOTTOM-MOUNTED MAGNETIC AGITATOR XXL

Innovation project Boehringer Ingelheim Hamburg-Harburg University of Technology and ZETA

„The need for optimized large-scale industrial fermenters has grown enormously and will continue to rise steadily. Firstly, because biocatalytic processes play a major role in the shift towards using renewable raw materials to produce basic chemicals and substances. And secondly, because the efficiency of microorganisms and cells for the production of substances has increased considerably in the last years. In order to meet the requirements of these accelerated metabolic processes a better supply of e.g. oxygen has to be guaranteed. For the execution of trials to enable the development of Boehringer's fermentation processes of tomorrow a transparent 15.000 L test facility was installed at the Technical University of Hamburg-Harburg."

(**Prof. Dr.-Ing. Michael Schlüter**, Institute for Mulitphase Flow, Hamburg-Harburg University of Technology)

"In a biopharmaceutical process all parameters have to be controlled strictly. Especially in industrial scale production it is of paramount importance to specify the production equipment as precisely as possible. At Boehringer Ingelheim this is achieved by means of computational fluid dynamics (CFD) and a worldwide unique transparent 15 000 L test plant, which could be installed at the Hamburg-Harburg University of Technology in collaboration with our partner Professor Schlüter. This enables us to make our production processes transparent and generate knowledge, which directly flows into the development of our processes."

(**Dr.-Ing. Thomas Wucherpfennig**, Project Manager Acrylic Reactor Plant and Flow Simulations, Late Stage Development Boehringer Ingelheim)

A central factor in achieving a production process of the highest efficiency in any stirred reactor is to ensure the greatest possible homogeneity of mixing. In order to draw up a specification for the mixing process, it is essential to accurately understand and define the hydrodynamic flow regime and the specific power inputs of the mixing rotors and their geometry.

A type of agitator, that is particularly suitable for aseptic processes, are magnetic agitators, in which the motive force is transmitted via magnetic fields without a physical contact between the motor and the impeller. This has the advantage that there is no connection between the sterile interior of the reactor vessel and the unsterile space outside, which reduces the risk of contamination associated with the mechanical seal of shaft-driven agitators.

In the current market, magnetic agitators are most often used for preparation systems of up to 20 m^3 working volume and for small fermenters and bioreactors of up to 3000 litres. Normally, magnetic agitators are used in cases that do not place very high demands on mixing time and mass transport. However, in recent times magnetic agitators have been used increasingly for more complex mixing applications, and this has driven their technical development.

ZETA has now developed the first magnetic agitator with a drive torque of more than 400 Nm for a bioreactor with a volume of 15 m^3. The aim of the present study was to carry out comprehensive tests of the performance range and the stability of the agitator.

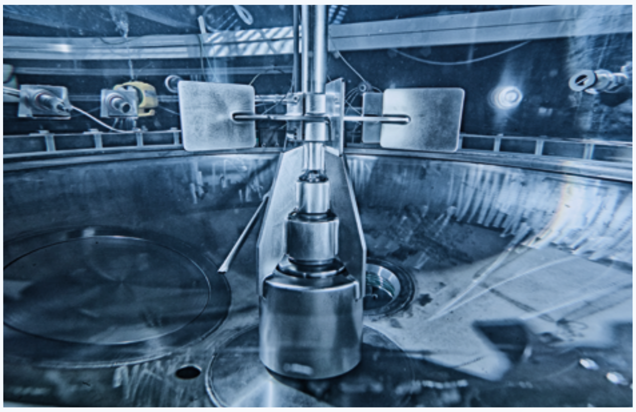
The ZETA bottom-mounted magnetic agitator for bioreactors (BMRF) is constructed in a small and compact design. One of the main key performance indicators of magnetic agitators is the maximum power input, which rises with increasing rotational speed and viscosity of the liquids. When the admissible torque value, which is transferred from the magnets to the agitator shaft, is exceeded, the magnetic field is disrupted and the impeller starts to slip.

A major goal of the test series was to quantify this performance limit for the agitator BMRF 40000.

Method

The newly developed agitator was tested in a test vessel with a total volume of 15 m^3 with a series of different impeller geometries to determine their power transfer to the stirred liquid and their mixing characteristics. The vessel wall is made of acrylic glass, in order to allow the use of optical measurement methods in the whole interior space of the vessel (see Figure 7). The mixed liquid was water (density $\rho = 999{,}44\ kg/m^3$, viscosity $\eta = 1{,}22$ mPas) at T = 12,5 °C.

The following combinations of impeller stages were tested:



In order to measure the actual power input of each impeller combination into the liquid, it is necessary to know the loss of power generated by the bearing. To do this, the agitator is submersed in water with the water level lying slightly above the agitator shaft. Then the power input of the agitator is measured at different rotational speeds.

A measuring flange between the drive and the bearing serves to measure the transferred torque and the actual rotation speed.

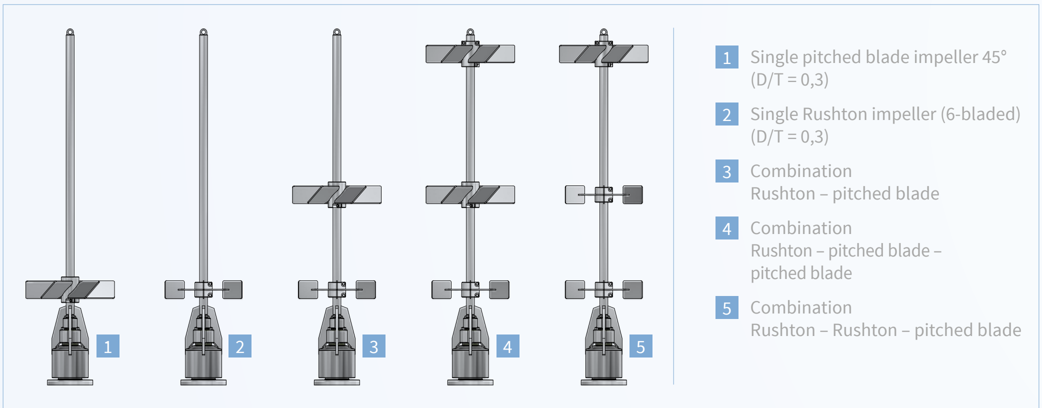


Figure 1: Combinations of impeller stages

The agitator is driven by a magnetic field, the impeller assembly is located and rides on a bearing shell with ceramic surfaces. In principle, the higher the viscosity and the rotational speed, the higher the power input, whereby also the gassing rate has an influence on this process.

The goal of the homogenization process in a bioreactor is to maximize the biological productivity, which can be guaranteed thanks to ideal mixing conditions (equalization of concentration and temperature differences) and short mixing times. For mass transfer the need is to achieve the best possible phase transfer of gas bubbles into the liquid (oxygenation) and vice versa (CO_2 stripping). These processes are highly complex and interdependent.

The torques of the individual impeller combinations were measured and recorded while increasing the rotation speed stepwise. Basing on the recorded values, the corresponding power input was determined. Figure 2 shows results for a pitched blade impeller, illustrating the increases in torque; broadly similar patterns were observed with the other impeller types. After a brief transitional phase the measured torque in a plausible way changes with the rotational frequency.

The performance of an impeller is described by the dimensionless Newton number (Ne value). To determine the Newton number, the mean torque M at steady state is calculated and the following equation is used:

$$Ne = \frac{P}{\rho\, d^5 n^3} = \frac{2\pi n M}{\rho\, d^5 n^3}$$

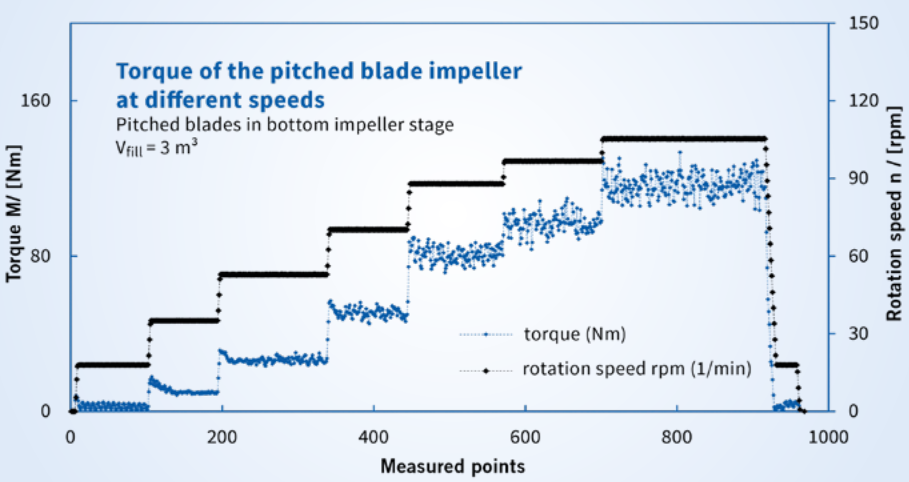


Figure 2: Example of Dynamic Torque Measurement

Preparing the apparatus for testing was very effective. The installation and functional setup of the bottom-mounted magnetic agitator were completed in half a day. Installation and deinstallation of comparable agitators with another technology (with mechanical seals) takes several days. Thanks to the compact design of the BMRF the agitator could be installed in an existing fermenter system. An already existing plug-in flange could be used and therefore there were no impact on the geometry of the sparger system.

In the course of the test series, the characteristics of the 6-bladed Rushton impeller and the pitched blade impeller as well as combinations of multiple stages were compared. Conventional calculation methods for multi-stage impellers assume that the total power input of the impeller is equal to the sum of the power inputs of the stages. However, this is only true, if the individual stages of the impeller are far enough apart that they do not influence one another hydrodynamically. The test series was designed to characterize the interactions between the impeller stages.

When changing the rotation direction, pitched blade impellers produce a flow parallel to the central axis. The rotation of a pitched blade impeller in a counterclockwise direction creates a flow parallel to the central axis going upwards (up-pumping). If the rotation direction changes, a downward flow is created (down-pumping). For the impeller combination Rushton – pitched blade (combination 3), the power inputs for both directions of rotation were compared.

The power input of the following impeller combinations was tested:

- Single-stage pitched blade (combination 1)
- Single-stage Rushton (combination 2)
- Rushton – pitched blade (combination 3)
- Rushton – pitched blade – pitched blade (combination 4)
- Rushton – Rushton – pitched blade (combination 5)

These impeller configurations were tested for two process conditions, gassed and ungassed. A gassing rate of 120 L/min was set, corresponding to a fermenter gassing of approximately 0.008 vvm (volume per volume and minute).

Another important question in this research project was, which rotational speed could be reached with a three-stage magnetic agitator designed for a bioreactor of 15 m³. In this case the focus was not only set on simply reaching the rotational frequency, but also whether the stability/oscillation of the impeller shaft would be acceptable.

The stability of the impeller shaft was monitored by means of optical measurements of the upper section of the shaft with a camera. The degree of oscillation of the shaft was determined at various speeds and then evaluated by means of digital image analysis. This finally allowed the lateral oscillation of the impeller to be quantified.

This test procedure was followed both for combination 4 with a Rushton and two pitched blade stages and combination 5 with two Rushton and one pitched blade stages.

Results

The bearing torque increases with increasing rotation speed, but at 4-13 Nm it is negligible compared to the torque of the different combinations of impeller stages in the liquid (see Figure 3).

The characteristics of the individual impeller stages – Rushton and pitched blade – were found to be as expected. The pitched blade impeller (combination 1) showed Ne = 1.8 and the Rushton impeller – Ne = 3.7 (see Figure 4).

If Rushton and pitched blade impeller stages are combined, they influence each other, what is reflected in the total power consumption of the agitator (see Figure 5).

With the combination Rushton – pitched blade (combination 3) a higher power input was observed in the up-pumping mode than for the down-pumping mode, as was expected. The difference in power input between the two modes was about 20 %. In the rotation direction, that corresponds to up-pumping, the upper pitched blade impeller stage evidently has a smaller effect on the lower Rushton stage than in the opposite rotation direction, given the spacing between the two stages used in this case.

The low gassing rate of approximately 0.008 vvm had, as expected, a very small effect on the power consumption of the agitator. Table 1 summarizes the power inputs for the different impeller combinations without gassing.

For the three-stage magnetic agitator the rotation speed was increased to find the threshold, at which the magnetic coupling breaks down. The target in the research design was a sustainable steady speed of 80 rpm. This was achieved both with combination 4 (Rushton – pitched blade – pitched blade) and with combination 5 (Rushton – Rushton – pitched blade). Even at an applied torque of M = 500 Nm no slipping of the magnetic coupling was observed.

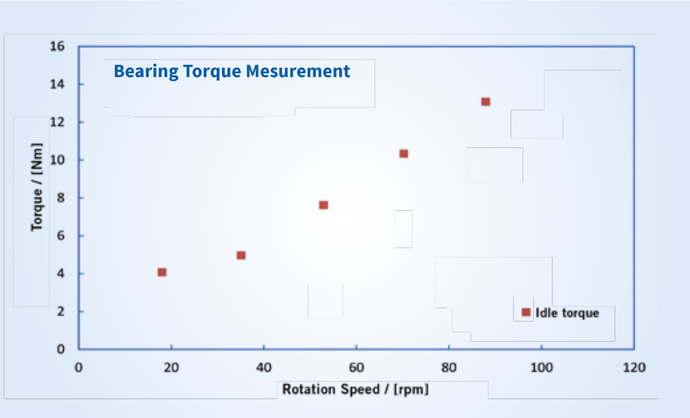


Figure 3: Torque of the Bearing at Different Speeds

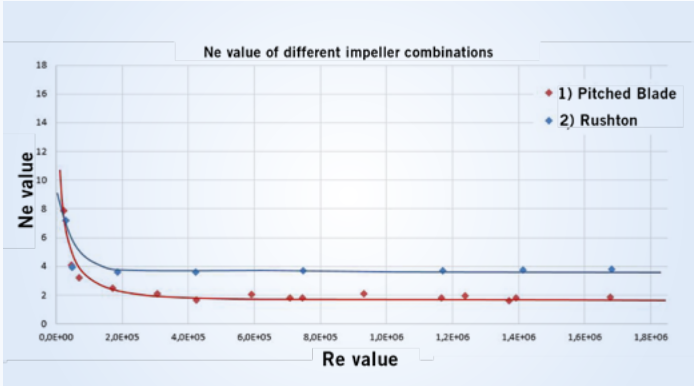


Figure 4: Comparison of the Ne Values of Single Impeller Stages: Pitched Blade (Combination 1) and Rushton (Combination 2)

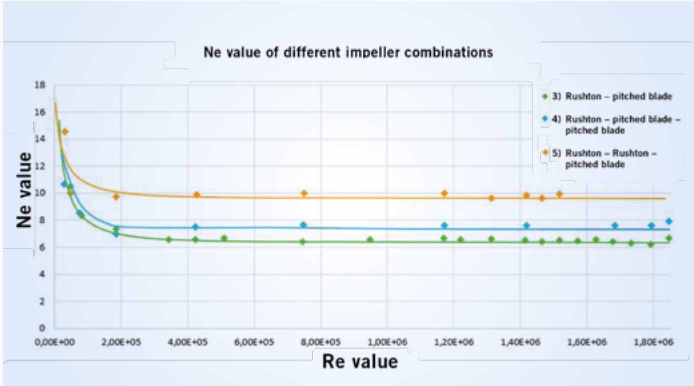


Figure 5: Comparison of Impeller Combinations

ZETA has now developed the first magnetic agitator with a drive torque of more than 400 Nm for a bioreactor with a working volume of 15 m³.

Figure: Test vessel at Hamburg-Harburg University of Technology

COMBINATIONS	NEWTON NUMBER no gassing	NEWTON NUMBER with gassing 0.008 vvm
1) Single pitched blade	1,8	Gassing with low volume flow rates did not have a relevant influence on the Newton number.
2) Single Rushton	3,7	
3) Rushton – pitched blade	6,9	
4) Rushton – pitched blade – pitched blade	7,6	
5) Rushton – Rushton – pitched blade	9,8	

Table 1: Results of Power Measurements

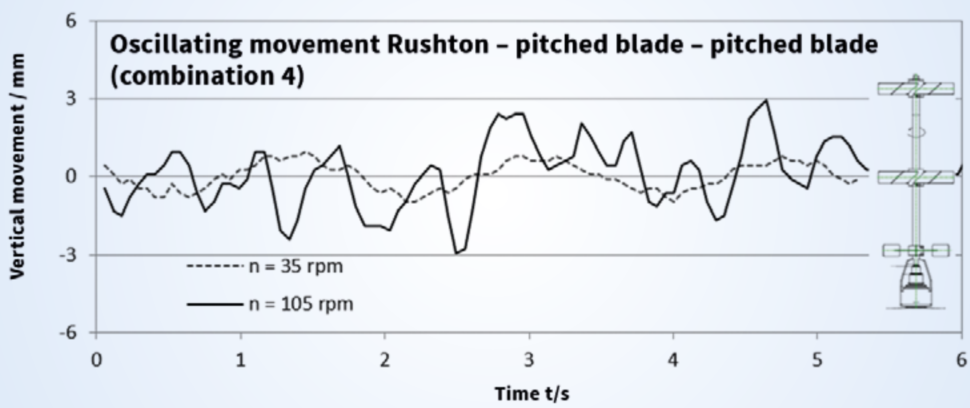


Figure 6: Oscillation of Combination 4

IMPELLER COMBINATION	SPEED [rpm]	AMPLITUDE [mm]
Rushton, combination 2	35 88 105	± 0,5 ± 0,4 ± 0,5
Rushton – pitched blade, combination 3	105	± 1,3
Rushton – pitched blade – pitched blade, combination 4	35 88 105	± 1,0 ± 0,6 ± 3,0

Table 2: Overview of Impeller Oscillation

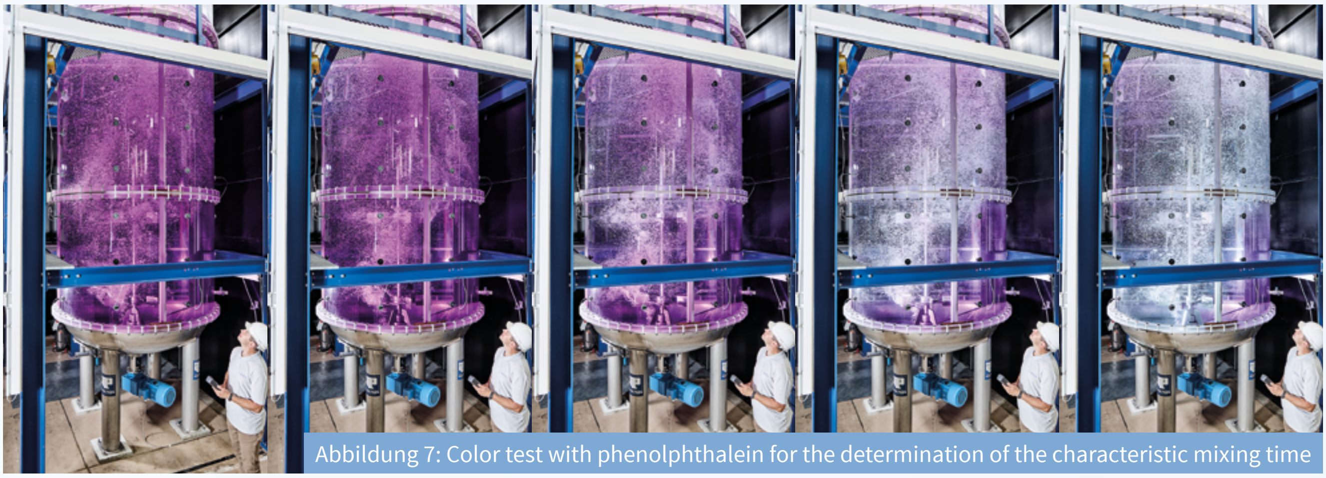


Abbildung 7: Color test with phenolphthalein for the determination of the characteristic mixing time

With combination 4 (Rushton – pitched blade – pitched blade) a speed of n = 88 rpm was achieved with a torque of M = 340 Nm. With combination 5 (Rushton – Rushton – pitched blade) the torque at this speed was M = 450 Nm. With this combination, even a speed of n = 110 rpm was reached, with a mean torque of M = 555 Nm and peaks of up to 600 Nm.

The agitator model tested did not exhibit critical oscillations that could threaten the stability of the impeller in operation. The tests showed that the operationally relevant speeds of n ≤ 80 rpm did not cause any oscillation of the impeller. With the single Rushton stage (combination 2), the oscillation of the impeller shaft had an amplitude of only 0.5 mm. Even at a speed of up to 105 rpm this amplitude did not increase (see Table 2 and Figure 6).

A larger effect on the oscillation of the impeller was caused by changing the number of impeller stages. With two stages, the amplitude of oscillation increased to approximately 1.3 mm at 105 rpm. With three impeller stages, the amplitude increased further, to a maximum of 3 mm, which can still be seen as uncritical.

Conclusion

The test series demonstrated the performance and the market readiness of the new ZETA bottom-mounted magnetic agitator BMRF for large bioreactors with a working volume of 15 m^3.

The BMRF has a negligible loss of power in the impeller bearing.

The expected torque transmission across the magnetic coupling was not only confirmed experimentally, but was exceeded by more than 50 %.

Even with a very compact design, the new agitator performs with stable running characteristics across the whole range of speeds used, with three-stage impellers. The design of the agitator enables it to be installed and deinstalled rapidly in any new and existing bioreactors without requiring changes in the geometry or functionality of existing agitator flanges or sparger systems.

ZETA has developed a valid testing method, applicable for magnetic agitators of all sizes, to determine the operating characteristics and power input of the impeller, and thus to enable rational planning of any mixing process. The test method can be applied both to existing and new stirred reactors.

The characterization of individual impeller stages and the whole impeller is the methodological basis for a calculation of the mixing time, the mass transfer values (liquid, solid and gaseous) as well as for scaling of impellers and mixing processes.

The BMRF 40000 combines aseptic process capability with large-scale power transmission with stable and precise running.

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