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Agitator Design Principles for Pharmaceutical and Biotechnology Applications

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Agitator Design Principles for the Bio/Pharm Industries

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PDHengineer Course No. BP-10001

Introduction

This course is intended to aid those in the bioprocessing, pharmaceutical and food industries who must specify, purchase, operate, troubleshoot or perform research involving agitation equipment. Typical applications in these industries might include, for example, simple tanks containing CIP solutions, broth and slurry tanks, compounding tanks and fermenters/bioreactors. The application technology ranges from simple to complex, and the construction details range from standard to highly sanitary. A basic Introduction to general agitator design principles is given, but the focus is primarily on applications found in the Pharmaceutical/Bioprocessing Industries.

The course begins with a basic introduction to agitation terminology and principles, then progresses through design concepts for liquid motion, gas dispersion and scale-up. Considerable time is devoted to fermenter and bioreactor design, including how to pilot in such a way as to get the kind of data which is useful for agitation scale-up and energy cost minimization. An introduction to advanced tools such as Computational Fluid Mixing (CFM) is given, and sanitary design issues are addressed. Solids suspension is not covered, as serious solids suspension applications are rare in these industries, and are covered in more generic agitation courses available in the marketplace. Likewise, mechanical design is not covered, both due to time limitations and the availability of such information in more generic agitation courses.

Chapter One: Agitator Design Basics

In this section, we will cover nomenclature, standard symbols, basic concepts, principle dimensionless numbers and the main classifications of flow patterns. We will also cover the basics of heat transfer calculations.

To begin, it is useful to identify the major components of an agitated tank, as shown in Figure 1.

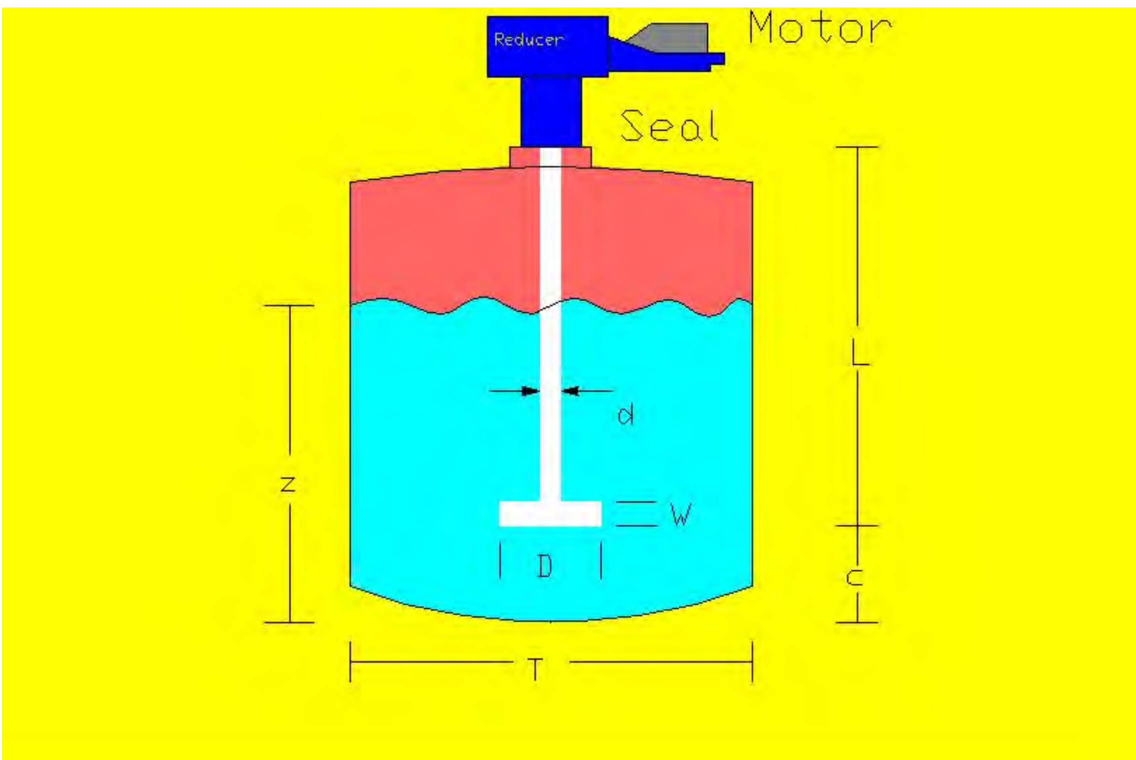


Figure 1, typical agitated tank

Let us follow the flow of power through the system, identifying the nomenclature and standard symbols as we do so. Note that the term "agitator" refers to the entire machine; some people incorrectly use this term to apply to the impellers only.

Power is provided by means of a prime mover. Though any device which provides rotary power can in principle be used (the author has seen such things as hydrostatic drives, steam turbines and internal combustion engines used), the most common prime mover is the simple electric motor. Most commonly, agitators are fixed speed, though multispeed motors or variable speed drives may be used where there is a need to change speed during different parts of the process, a desire to fine-tune results, or simply to minimize energy consumption.

In most cases, (except in small tanks, typically less than 2000l capacity) motor speed is too high to drive the shaft directly. Therefore, the power is transmitted through a speed reducer, which is normally a gear drive. This reducer, in addition to reducing speed and increasing torque, must usually support all of the shaft loads, which include not only torque, but bending moment, downward load (weight) and pressure thrust in a closed tank. These duties are normally best served by using a gear drive specifically designed for agitator service, rather than a standard speed reducer.

In many cases, the agitator is mounted on a closed top tank, so it will have a shaft seal. This may be a lip seal, packing or various types of mechanical seals. Some agitators are mounted on open-top tanks, and do not have a seal.

The power is transmitted to the impeller or impellers by a shaft, with diameter “d” and extension “L” from the mounting surface. This shaft must transmit torque, withstand bending moment and not operate at a speed close to its natural frequency. In addition to solid, constant diameter shafts, agitators may have stepped diameter or even hollow shafts.

Agitation is created within the tank by the action of an impeller or impellers, turning at the shaft speed, “N”. Each impeller has a diameter, “D”, a blade width “W”, and an off bottom clearance “C”.

Most agitated tanks have a cylindrical shape. The tank diameter is referenced by the symbol “T”, and the liquid level is referenced by “Z”. Other dimensions used to lay out the tank geometry include the mounting height or nozzle projection, straight side and head depths. These are not usually given standard symbols.

There are some other important variables and symbols used in agitator design, not shown on the tank sketch. These include the impeller pumping rate, “Q”, liquid density, “ρ”, liquid viscosity, “μ”, and power draw, “P”.

These symbols are summarized below.

Symbol	*Meaning*	*Symbol*	*Meaning*
D	Impeller Diameter	N	Shaft Speed
T	Tank Diameter	L	Shaft Extension
d	Shaft Diameter	Q	Impeller Pumping Rate
C	Off Bottom Clearance	ρ	Liquid density
Z	Liquid Level	μ	Liquid Viscosity
W	Impeller Width	P	Power Draw

The complexity of agitated tank geometry makes analytical solution of the equations of continuity and the Navier-Stokes equation all but impossible. Progress has been made using numerical methods to solve these equations, but even these methods currently have limitations, which will be discussed in chapter 11.

The most common way to solve agitation problems is to correlate experimental data using expressions involving dimensionless numbers, and then use these correlations to solve a variety of real-world problems. The next several pages will cover the principal dimensionless numbers, their significance and how they are used.

Dimensionless numbers, as their name implies, are numbers derived from ratios of quantities such that all units cancel out. Therefore, any consistent set of units can be used; the equations do not depend on any particular set of units. For example, a very simple dimensionless number could be the aspect ratio of a cylinder, which could be represented by H/D, where H is its height and D is its diameter. It does not matter whether the height is measured in meters, inches or furlongs; as long as the diameter is measured in the same units as the height, the aspect ratio is the same. The units *must* cancel; a dimensionless number has no units.

In agitation technology, there are a number of dimensionless units which are in common use. These include:

1 Power Number, N_P
2 Pumping Number, N_Q
3 Reynolds Number, N_{Re}
4 Froude Number, N_{Fr}
5 Nusselt Number, N_{Nu}
6 Prandtl Number, N_{Pr}
7 Geometric Parameters: D/T, C/D, etc.

Below we will explain these in more detail.

1. Power number, N_P

This is defined by $N_P = P/\rho N^3 D^5$
It is proportional to the ratio of power draw to liquid density and impeller parameters, including shaft speed. Its principal use is to calculate power draw. As such, it is used in all agitator designs. It is a function of impeller type, Reynolds number and various geometric parameters, such as off bottom clearance to impeller diameter ratio (C/D) and ratio of impeller diameter to tank diameter (D/T).

At high Reynolds numbers (low viscosity), it becomes constant, indicating that for turbulent flow, power draw is directly proportional to liquid density, the cube of shaft speed and the fifth power of impeller diameter.

At low Reynolds numbers (high viscosity), the power number becomes inversely proportional to Reynolds number and the geometric effects disappear. This means that in laminar flow, power is independent of density but is directly proportional to viscosity, shaft speed squared and impeller diameter cubed.
A typical Power Number versus Reynolds number curve is shown in Figure 2.

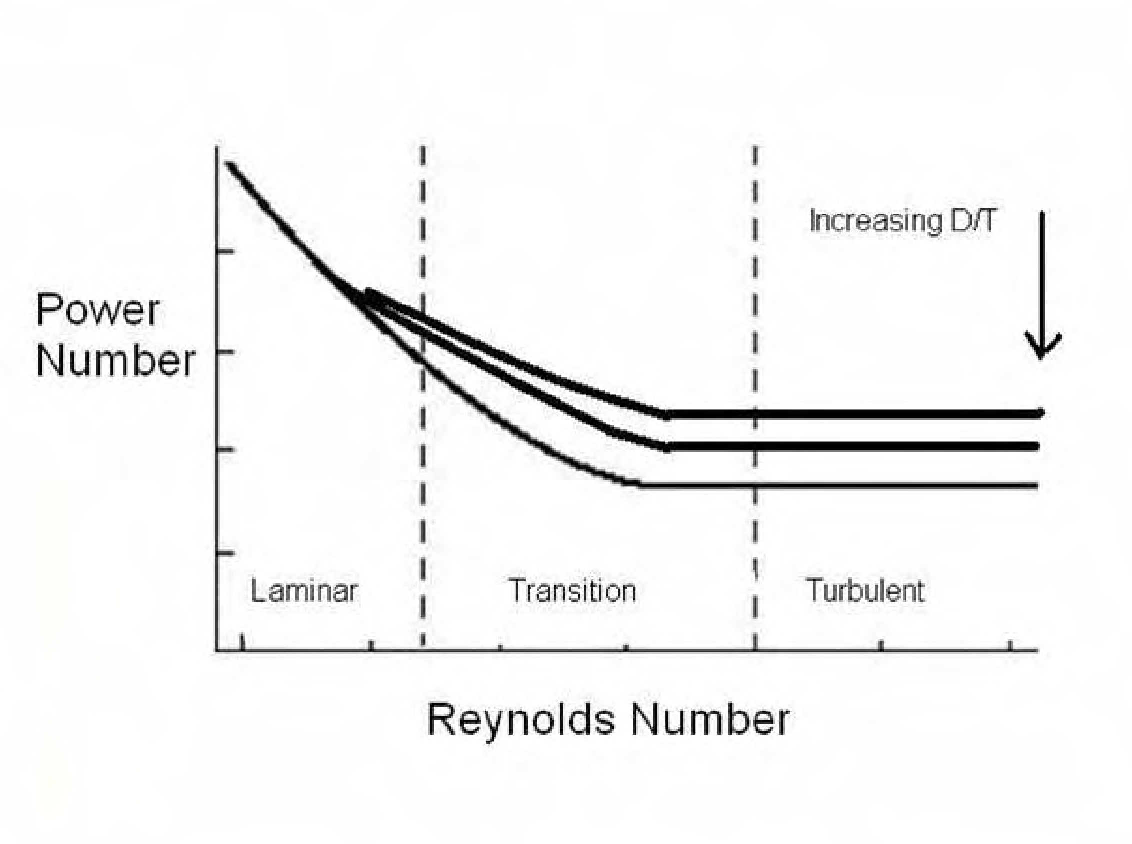


Figure 2: Power Number Curve (typical)

Power numbers have been published for some common impellers. Equipment manufacturers do not always publish such data for their proprietary impellers. Below is a table listing some turbulent power numbers for some common impellers, as a function of D/T. (We will define these impeller types later). More data may be found in the appendix accompanying this course.

D/T	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-blade
0.25	0.33	1.06	1.37	5.5
0.3	0.32	1.05	1.37	5.5
0.4	0.29	1.0	1.37	5.5
0.5	0.27	0.98	1.37	5.5

Figure 3: "Generic" Turbulent Power Numbers

2. Pumping Number, N_Q

This is defined by $N_Q = Q/ND^3$

It may be thought of as being proportional to the ratio of the impeller pumping rate to the impeller swept displacement. Its principle use is to calculate flows and characteristic velocities inside an agitated tank. The pumping number is used for calculations in flow velocity controlled problems, such as liquid blending and motion. It is a function of impeller type, Reynolds number and geometric parameters. Pumping number is constant in both turbulent and laminar flow, but it varies in the transition flow range. It is much higher in turbulent flow than in laminar. In addition, it is mostly independent of geometric effects in laminar flow but shows a decreasing value with increasing D/T in turbulent flow, indicating that the return flow impedes the discharge flow as the impeller gets larger, especially for axial flow impellers.

Figure 4 illustrates the shape of a typical pumping number curve.

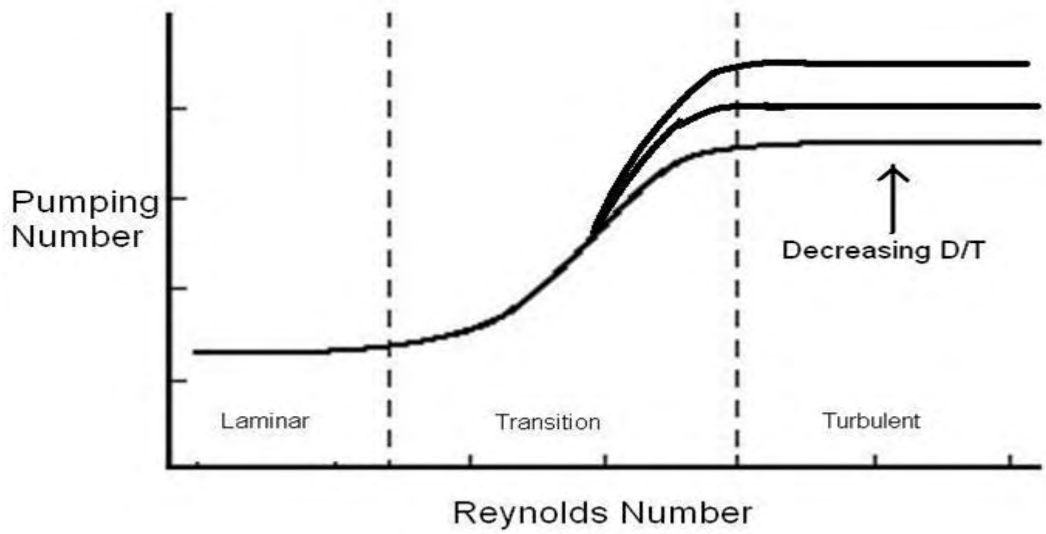


Figure 4: Pumping Number Curve (typical)

Just as equipment manufacturers do not always disclose their power number curves, they also do not always disclose their pumping number curves. Figure 5 lists some turbulent flow values for some common generic impellers. More data are available in the appendix. Users should be skeptical of manufacturer pumping number claims that are substantially higher than those shown herein for a given class of impeller. Pumping numbers above 0.6 are quite difficult to obtain for efficient hydrofoil impellers. As a point of reference, a pumping number of 0.785, or π/4, corresponds to a 1:1 helicoid pitch impeller with zero slippage.

D/T	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade
0.25	0.57	0.80	0.88	0.72
0.3	0.55	0.73	0.80	0.72
0.4	0.53	0.63	0.68	0.72
0.5	0.51	0.56	0.60	0.72

Figure 5: “Generic” Turbulent Pumping Numbers

3. Reynolds Number, N_{Re}

Defined by the equation $N_{Re} = D^2N\rho/\mu$, this number is proportional to the ratio of inertial to viscous forces. Though not used directly to calculate performance, virtually all other dimensionless numbers of design significance are functions of the Reynolds number. These include pumping and power numbers, as well as Nusselt numbers used for heat transfer calculations. The Reynolds number defines the flow regime and level of turbulence. High Reynolds numbers (> 10,000, for example) are characterized by mostly turbulent flow. Low Reynolds numbers (<10) are principally in laminar flow. In between, there is a very broad transition range, which is often characterized by turbulent flow near the impeller and laminar flow near the tank walls.

4. Froude Number, N_{Fr}

This is defined by $N_{Fr} = N^2D/g$, where g is the acceleration due to gravity. This number is proportional to the ratio of inertial to gravitational forces. One use is to correlate such things as surface deformation or vortex formation, which can be useful for incorporating dry powders. Another is to correlate power draw in gas-liquid systems, where gravity has a significant influence due to the low density of gas bubbles and their strong tendency to rise.

5. Nusselt Number, N_{Nu}

This can be defined by N_{Nu} = hT/k or hd_{tube}/k, or similar groups depending on the heat transfer surface. Here h means the convective heat transfer coefficient and k is the liquid thermal conductivity. Nusselt number is used exclusively in correlations for predicting the heat transfer coefficient. It is a function of Reynolds and Prandtl numbers, geometric ratios and impeller type. Later, we will give several useful correlations for heat transfer.

6. Prandtl Number, N_{Pr}

This is defined by $N_{Pr} = C_P\mu/k$, where C_P is the specific heat capacity of the agitated fluid at constant pressure. This number is dependent on fluid properties only, and is a key group in heat transfer correlations.

7. Geometric ratios

Many different ratios are used. Among the more common ones are D/T, Z/T, W/D, C/D and C/T. Most performance correlations, such as power number, pumping number and dimensionless blend time require geometric ratios as part of the relationship.

Heat transfer calculations

Heat transfer calculations are needed for many configurations in agitated vessels. Common surfaces used for heat transfer include vessel jackets, internal helical coils, vertical tube bundles and panel coils used both as baffles and heat transfer surfaces. In general, most surfaces within the tank will have a process-side heat transfer coefficient (h) about 50% greater than found on a vessel jacket.

Below are correlations for the most common surfaces.

Jacketed Heat Transfer to Side Wall

$N_{Nu} = K(N_{Re})^{(2/3)}(N_{Pr})^{(1/3)}(\mu/\mu_w)^{0.14}(T/Z)^{0.15}$

where K depends on impeller type and μ_w is the viscosity of the fluid at the wall temperature (Either guess at this or make an assumption and iterate. However, with an exponent of 0.14, I usually just guess.)

Although impeller types have not been defined yet, they are mentioned briefly here for the purpose of defining the values of K.

For a Rushton turbine (6 blades at 90 degrees mounted to a disc, W/D=0.2) and similar radial turbines, K is about 0.74

For typical 4-bladed pitched blade turbines (45 degree blade angle, W/D=0.2), K is about 0.45.

For generic narrow-blade hydrofoils, K is about 0.31.

Though no data are available in the literature, the author's estimate of K for wide blade hydrofoils is about 0.4

Jacketed Heat Transfer to Vessel Bottom

$N_{Nu}=K(N_{Re})^{(2/3)}(N_{Pr})^{(1/3)}(\mu/\mu)^{0.14}$

As above, K is dependent on impeller type. Here are typical values for the same impellers described above:

K = 0.5 for Rushton

K = 1.08 for pitched blade

K = 0.9 for narrow hydrofoil

K ≈ 1.0 for wide hydrofoil (author's estimate)

Helical Coil Correlation

Defining Nusselt number as $h_c d_t/k$,

$N_{Nu}=K(N_{Re})^{(0.67)}(N_{Pr})^{(0.37)}(D/T)^{(0.1)}(d_t/T)^{(0.5)}$

Where K is as follows:

K = 0.17 for pitched or radial turbines
K= 0.14 for narrow hydrofoils
K ≈ 0.15 for wide hydrofoils (author's estimate)

In the case of more than one bank of helical coils, the author recommends a factor of $(0.82)^{(n_b-1)}$ be applied to the resulting Nusselt number.

Vertical Tube Correlation

Defining Nusselt number as $h_c d_t/k$,

$$N_{Nu}=K(N_{Re})^{(0.65)}(N_{Pr})^{(0.3)}(D/T)^{(0.33)}(2/n_b)^{(0.2)}(\mu/\mu)^{0.14}$$

Where n_b is the number of tube baffles.

K is as follows:
K = 0.09 for pitched or radial turbines
K = 0.074 for narrow hydrofoils
k ≈ 0.08 for wide hydrofoils (author's estimate)

If there is more than one bank of tubes per bundle, a factor of $(0.82)^{(n_b-1)}$ should be applied to the resulting Nusselt number.

A Word on impellers

All of the above correlations have lower values of K for efficient hydrofoil impellers than for less efficient pitched or radial turbines. This may lead some to think that the actual heat transfer is less. However, the low power number of hydrofoils allows them to be applied at larger diameter than the less efficient turbines for a given power draw and shaft speed. The net result is about a 25% higher process-side film coefficient.

Flow Patterns

So far we have covered some fundamental concepts of impeller performance, such as dimensionless correlations for power and pumping. Equally important to an understanding of agitation is the flow pattern produced.

Agitator flow may be broadly grouped into three principal patterns: Axial, Radial and Mixed flow.

Axial flow is defined as having the majority of the flow in a direction parallel to the agitator shaft and tank wall. It is most useful for general mixing and solids suspension, and is in fact the most widely used flow pattern. An illustration of this pattern is provided in figure 6.

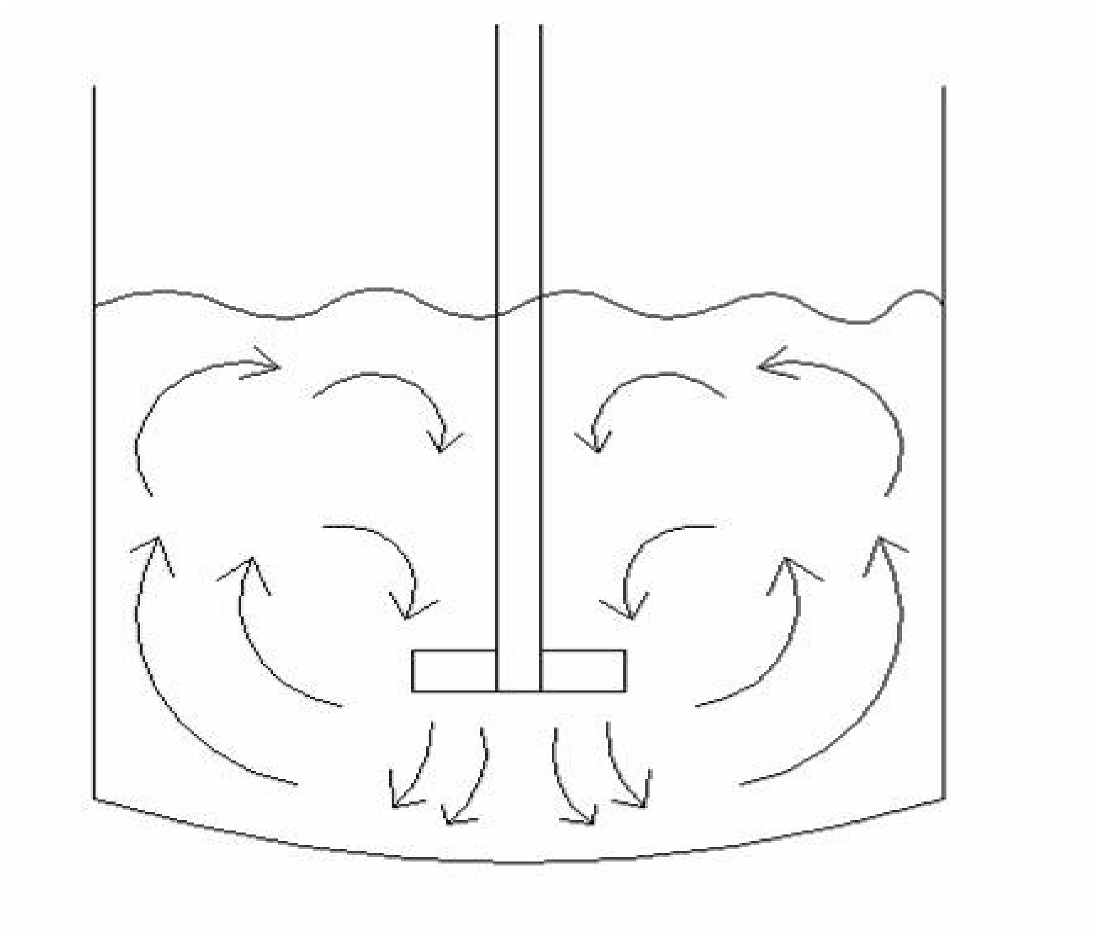


Figure 6: Axial Flow Pattern

Radial flow is defined by having the impeller discharge normal to the shaft. It is used for applications requiring shear, gas dispersion (which does *not* actually require shear) and mixing at very low liquid levels. An illustration of this flow pattern is provided in figure 7.

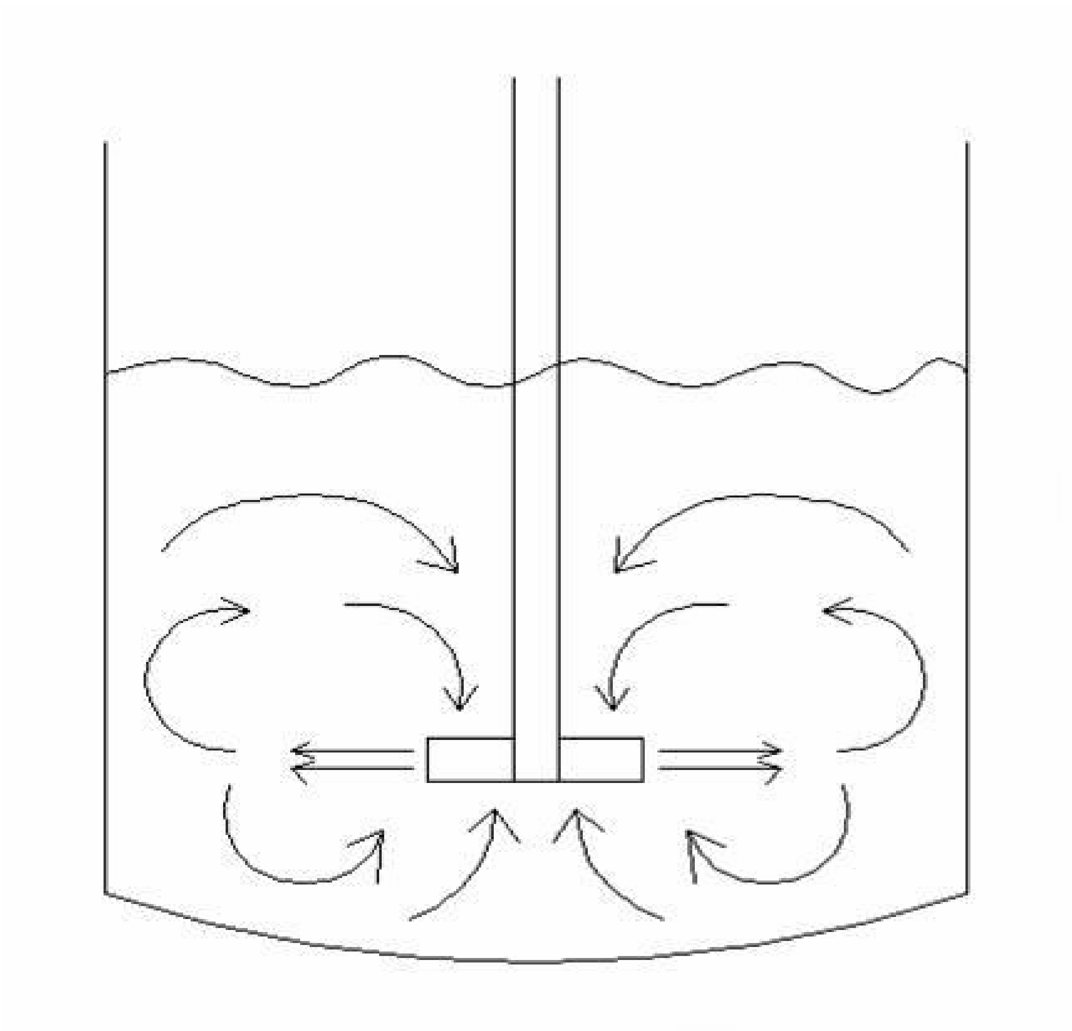


Figure 7: Radial Flow Pattern

Mixed flow is somewhere between axial and radial flow. The impeller discharge is about 45 degrees to the agitator shaft. It can be used for general purpose design. The main use today is in applications where surface vortexing is desirable, such as in incorporating dry powders or pulling in gasses from above the liquid surface. Care must be taken using this flow pattern for solids suspension; if the impeller is too large or too high off bottom, flow reversal will occur, leading to a pile of solids forming in the bottom center of the tank. Figure 8 illustrates this flow pattern.

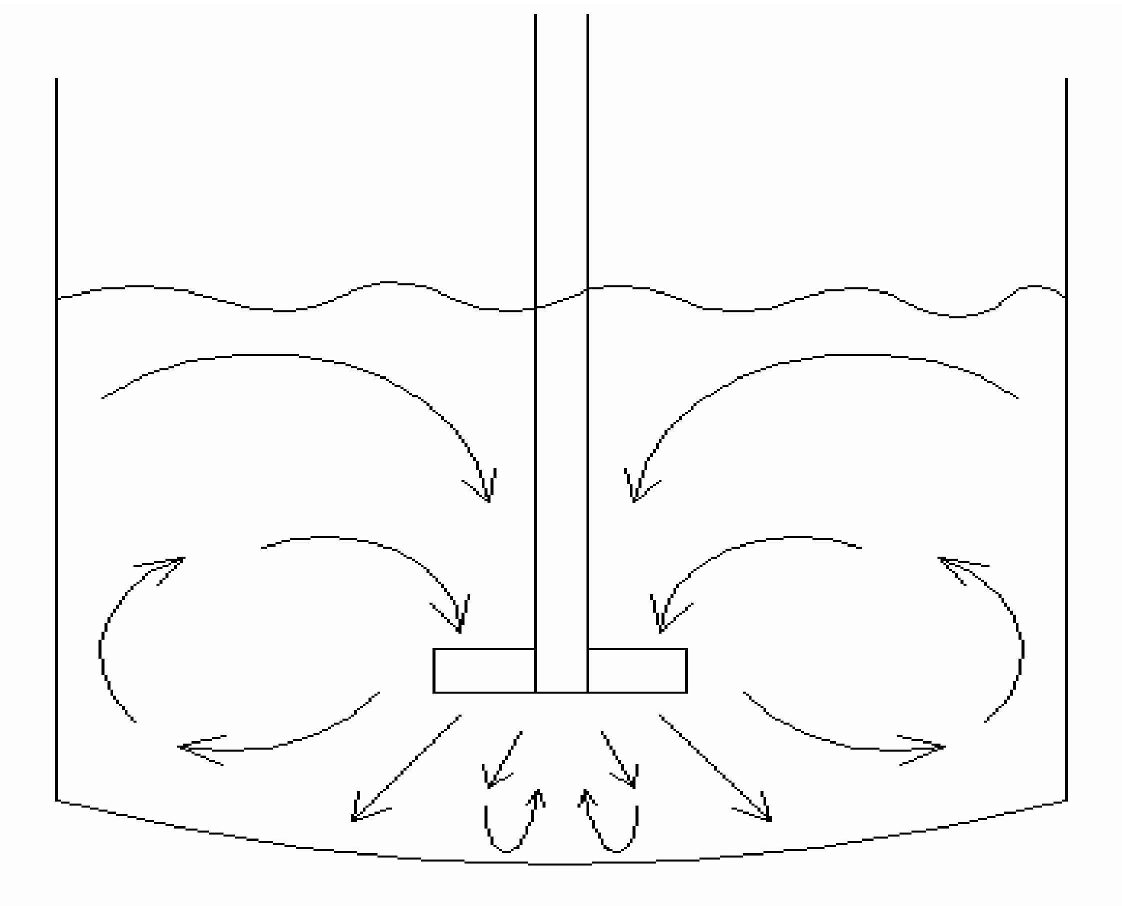


Figure 8: Mixed Flow Pattern

Impeller Examples

Agitator impellers are classified mainly by the flow patterns they produce. Therefore, agitator impellers may be classified as axial flow (further subdivided into high and low solidity styles), radial flow and mixed flow. Several agitator manufacturers have given Benz Technology International, Inc. permission to use illustrations of their impellers in this course and other publications. The use of these illustrations does not constitute an endorsement of these products or companies by Benz Technology International, Inc.

Since axial impellers are classified also by solidity, we will define it here. Solidity is the fraction of the impeller swept circle covered or occluded by the impeller in plan view. Most high solidity impellers on the market have a solidity of at least 0.8; it is possible to go as high as 1.0 by having fully overlapping blades. Low solidity impellers typically have a solidity of less than 0.2. As solidity increases, the pressure potential of an impeller increases. Therefore the flow decreases for a given power draw and shaft speed.

Figure 9 illustrates a typical high solidity axial flow impeller, the MaxFlo series by Chemineer, Inc. (Photocredit Chemineer, Inc.)

Figure 9: High Solidity Impeller (Chemineer MaxFlo Series)

Figure 10 illustrates a low solidity axial impeller, the Chemineer HE-3. (Photocredit Chemineer, Inc.)

Figure 10: Low Solidity Axial Flow Impeller (Chemineer HE-3)

There are many different kinds of radial flow impellers on the market, with differences in power number and gas handling characteristics, among other things. Below we illustrate four offered by Chemineer, Inc.: the S-4, D-6 (also called “Rushton”), CD-6 and BT-6. (Photocredit by Chemineer, Inc.)

All of these, as shown, would rotate in a clockwise direction when viewed from above. The leading edge of the curved radial turbines is the concave side.

Figure 11: Radial impellers by Chemineer, Inc.
(Clockwise from upper left: S-4, D-6, BT-6, CD-6)

The most common type of mixed flow impeller is the simple 45 degree pitched blade turbine, shown below in figure 12. (Photocredit Chemineer, Inc.)
Other types include those with the blade pitch reversed along a split line between the inner part of the blades and the outer part (no illustration available).

**Figure 12: Mixed flow impeller
(Pitched blade turbine)**

Agitator Design Procedure

At this point, we have covered some fundamental relationships in agitation. However, it is difficult to apply these relationships to practical design problems without organizing them into some kind of logical procedure. The following procedure illustrates the steps needed to solve the main categories of fluid agitation problems.

Classify the problem

The main problem classifications are based on the phases in contact with each other. Blending of miscible liquids is classified as a liquid motion problem. Suspending of solids in liquids is a solids suspension problem. Contacting liquids with gas is a gas dispersion problem. Each of these problems can be solved using similar steps, but the magnitude variables and equations are different.

Less common problems include immiscible liquid contacting, dry solids incorporation, and competitive-consecutive reactions. Though these are sometimes possible to design within one of the first three classifications listed, detailed procedures for these classifications are beyond the scope of this course.

Define problem magnitudes

The principal problem magnitudes are size, difficulty and required process result. These magnitudes will vary with each problem classification.

Size is the mass of fluid to be agitated (volume times density.) It is the same for each classification. Note, however, that for solids suspension problems, the density to be used is the slurry density.

Difficulty is the measure of resistance to accomplishing the process result. For liquid motion problems, the difficulty is the fluid viscosity. For solids suspension, it is the product of the weight mean settling velocity times the density difference between the solid and the liquid. For gas dispersion, it is the amount of gas to be dispersed, expressed as a superficial gas velocity.

Desired process result is what the agitator must do to satisfy the process needs. If at all possible, it should be stated in purely physical terms, as agitators ultimately just create motion in the tank; they do not “cause” chemical reaction, heat transfer or mass transfer to take place. Examples of such results are characteristic liquid velocity for liquid motion problems, level of solids suspension for solids suspension problems, and degree of gas dispersion for gas dispersion problems.

If the process result must be stated in chemical process terms, the relationship between these and agitation parameters often must be experimentally determined. The relationship may be very specific for each process. Such relationships often involve a great deal of experimental effort and may only be accurate to about +/- 30%.

Calculate possible process designs

For any given set of problem magnitudes, there are in principle an infinite number of designs that will satisfy them. These involve combinations of various impeller sizes, types and shaft speeds. In practice, actual agitator drives have a fixed number of speeds available to choose from. In general, for most problem classifications (except gas dispersion), larger impellers turning at slower shaft speeds will satisfy the problem magnitudes (giving equal process results) at a lower power consumption, though possibly requiring more torque and a higher capital cost. Years of experience have shown, however, that these energy savings have limits at large D/T ratios. In particular, attempting to save energy by using a D/T ratio greater than 1 will not be successful. (Just checking to see if you are paying attention!) Actually, most low viscosity applications will have flow pattern problems with a D/T ratio above 0.5, so this is often the practical limit for saving energy.

Design the mechanical system

Mechanical design consists of selecting the drive and designing the shaft and impellers. Shaft design must consider stress (shear and tensile) and lateral natural frequency. All designs must avoid operating within 20% of a lateral natural frequency. In large tanks (above 12,000l) it is customary to operate below the first lateral natural frequency. These restrictions may make some designs that will satisfy the problem magnitudes infeasible or impractical. For example, it is impossible to build a unit with d>D.

Detailed mechanical design is beyond the scope of this course.

Economic optimization

Among the (hopefully) several designs that have proven both to satisfy the problem magnitudes and mechanical feasibility requirements, there will likely be differences in capital and power costs. Economic optimization looks at the combined present worth of the capital cost plus operating costs, based on how many hours per year the unit will be operated, how many years the service life is expected to be, and the interest rate used for calculation. Each company probably has standard ways of evaluating such costs.

Although many process engineers are under pressure to keep the capital cost as low as possible, when the present worth of power cost is added in, it is often possible to justify paying a substantial premium to buy a lower-power option. In my experience, it usually costs less than a 20% premium over the lowest capital cost option to cut the power in half.

In the next chapter, we will illustrate all of these principles for a liquid motion problem. If this chapter seemed a bit like drinking water from a fire hose, take heart: it won’t get much worse!

Chapter 2: Agitator Design for Liquid Motion

This chapter will apply the design procedure from the last part of Chapter 1 to problems classified as liquid motion.
First, we will define the problem magnitudes for liquid motion.

1) Size = mass of fluid to be agitated = volume* density
2) Difficulty = viscosity of fluid
3) Process result. Normally this is the ability to overcome fluid property differences and provide complete motion in the tank so as to avoid stratification.

This kind of process result can be related to the characteristic fluid velocity created by the agitator. Now we will show how to calculate this velocity.

We start by calculating the pumping capacity, using the definition of pumping number:

$N_Q = Q/ND^3$

Therefore, $Q = N_Q ND^3$

The pumping number defined above is experimentally measured for each impeller type, and is almost always based on a “square batch” cylindrical geometry, where Z=T. It is an assumption in this procedure that a given impeller will pump the same in other geometries of the same liquid volume. While difficult to prove theoretically, many years of practical experience show that this assumption produces agitator designs that work.

The volume of a square batch cylindrical geometry can be expressed as:

$\text{Volume} = \pi T^3/4$

For non –square batch geometries, solve for T in the above equation; this will be referred to as T_{eq} below.

Characteristic velocity (V_C) is agitator pumping rate divided by the cross sectional area of a cylindrical square batch tank having the same volume:

$V_C = 4Q/\pi T_{eq}^2$

This number is very useful as a measure of overall agitation intensity in the tank. It relates well to the ability to overcome fluid property differences, such as density difference or viscosity ratio. Insufficient velocity will result in “layering” of the tank contents and mixing will occur mainly by diffusion. When these differences are overcome, blending will normally occur quite rapidly.

Scale of Agitation

If V_C is expressed as feet/minute, experience suggests that a range of 6-60 covers at least 90% of blending and motion applications. A “Scale of Agitation” with a range of 1-10 can be calculated by dividing by 6 feet per minute. (It is called ChemScale by Chemineer, Inc., which pioneered this concept in the late 1960s). This scale is now widely used throughout industry.
In practice, a scale of 1 is quite mild, 3 is normal, 6 is vigorous and 10 is both violent and unusual.

Scale of agitation can be related to ability to control fluid property differences as follows:

A scale level of 1 can handle a specific gravity difference of about 0.05 and a viscosity ratio of about 20. A scale level of 3 can handle about a specific gravity difference of 0.2 and a viscosity ratio of 100. A scale level of 10 can handle about a specific gravity difference of 1 and a viscosity ratio of about 25000.

These differences (corresponding to a scale level of 10) are quite unusual to encounter. Most applications requiring such high levels of agitation are those which have the risk of a runaway reaction, where temperature uniformity is required. Many polymer reactors fall into this category.

Scale of agitation can be used as a scale-up tool for motion controlled applications. Once the scale of agitation has been determined, the rest of the calculations are straightforward.

Why not just specify power?

Some might ask at this point, why not specify power or power/volume instead of going through pumping calculations. Basics physics provides the answer:

1) Power = flow*head
2) Small D, high N creates more head
3) Small D, high N requires more power for a given flow than large D, low N

Many combinations of diameter and speed will give equal flow, but power will be higher with high speed, small diameter. One can observe this by trying to create the same level of motion in one's coffee cup using a toothpick versus a spoon.

For a given impeller type, often equal results will be obtained at roughly the same torque investment.

Geometry Effects

Although the basic sizing calculations are based on a square batch, tall batch geometries may require multiple impellers. It is assumed that the same power and speed will give the same process results in a tall geometry as in a square batch by using the appropriate number of impellers.

A single impeller can handle a certain batch height before the flow pattern becomes staged or zoned. Additional impellers can extend this, but the flow zones are not quite additive; the maximum Z/T is not the value for a single impeller times the number of impellers. Table 1 gives geometry guidelines for the zone of control of the bottom impeller and the incremental zones added by upper impellers, for pitched blade and hydrofoil impellers, as a function of Reynolds number.

Impeller type	Reynolds Number	Z/T, 1st impeller	Z/T incremental impellers
Hydrofoil	>1000	1.4	1.1
Hydrofoil	300-1000	1.1	0.9
Pitched Blade	>800	1.2	1.0
Pitched Blade	100-800	0.8	0.7

Table 1: Geometry Guidelines

Sample Problem

The procedure will now be illustrated by use of a sample problem.

A vertical cylindrical tank will be used to agitate a waterlike solution (low viscosity) with a specific gravity of 1.2. Minor additions will be made of solutions of up to a 1.45 specific gravity. The tank diameter is 84" and the liquid volume is 2200 gallons. Because of the maximum specific gravity difference of 0.25, we will design for a scale level of 4. If the impeller diameter is set at 34.6", what shaft speed and motor power are required? Calculate both for a generic low solidity hydrofoil impeller and a standard pitched blade turbine. (The reader is encouraged to try to solve this problem without looking at the solution, then compare to the solution which follows.)

Sample Problem Solution

1) Convert actual batch geometry to square batch: 2200 gallons/(7.48 gallons/cubic foot) = 294.1 cubic feet = $\pi T_{eq}^3/4$; T_{eq} = 7.208 feet = 86.5".
2) D/T_{eq} = 34.6/86.5 = 0.4
3) From Chapter 1 (basics) or from the appendix, look up the pumping numbers. For a narrow hydrofoil, N_Q = 0.53; for a pitched blade turbine it is 0.68
4) Solve for required characteristic velocity at scale level of 4: V_C = 4*6 feet/minute per scale level = 24 feet/minute.
5) Solve for required impeller pumping rate based on definition of characteristic velocity: $V_C = Q/A = 4Q/\pi T_{eq}^2$ = 24'/min; $Q = 24\ \pi T_{eq}^2/4 = 6\pi T_{eq}^2 = 6\pi(7.208\text{ feet})^2 = 979\text{ ft}^3/\text{min}$ = 7325 gpm.
6) For the narrow hydrofoil, $Q = N_Q N D^3 = 0.53\ ND^3$; $N = Q/(N_Q D^3) = 979\text{ ft}^3/\text{min}/(0.53*(2.88\text{ ft})^3)$ = 77.3 rpm.
7) Likewise, for the pitched blade turbine, $N = 979/(0.68*2.88^3)$ = 60.3 rpm.
8) Calculate power from the definition of power number: $N_P = P/\rho N^3 D^5$; $P = N_P\ \rho N^3 D^5$. This step is generally easier to perform in SI units, so as to avoid using g_C or lb mass and lb force conversions.
9) For the hydrofoil, the power number at a D/T of 0.4 is 0.29 (from Chapter 1 or the appendix). Thus, $P = 0.29(1200\text{ kg/M}^3)(77.3\text{ rpm}/(60\text{s/min}))^3(34.6\text{in.}/(39.37\text{in./M}))^5 = 390\text{ kg-M}^2/\text{s}^3$ = 390 watts = 0.52 Hp.
10) Similarly, for the pitched blade turbine, $P = 1.37(1200\text{ kg/M}^3)(60.3\text{ rpm}/(60\text{s/min}))^3(34.6\text{in.}/(39.37\text{in./M}))^5$ = 875 watts = 1.17 Hp.

Comparisons

From the above problem we can make the following comparisons:

1) The pitched blade turbine requires 2.2 times the power of the narrow blade hydrofoil at equal impeller diameter for this case, so its operating cost will be higher.
2) The pitched blade turbine requires 3 times the torque, so it will require a larger gear drive and probably a larger shaft diameter, so its capital cost will be higher.
3) The pitched blade turbine turns 73% as fast; its tip speed is

lower, and its maximum shear rate will therefore be lower.

Use of commercial software

Most agitator manufacturers have their own software, which may be specific to their products and is not available to the general public. Moreover, data on proprietary impellers is seldom available. However, there are some commercial agitator design software packages available, such as that offered by ReyNo, Inc. (Disclosure: Benz Technology International, Inc. represents ReyNo Inc. software) Such software allows rapid evaluation of alternatives especially in transition flow ranges, where results often must be iterated due to changes of pumping and power numbers as a function of Reynolds number.

Impeller efficiency

In this chapter, we have seen that there can be very large differences in impeller performance. Now we will discuss a way to quantitatively compare them. Some people use the term “efficiency” to compare performance. How does this apply to agitators?

In the strictest engineering sense, efficiency = output power/input power. To use this concept, we must clearly define system boundaries so that “input” and “output” are unambiguous. This is problematic for agitators.

If we define the system boundary to be the impeller itself, all of the power reaching the impeller via the agitator shaft is transmitted by the impeller to the fluid as some combination of flow times head. In this sense, all impellers are 100% efficient.

On the other hand, if we define the system to be the entire agitated tank, there is no net flow created by the agitator; it all turns into heat. (To prove this, imagine a steady state agitated tank. Then imagine suddenly removing the agitator. The flow will come to a stop. Where did the energy go?) Thus, all typical agitated tanks have an efficiency of zero. (The exception is the special case of a tank equipped with an agitator that actually pumps liquid through it, but this arrangement is not found in the pharmaceutical industry. Moreover, such an arrangement is technically a kind of pump. In fact, an agitated tank is analogous to a deadheaded centrifugal pump.)

So, we need some other way to compare impellers besides efficiency; the concept does not work well for agitators.

One way is to compare impeller pumping at equal impeller power and equal shaft speed. (Impellers with different power numbers will have unequal diameters). This method is equivalent to comparing two identical agitators in terms of power draw, shaft speed and gear drive size; the only difference is the impeller used to load the machine. Thus, operating cost is the same and capital cost is similar.

We will call this comparison concept “effectiveness”. It can be shown that, at equal shaft speed and power, the impeller pumping relates to its power and pumping numbers as follows: $Q = CN_Q/N_P^{0.6}$
We will therefore define effectiveness as $N_Q/N_P^{0.6}$.

Effectiveness example

The table below compares 3 different impellers: a pitched blade turbine, a narrow blade hydrofoil and a wide blade hydrofoil. The comparison uses D/T ratios chosen to give equal power draw at equal shaft speed. The power draw at fixed shaft speed is proportional to the group $N_P(D/T)^5$, which is used to verify that the comparisons are at equal power.

Impeller Type	D/T	N_P	$N_P(D/T)^5$ x 1000
Pitched blade	0.300	1.37	3.33
Narrow hydrofoil	0.409	0.29	3.32
Wide hydrofoil	0.316	1.05	3.32

Table 2: Effectiveness example at equal power and shaft speed

Comparison results

Table 3 shows the effectiveness parameter comparison results.

Impeller Type	D/T	N_P	N_Q	$N_Q/(N_P)^{0.6}$
Pitched blade	0.300	1.37	0.80	0.662
Narrow hydrofoil	0.409	0.29	0.53	1.11
Wide hydrofoil	0.316	1.05	0.72	0.70

Table 3: Comparison Results

Relative Results

If we compare the effectiveness on a relative basis, which is equivalent to comparing relative pumping at equal power and speed, we get the following:

1) Pitched blade turbine: 1.0
2) Narrow hydrofoil: 1.68
3) Wide hydrofoil: 1.06

Data needed to compare impellers

If we are to be able to compare the effectiveness of various impellers, we need power number and pumping number as a function of impeller type, D/T and Reynolds number. Such relationships have been published for some impellers, but many manufacturers have proprietary impellers for which such data are not available. This leaves the end user in the unenviable position of taking vendor claims on faith. However, as a general rule, impellers that look basically similar and have close to the same power number will probably have similar pumping performance. It is fairly easy for an end user to measure power number. It is not so easy to measure pumping number. Such measurements can be made with a variety of techniques, such as laser-Doppler velocimetry, digital particle image velocimetry, particle streak photography, hot wire anemometers, etc. Various texts treat these methods, which will not be detailed here.

Chapter 3: Gas Dispersion Principles and Issues

This chapter is a brief introduction to the major principles and issues common to gas dispersion applications. More detail will be given in sections on fermentation, fermenter impeller design and cell culture design.

Misconceptions

There are several misconceptions commonly believed about gas dispersion. We will clear some of these up before proceeding further.

1) Gas bubbles cannot be "sheared" Therefore, shear is not a part of gas dispersion design, and impellers designed to create shear are unnecessary.
2) Only a denser material than the continuous phase can be sheared; therefore impeller tip speed is irrelevant in dispersion calculations (though it may affect other things)
3) Axial flow impellers *can* disperse gas, and will create just as high a mass transfer rate as radial impellers at equal power input, provided they are not flooded. Axial impellers cannot generally handle as much gas as radial, they do not drive the bubbles to the wall as effectively, and their relatively low power numbers make it difficult at times to invest the relatively high power inputs required for gas dispersion.

Dispersion Mechanisms

Almost all power drawn by impellers in a gas-liquid system is due to drag in the liquid; the gas has such low density that it contributes little to drag or power draw. Also, the gas properties do not control bubble formation; the interfacial tension and density of the liquid do. Dispersion mechanisms operate principally on the liquid, not the gas. The principle mechanism responsible for dispersion of gas is the creation of turbulent eddies in the liquid, which catch gas in their low pressure zones. The bubbles elongate in these eddies until surface tension forces result in a collapse of larger bubbles into a "string" of smaller bubbles.

Turbulent eddy formation, based on isotropic turbulence theory (which assumes the fluctuating velocity components making up the turbulence are evenly distributed in all spatial dimensions), should be directly related to power dissipation per unit mass. While an agitated flow field is not exactly isotropic, the power/mass parameter still works very well at predicting such things as bubble size and interfacial area.

Power Draw Effects

The presence of gas in an agitated tank affects power draw. Generally it is a reduction in power draw, but at very low gas flow rates, the power draw may go up somewhat, due to higher head imposed on the impeller.

Gas can reduce power draw in two ways:
1) Reduction of bulk density due to gas holdup. This effect occurs with all impeller styles.
2) “Streamlining” of the apparent impeller shape by formation of gas pockets on the low pressure side of the blade. This is analogous to reducing drag coefficients on a car. Impellers which can form gas pockets experience this effect; if no gas pockets form, this effect will not happen.

Evolution of radial flow impellers

Originally, most agitators had radial flow impellers (typically Rushton style, named for Professor Henry Rushton, whose graduate student developed the design as an assignment), regardless of application. By the 1960s, however, the Rushton style was replaced by axial and mixed flow impellers for most applications except for gas dispersion. Rushton style impellers have been extensively used in fermentation since the commercialization of Penicillin in the 1940s.

The Rushton impeller has flat blades affixed to a central disc. Research by John Smith, Klaus V’ant Riet and others in the 1980s led to the idea that gas pockets could be reduced by using concave blade shapes, with the concave side being the leading side. Smith studied an impeller which had symmetrical concavity based on cylindrical sections. Later, others made the concavity deeper than cylindrical sections in an effort to more nearly approximate the gas cavity shape.

(Scaba SRGT, ICI-Middleton and Ekato Phasejet are all examples of this concept.) Chemineer took it a step further with their BT-6 impeller, which added the feature of being asymmetric about the disc, due to gravity acting in only one direction on the gas. We will illustrate some of these impellers from a viewpoint of what happens to the gas pockets at high gas flow rates.

Rushton impeller

Figure 1 shows a large gas pocket formed behind a blade of a Rushton impeller. Such pockets or cavities cling to the back of the blade at high gas flow rates. They cause considerable streamlining and power draw reduction. When gas flows get too high, the pockets can bridge between blades, resulting in flooding and severe mechanical instability. Such cavities also result in lower gas handling capacity than would be obtained if the pockets could be reduced or eliminated. That is why researchers investigated the idea of concave bladed impellers.

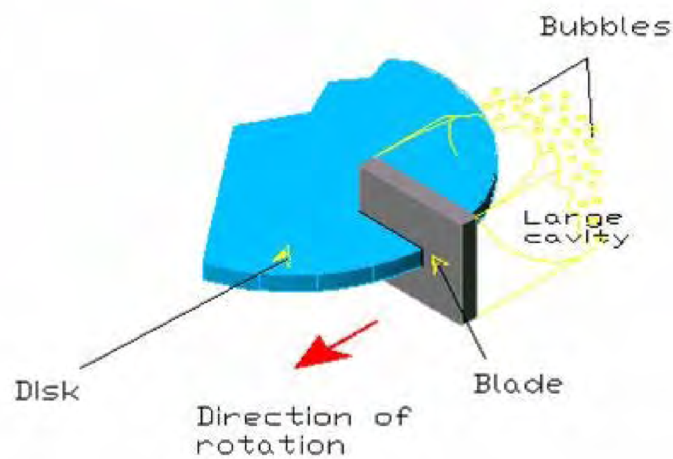


Figure 1: Rushton blade with large cavity

Modified Smith turbine (Chemineer CD-6 and similar)

The original Smith turbine had a concavity of about 120 degrees. The Chemineer CD-6 and similar turbines today commonly have a concavity of 180 degrees as shown in Figure 2. The concave shape reduces the cavity size, reduces streamlining and results in much less power drop when gassed. It also increases net pumping and more than doubles gas handling capacity compared to a Rushton.

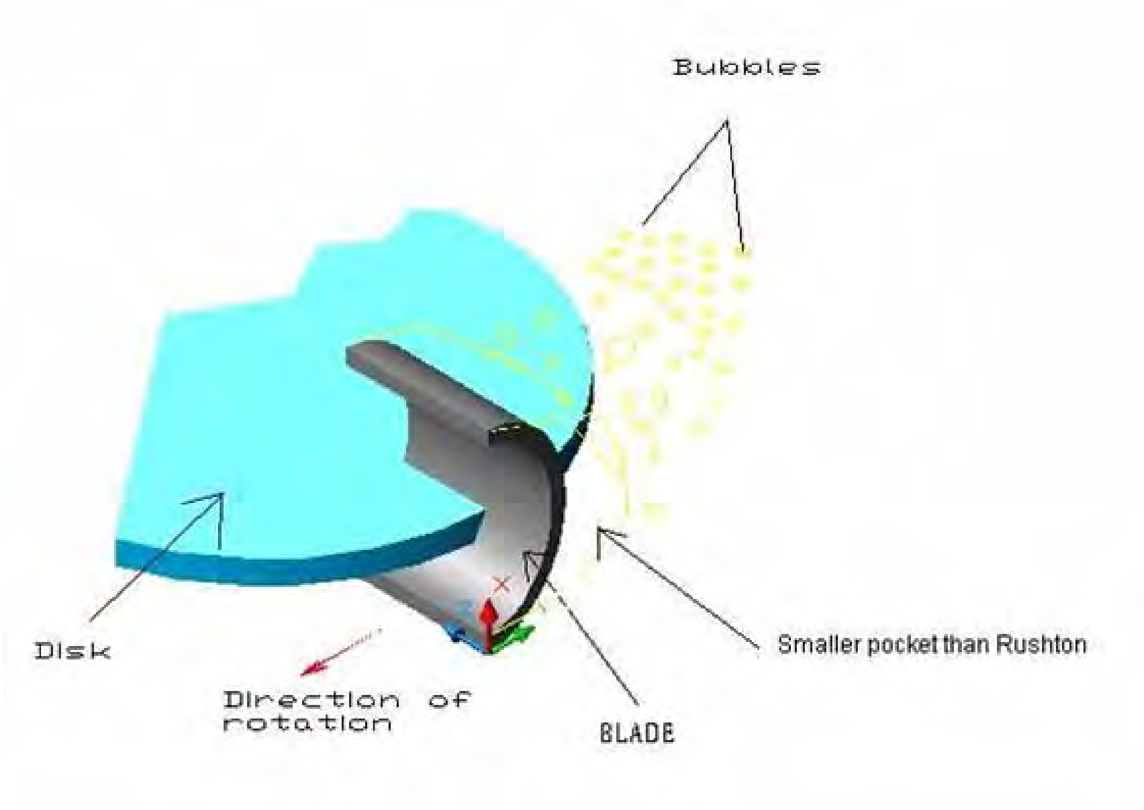


Figure 2: 180 Degree Concave Blade Pockets

Deep concave turbine example: Ekato Phasejet

As previously mentioned, there are several varieties of impellers which have deeper blade sections than semi-cylindrical, which are symmetrical about the disc plane. One such impeller is the Ekato Phasejet. Figure 3 is a photo of an

actual impeller, though the U.S. patent illustration shows a serrated conical disc instead of a simple flat one. Although no data are given on gas pocket formation, it is expected that gas cavities will be smaller than on the 180 degree turbine in figure 2. The gassed power drop is between the 180 degree turbine and that of the Chemineer BT-6. Gas handling capacity is probably between these two as well, though no published data are available.
The photo is by Ekato, Inc.

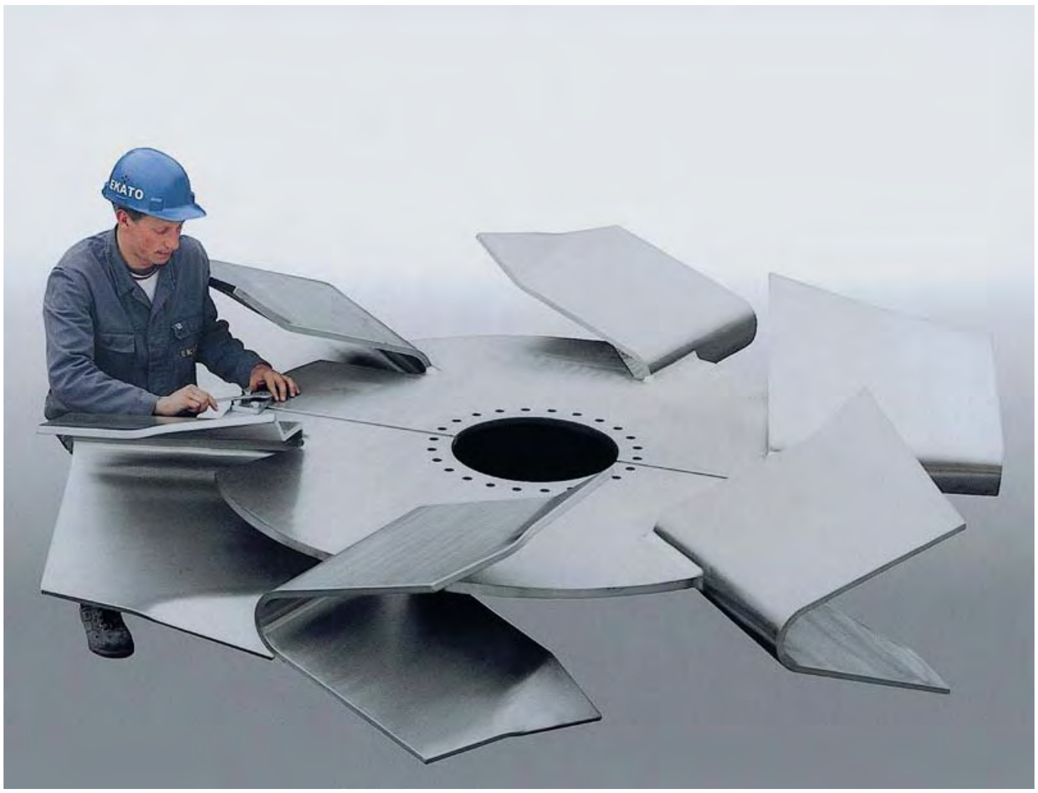


Figure 3: Ekato Phasejet

Chemineer BT-6

In the late 1990s, Chemineer introduced the BT-6, which is a deep concave impeller with asymmetric blade shape. The blade curvature is different above and below the disc, and the top half of the blade overhangs the lower half. This design is based on studying the cavity shape and trying to eliminate the cavities so as to minimize power drop. It is also based on the idea that gas rises, so there is a need to “catch” the gas with the overhang. As shown in Figure 4, the gas pockets appear to be eliminated. The impeller has high pumping and can handle more than 5 times the gas flow compared to the Rushton. It likely has the least reduction in power draw due to gassing of anything on the market; the power draw reduction appears to match the density reduction due to gas holdup.

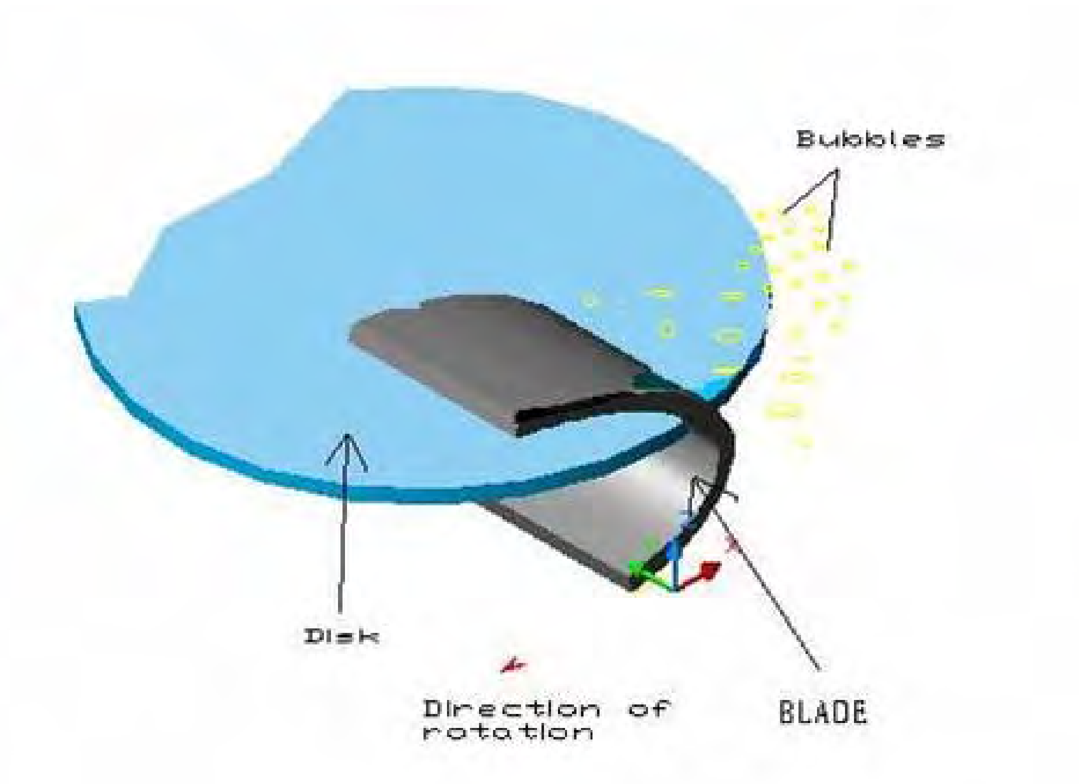


Figure 4: BT-6 pockets (or lack thereof)

Typical power draw effects: examples

Here we introduce a new dimensionless group, the Aeration Number (sometimes called the gas flow number), N_A, which equals Q_G/ND^3. Here Q_G is the actual volumetric gas flow at the impeller. The Aeration Number is proportional to the gas flow divided by the impeller pumping capacity. It is used in flooding correlations and power draw correlations. Below we will compare the ratio of gassed to ungassed power of several impellers under highly aerated conditions typical of fermenters. Specifically, for these comparisons the Aeration Number is

0.16 and the Froude Number is 0.5.

1) Rushton: 0.4
2) 180 degree concave: 0.65
3) Ekato Phasejet: 0.80
4) Chemineer BT-6: 0.84
5) Narrow blade hydrofoils: 0.76
6) Wide blade hydrofoils: 0.77

Importance of actual power draw

At this point, some might ask, Why not simply design the agitator for its ungassed power, and let it unload when gassed? The answer has to do with mass transfer. The overall mass transfer coefficient in a gas-liquid system depends on the *gassed* power draw. Specifying motor size only could result in insufficient power for the target mass transfer if the system unloads substantially with increasing gas flow. So, impellers should be sized to deliver the required power draw under peak gas flow conditions. When impellers are sized to give a target gassed power draw, how the motor is to be sized can be very important. If the motor is to be sized for the ungassed power draw, it could mean very oversized equipment. For example, if a Rushton impeller were used, the motor might have to be 2.5 times as powerful as needed for the gassed condition. The gear drive, shaft, etc. would also have to be similarly sized. Impellers which unload less would not require the same degree of oversizing, which gives them an advantage. Besides using impellers which unload less, it is possible to avoid such extreme oversizing by using two-speed motors or variable speed drives, so that the agitator speed is reduced when running at reduced gas flow rates. However, most multispeed motors and variable speed drives are constant torque devices rather than constant power, so less power is available at reduced speed.

In addition, proper distribution of power among multiple impellers is critical. Too little in the upper impellers can result in coalescence and insufficient mass transfer in the upper zones of the tank. Too little in the bottom fails to make effective use of the increased driving force there. For any given impeller system, there is an optimum power distribution. This distribution is generally considered to be proprietary. Benz Technology International Inc. uses specific power distributions which have been found to be optimal.

Flooding

Another consideration is impeller flooding, a condition in which more gas is entering the impeller than it is effectively able to disperse. There are several definitions of flooding in common use. The one we will use is the point where the gas bubbles are not driven to the tank wall roughly within the plane of the impeller. (Some mass transfer enhancement happens at conditions just below this requirement, so this is a slightly conservative definition.)

Complete Dispersion

This is defined as a condition whereby the lower impeller is able to drive at least some bubbles to the tank bottom.

Illustration of flooding and complete dispersion

Figure 5 illustrates the transitions from the flooded condition (left tank) to just dispersed (middle) and completely dispersed (right). The transition can be thought of as the result of increasing shaft speed at constant gas flow (left to right) or as increasing gas flow at constant shaft speed (right to left).

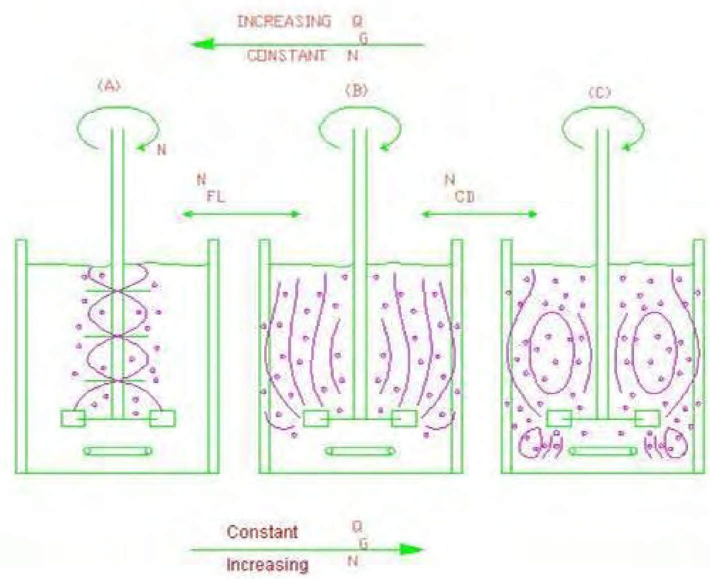


Figure 5: Flooding, complete dispersion

Holdup or gas volume fraction

When gas is dispersed into liquid, it reaches a steady-state condition wherein some of the gas remains in the liquid for a time. This volume fraction, expressed as the ratio to liquid volume, is called holdup. In common industrial applications, it ranges from 0 to about 0.6. In aerobic fermenters, the normal range is 0.1 to 0.2, though some can be much higher.

Room must be allowed for in the vessel design both for holdup and gas disengagement. Holdup correlations are broth-specific. Holdup is not the same as foam, which often must be addressed by use of antifoam compounds.

In practice, this author has observed that end users will keep increasing the broth volume until broth comes out of the vent, thus establishing the true maximum capacity of the vessel.

Gas/Liquid mass transfer

Enhancement of gas/liquid mass transfer is usually the primary job of agitators selected for gas dispersion, especially in aerobic fermenters. An important secondary function is liquid blending, so as to minimize gradients in composition, especially the dissolved gas concentration. With living systems, severely unequal dissolved oxygen concentrations can stress or even kill cells as they pass from high to low DO zones, and the product distribution can be affected.

The main governing equation for mass transfer, in simple form, follows, where M is the mass transfer rate per unit of liquid volume:

$$M = k_l a(C_{sat}-C)$$

In this equation, k_l is the liquid film coefficient and a is the interfacial area per volume. Generally it is impossible to experimentally separate these variables, so most correlations combine them into $k_l a$, which has units of reciprocal time. C_{sat} is the saturation concentration of the gas in the liquid adjusted to local temperature, pressure and composition. C is the actual dissolved gas concentration. The expression in parentheses is called the driving force; if it is zero, no mass transfer will take place.

For tall vessels (>3M height; some fermenters are more than 30M tall), the driving force should be expressed as a log mean, as there is a substantial gradient in absolute pressure:

$$((C_{sat}-C)_1-(C_{sat}-C)_2)/\ln((C_{sat}-C)_1/(C_{sat}-C)_2)$$

For most gas-liquid systems at low pressure, the gas saturation obeys Henry's law, which states the concentration at saturation is proportional to the absolute partial pressure of the gas. The proportionality constant is called the Henry's law constant, H:

$$C_{sat}= \pi_{gas\ solute}/H$$

The value of H is a function of the gas-liquid system, the temperature, and the presence of other dissolved species. The CRC Handbook of Chemistry and Physics and Perry's Handbook are good references. Also, it can be experimentally measured for specific systems by letting them go to saturation.

A useful relationship is that 1 standard cubic foot of air (60F, 1 atm) contains 1.195 gram moles. Air at 21% oxygen contains 0.251 gmol of oxygen per standard cubic foot.

How does this relate to agitation?

The overall mass transfer coefficient is a function of agitation, gas flow and maybe other parameters. The most common form of correlation is:

$k_l a = A(P/V)^B (U_s)^C$

Where P = agitator power, V = liquid volume and U_s is the superficial gas velocity (gas volumetric flow divided by tank cross sectional area). The constants A, B and C must be experimentally determined; they depend on broth composition. Published equations for air/water systems may be used for estimates, but they are often only +/- 60% accurate. One such equation, using units of watts, seconds, meters, and kg (instead of volume) uses values of 0.946 for A and 0.6 for both B and C. For modestly viscous fluids, the result can be multiplied by viscosity in Cp to the -0.5 exponent. Do not use this for viscous gums, such as xanthan.

The correlation constants do not appear to be significantly dependent on impeller type. The principle agitation parameter is invested power.
Commonly, B and C will be about 0.6, +/- 0.2

Even a broth-specific correlation will often be no more than +/- 30% accurate due to the many variations in living systems, so safety factors and judgment are needed. Solving the mass transfer equation for agitator power is one major design goal. Note that there are combinations of airflow and power that will produce equal results.

Some people have written that the constants seem to vary as a function of scale. This author believes it is more likely that the constants vary somewhat with actual values of P/V and gas velocity, which tend to be different at different scales of operation.

Summary of chapter 3

1) Design for gas dispersion must take into account agitator power required for mass transfer
2) Power reduction due to gassing affects impeller/motor sizing schemes
3) Flooding must be avoided for good results
4) Holdup affects power, vessel size needed
5) Solving mass transfer equations leads to agitator power requirements

Chapter 4: Agitation Scale-Up

What is scale-up?

Many definitions of scale-up have been described in technical literature and texts. Some are based on dynamic similarity; some are based on kinematic similarity, etc. For our purposes, scale-up consists of the production of equal results in a larger scale to those which were achieved in a smaller scale. Not all results can be scaled simultaneously and different kinds of results scale-up differently.

Scale-up results: examples

Generally, the kinds of results which might be scaled include physical and process results. Techniques may differ for each one.

Examples of process results include rate of production, yield, purity, mass transfer rate, product distribution, cell viability, crystal nucleation rate, crystal size, crystal growth rate, and many more.

Physical results depend more directly on agitation and may sometimes be related to process results. There are many possible physical results which can be scaled, including mass transfer coefficient, degree of solids suspension, bubble size distribution (gas-liquid), droplet size distribution (immiscible liquid-liquid), composition uniformity, blend time, maximum shear rate, average shear rate, eddy size distribution, heat transfer coefficient, heat transfer rate, cooling or heating time, solid particle attrition rate, solid particle size distribution, etc.

Process Result Scale-Up

Scaling up process results is intrinsically very complex. To do so requires an intimate knowledge of all system relationships. Rather than being a true scale-up, such an activity more closely resembles a design procedure. It may not be possible to duplicate process results exactly in two different scales of operation.

Here are a couple of examples of process result scale-up and limitations:

1) Aerobic Fermentation. For this process it is possible to scale-up on the basis of an equal mass transfer rate per liquid volume, which often leads to roughly the same process result. However, it is impossible to maintain equal dissolved oxygen distribution, which may result in several inequalities, such as different yield or product distribution. Cell viability may be an issue in some cases due to low DO at the top of the vessel.

2) Competitive–Consecutive Reaction. Over a very small range of scales, this might be possible. Over a larger range, it is not possible to maintain equal product distribution. The theoretical size of equipment required becomes very large very quickly. Even if such equipment is installed, it may not work because the tank may become aerated due to surface entrainment, making the true degree of agitation less than predicted.

For process scale-up, the following variables can be manipulated in most cases: agitation parameters such as impeller diameter, types of impeller, number of impellers and shaft speed; tank geometry (such as changes in aspect ratio or baffling); process conditions such as temperature (including cooling medium) and pressure; feed rates and compositions. Such an array of variables gives many degrees of freedom. However, scale-up of the agitation system tends to be based more on physical results.

Physical result scale-up

There are fewer variables available for manipulation for physical results. These include shaft speed, N; impeller size, D; number of impellers, type(s) of impellers, tank geometry, and in some cases, fluid properties such as density and viscosity. (In these cases, a substitute fluid is used instead of the process fluid to mimic certain fluid behaviors at different Reynolds number values).

In most cases, it is possible to duplicate 1 or 2 physical results upon scale-up. It is almost impossible to duplicate 3 or more physical results except over a very small scale range. We will look at some of these cases next.

Scaling a single physical result

The simplest and surest way to scale a single physical result is on the basis of geometric similarity. This method fixes all dimensions, such as tank diameter, impeller diameter and liquid level in the large scale. The only variable left to adjust is shaft speed.

Figure 1 illustrates the concept of geometric similarity.

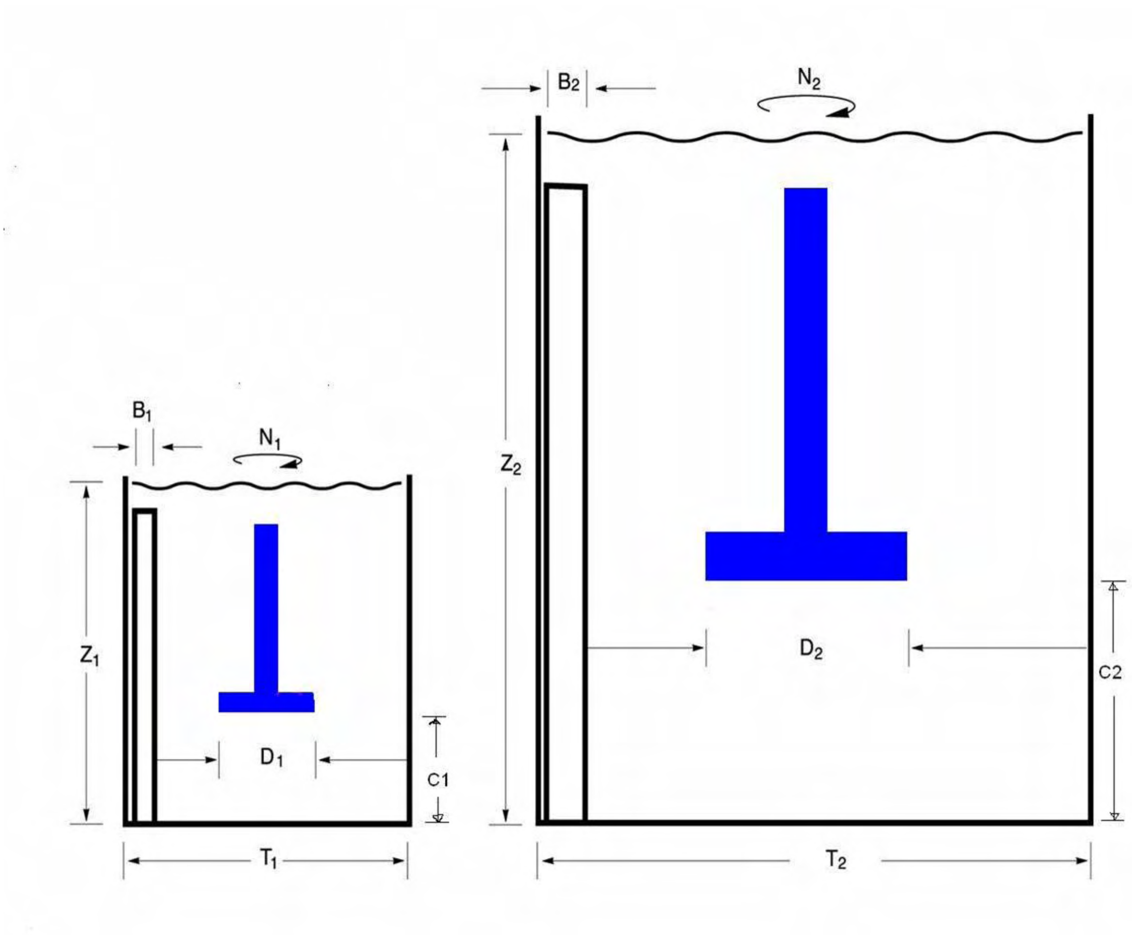


Figure 1: Geometric Similarity

In this figure, all corresponding dimensions are related by the same ratio, R:

$R = T_2/T_1 = D_2/D_1 = Z_2/Z_1$, etc.

In case exact geometric similarity cannot be maintained, good results will be obtained by defining R as (Volume ratio)$^{1/3}$ and using this value of R to define the full scale impeller diameter. Of course, the impeller style and internal ratios, such as W/D, must also be geometrically similar. In the event the full scale geometry is so different as to require a different number of impellers, it is sometimes reasonable to divide the tank into sections or zones conceptually to scale multiple impellers. For example, if the small scale tank has a Z/T ratio of 1 and the full scale has a Z/T ratio of 2, scale as though the full scale is 1:1 based on tank diameter but add a second impeller.

Scaling shaft speed, N

Since we have fixed the geometry upon scale-up, the only variable we can manipulate is shaft speed. Shaft speed scaling follows the simple exponential scaling rule below:

$N_2/N_1 = (1/R)^n$ or $N_2 = N_1(1/R)^n$

The value of n, called the scaling exponent, depends on the physical result to be scaled. It can be derived from fundamental equations or determined empirically for some results. Smaller values of n lead to higher shaft speeds and therefore larger agitators upon scale-up.

Several scaling exponents are in common use. These will be described below. The symbol "≈" will be taken to mean "is proportional to", as my font package regretfully does not have a symbol for this.

1) $n = 2$
This result gives equal Reynolds number, which can readily be seen by inspection of the Reynolds number definition, $D^2N\rho/\mu$. Mostly, this is used for academic research into flow patterns and turbulence, as no useful process-result related physical results scale this way. Sometimes it is necessary to have equal Reynolds number while simultaneously scaling another result. Viscosity is often changed to accomplish this.

2) $n = 1$
This rather common scaling rule actually gives several kinds of equal physical results, which will be shown below.

1. Equal tip speed (πND). Since maximum shear rate is proportional to tip speed, this scaling rule coincidentally gives equal maximum

shear rate.

2 Equal torque/volume ($\approx N^2D^5/T^3$) $\approx N^2D^2$

3 Equal impeller thrust/area ($\approx N^2D^4/T^2$) $\approx N^2D^2$

4 Equal characteristic velocity ($\approx ND^3/T^2 \approx ND$); equal scale of agitation

5 Equal ability to overcome fluid property differences (empirical)

3) n = 2/3

This exponent is often used for gas dispersion. It has both theoretical and empirical significance:

1 Equal power/volume ($\approx N^3D^5/T^3 \approx N^3D^2$)

2 Equal drop size in liquid/liquid dispersion (drop size/D $\approx N_{We}^{-3/5}$; $N_{We} \approx N^2D^3$; drop size $\approx N^{-6/5}D^{-4/5}$

3 Equal overall mass transfer coefficient in gas liquid systems (partly empirical, partly based on isotropic turbulence theory, which predicts dependence on power/mass)

4 Equal dry solids incorporation rate/tank cross sectional area (empirical)

4) n = ½

Not very commonly used. It is derived from the Froude number:

1 Equal Froude number (N^2D/g)

2 Geometrically similar vortex depth (rigorously correct only if equal Reynolds number simultaneously exists, which requires different kinematic viscosity fluids in each scale. However, if both scales have fully developed turbulent flow, Reynolds number drops out as a correlating parameter.)

3 Equal agitated side heat transfer coefficient ($\approx N_{Re}^{2/3} \approx D^{4/3}N^{2/3}$)

5) n = 0

Very rarely used, as it results in extremely large equipment over even a small scaling range. Not usually practical. Actual agitation may be less than expected when scaling this way, due to aeration of the liquid.

1 Equal shaft speed in both scales (N fixed)

2 Equal blend time (t_b*N = constant) in laminar flow or turbulent flow. This relationship does not hold if the flow is in transition upon scale-

up, as the dimensionless blend time, t_b*N, is constant in both laminar and turbulent flow (much higher values in laminar flow, however) but changes considerably in transition flow.

3 Equal product distribution in competitive-consecutive reactions; equal composition in reacting systems.

Solids suspension scale-up: a special case

Solids suspension does not scale-up using a fixed exponent for all cases. Instead, solids suspension has a variable scaling exponent, which depends both on the settling velocity of the solids and the relative scale of operation. The value of this exponent approaches 0.5 as the settling rate approaches infinity, and approaches 1.0 as the settling rate approaches zero.

Since there are so many factors affecting solids suspension, use of software such as that offered by ReyNo is recommended.

Cautionary note

The single-result method just given is rigorously correct only in turbulent flow, where certain groups remain constant and independent of viscosity. It will also work well if the Reynolds number is constant in most cases. Change in flow regime requires detailed knowledge of system behavior. However, most errors will be conservative when scaling up.

Single result example

Extremely different machine sizes and power draws will result from using different scaling exponents when starting from the same small scale and scaling to the same production scale. In the following example, the fluid to be agitated is waterlike, having a specific gravity of 1 and a viscosity of 1 cP. The impeller to be used will be a generic hydrofoil, with a power number of 0.33 and a pumping number of 0.54, at a D/T ratio of 1/3. The tank dimensions and small scale agitator speed are shown in Table 1.

Parameter	Small Scale	Large Scale
Tank Diameter, mm	300	3000
Impeller Diameter, mm	100	1000
Volume, l/gallons	21.2/5.6	21,200/5600
Shaft speed, rpm	720	To be determined

Table 1: Scale-up example data

To scale-up, we must determine the full scale shaft speed and power. We will show these in table 2 as a function of the scaling exponent used. We will also show the scale of agitation for comparison purposes. The smaller vessel has a scale of agitation of 3.

Exponent, n	N, rpm	Power, kW	Scale of agitation
1	72	0.57	3
2/3	155	5.7	6
1/2	228	18.1	10
0	720	571	30

Table 2: Full scale results

As one can see, the results are indeed very different as a function of the scaling exponent. The power varies over a 100:1 range, and the scale of agitation varies over a 10:1 range. It is highly unusual to need a scaling exponent less than 0.5.

For simple blending problems, an exponent of 1 would suffice, which in this case gives us a scale of agitation of 3, same as in the small scale.

Scaling two physical results

Because geometric similarity leaves us only one variable to manipulate, we cannot use it to scale two physical results simultaneously. We must manipulate the geometry in some way to scale two results. Possibilities include changing D/T ratio, type of impeller or number of impellers. No general rules apply; it depends on which two specific results are desired to remain constant.

Two-physical result strategy

Let us suppose we are trying to scale on the basis of equal mass transfer coefficient in a system where we are also concerned about shear. To do this, we may wish to scale on the basis of equal power/volume and equal tip speed. We note that $P/V = N_P \rho N^3 D^5/V$. We also note that tip speed = πND. Inspection reveals we cannot use geometric similarity, as these two results scale differently. To keep both results the same on scale-up, we can look at several options:

1. Use larger D/T ratio; lower speed, more torque for the power.
2. Use more impellers; this gives smaller diameter and lower tip speed for the power than a geometric P/V scale-up
3. Change impeller style to one with a higher power number so the diameter and tip speed are less than a geometric P/V scale-up. Example: go from a low solidity hydrofoil to a high solidity hydrofoil upon scale-up.

These ideas may not work if the scale ratio is too large. For example, using the same problem as used in the single physical result example, if we want to keep the tip speed the same, one possibility would be to use the same diameter and speed (1000 mm at 72 rpm) as used for the tip speed scale-up (n = 1), but change the impeller style to draw 10 times as much power (5.7 kW). The impeller would require a power number of 3.3. No axial impeller has such a high power number, so a radial impeller would have to be used. Such a substitution would make a complete change in the flow pattern, which could be problematic in some cases. Another possibility would be to use two larger axial flow impellers of a higher power number. For example, two 1333 mm diameter high solidity hydrofoil impellers with a power number of 1.0 (based on D/T = 0.4) would require a shaft speed of 52.7 rpm to draw 5.7 kW. This would give a tip speed of 3.68 M/s, which is slightly below the tip speed of 3.77 M/s used in the small pilot scale (and in the equal tip speed scale-up with a scaling exponent of 1.) The flow pattern would change somewhat, but not in a harmful way; it would still be axial flow.

Summary

Process scale-up requires a complete understanding of all relationships, and is quite difficult.
Single parameter physical scale-up is straightforward, but choosing the correct scaling exponent is critical.
Dual parameter physical result scale-up is possible for limited circumstances and limited scale ratios.
Scaling 3 or more physical parameters is almost impossible.

Chapter 5: Bioprocessing Application Classifications and Guidelines

With the information from the foregoing chapters in mind, we will list several classifications of problems common in the bioprocessing industries, and provide application guidelines for them.

Bioprocessing Agitator Application Classifications

Most bioprocessing applications fall under one of four categories:

1) Simple blending
2) Cell culture bioreactors
3) Anaerobic fermenters
4) Aerobic fermenters

We will comment on each of these in turn. Bioreactors and fermenters will be dealt with at greater length in other chapters of this course, as they involve more specialized calculations.

Simple blending

Many applications in the bioprocessing industry are simple blending, often of waterlike materials. Agitator design is not crucial in these applications, but still follows the blending and motion procedure, including the possibility of power use optimization. Examples of such applications include:

1) Media preparation
2) Buffer preparation
3) CIP (Clean-in-Place) preparation
4) Various hold tanks
5) Harvest tanks
6) Liquid product storage

Most of these applications can be handled by a liquid motion scale of agitation of 2-3. There are a few special cases which deserve additional comment.

In some cases, the harvest tank may contain organisms which are subject to shear damage. In such a case, a study should be undertaken to find out the maximum impeller tip speed that the cells will tolerate before damage is evident. Only designs which are below this maximum tip speed should be considered., However, since rupturing air bubbles create thousands of time the shear rate of anything produced by agitators, it is unlikely that shear damage will be created by an agitator if the cells have already withstood aeration.

If a dry powder must be incorporated, an upper pitched blade turbine may be needed to create a vortex on the surface, and a scale of agitation of 5 or more may be needed. (If the solids wet out easily, such as salt or sugar crystals dropping into water, no additional agitation will be needed.)

Cell Culture Bioreactors

These are divided into two sub-categories: immobilized and suspended.

When the cells are immobilized on supports, the vessel often has no agitator; it is operated as an airlift vessel. Sometimes the reactor has two chambers: one which has the cells, and another which is aerated. The aerated liquid then recirculates by pump action or by airlift induction so as to flow over the immobilized cells in the second compartment. In this case, if an agitator is used, it is designed for mass transfer. More detail is given in a dedicated chapter on this.

In the case of suspended cell cultures, the cells may be freely suspended or supported on an inert substrate, typically spherical in shape, which is suspended in the liquid. Usually, the mass transfer requirements are so low that the agitator is not designed for mass transfer. Instead, it just circulates the tank contents. Air is sparged outside the radius of the impeller so as to avoid rising through it or disturbing its flow pattern, which is typically axial flow.

The agitator is designed for minimum shear. In practice, this means using a hydrofoil at a large D/T ratio, typically about 0.5. Generally, high solidity hydrofoils are used, as they have a lower tip speed for a given diameter and scale of agitation. Variable speed drives are almost always used to give the lowest speed that still produces satisfactory results.

Bubble shear is a major issue. It is desirable to avoid small bubbles, which cause most of the shear damage. Although the bubble shear is much higher than agitator shear, and therefore the need for low agitator shear is questionable, agitators designed for low shear also produce a more uniform bubble size distribution and fewer small bubbles. Mass transfer limitations may occur if the bubbles are too large however.

Anaerobic fermenters

This is an area which needs much more research. Most agitator designs for anaerobic fermentation are regarded as non-critical. If the substrate is “clean”, having no suspended solids other than yeast cells, the agitator will produce product with no operating problems even at agitation scales less than 1, although a scale of about 2 is typical. When there are significant solids present, such as ground grain solids in dry-grind ethanol processes, the minimum scale of agitation required to keep the tank bottom reasonably clean and avoid bacterial infections is usually at least 3.

However, agitation in anaerobic fermentation does more than merely keep solids in suspension. Work done by Professor Enrique Galindo in ethanol fermentation suggests that increases in agitation are accompanied by increases in rate of production, product yield and maximum product concentration. People working in the industry have anecdotally reported similar results. I have also observed that in other anaerobic fermentations, increasing agitation reduces byproduct formation. To my knowledge, no one knows the mechanisms behind these results. Until we do, we cannot be sure how to scale them up. Galindo suggested power/volume based on his limited study, but that may not always be the case. Moreover, actual production scale units currently in operation have a much lower P/V than Galindo studied. That suggests there is much room for improvement. My suggestion would be to spend any left over capital on anaerobic fermentation projects (if anyone ever has extra money left over!) on larger fermenter agitators.

Aerobic fermentation

These applications have huge financial importance to the industries using them.

From a process viewpoint, they can make anything from extremely valuable specialized proteins or drugs valued at hundreds or thousands of dollars per gram, to commodities such as amino acids or enzymes valued at less than $1 per pound.

From an equipment design viewpoint, agitators designed for aerobic fermenters are among the largest, in terms of power for their tank volume, found in industry. Dissipating high levels of power can create high mechanical loads and a large amount of vibration.

The major design requirement for aerobic fermenters is mass transfer rate. A second requirement is liquid blending. Past experience is often used for scale-up. Proper piloting can aid in optimally sizing such equipment. Three chapters of this course concentrate on the issues unique to fermenter design.

Fermentation process technology continues to evolve. Agitation technology is changing also. Fermentation was originally commercialized using Rushton turbines. Since then, there has been an evolution towards axial/radial combinations to provide both good gas dispersion and good blending. The radial impellers have evolved in the direction of concave bladed designs, and the axial impellers have tended toward high solidity and up-pumping. There have also been all-axial designs. Chapter 9 is devoted to fermenter impeller system design.

Mechanical technology is changing also, principally to address vibration issues. Dynamic finite element design analysis is essential for large critical equipment. Such analysis can include not only component analyses but also system response, such as lateral and torsional natural frequency analysis. Lab and field measurement of forces and deflections are needed to validate computational models, and most major mixer manufacturers have this capability also.

Major agitator manufacturers employ a variety of process technologies.
Such might include “wet” gas/liquid simulations, LDV (Laser Doppler Velocimetry) and DPIV (Digital Particle Image Velocimetry) velocity measurements, complex gas/liquid calculations with proprietary software, and multiphase computational modeling.

Benz Technology International, Inc. adds some of its own technology and services to that provided by the mixer manufacturers. Examples include:

1) Recommendation and coordination of wet tests at mixer manufacturers
2) Recommendation and coordination of computational fluid dynamics runs by mixer manufacturers or by CFD software suppliers
3) Design, interpretation and scale-up of tests at customer facilities
4) $k_l a$ curve fitting
5) Use of software by ReyNo, Inc. and Chemineer, Inc.
6) Benz Technology International, Inc. software for power optimization, mass balances, etc.

Chapter 6: Sanitary Design Guidelines

This chapter focuses on sanitary design features sometimes needed in agitation equipment to aid in producing products that are cGMP-compliant. The GMP regulations do not call out exactly what equipment design features or materials are needed. Instead, they require that the equipment design, to paraphrase the essence of the regulations, be such that the equipment will not alter the strength, identity or purity of the product beyond its established specification limits. It is up to each facility subject to the cGMP regulations to validate the process and equipment design. This chapter is not a substitute for that process. Rather, it is an attempt to define terms that must be understood and illustrate features which are often specified to aid in compliance. There is always a conflict between expense and process need. Some processes or steps within a process can be perfectly compliant with no sanitary design features. Others require the best sanitary design available.

To avoid confusion, we will begin by defining some terms that have often (erroneously) been used interchangeably:

1) Aseptic: having no *undesirable* living organisms present.
2) Sanitary: easy-to-clean. Not prone to trapping substances in pockets or cavities.
3) Sterile: having no living organisms present

The terms aseptic, asepticity, sterile and sterility refer to process conditions, not equipment design. Asepticity is desired in processing steps such as fermentation. Sterility is impossible in fermentation; desirable organisms are a necessary part of the process. Sterility is desired or even mandated in the final product, unless the final product itself is living cells, such as various yeasts and food cultures. Sterility is also usually required in media, buffers, etc.

“Sanitary” describes equipment, not the process. Many pharmaceutical processes benefit from or require sanitary equipment design. However, sanitary design is not always required to achieve sterility or asepticity. Liberal application of steam, bleaches or other biocides will kill any organisms present in the equipment. Injection of a carefully controlled culture of the desired organism into a thoroughly sterilized tank with a sterile medium can result in successful aseptic growth even with very ordinary equipment design. Such is generally the practice for equipment used to make commodity products such as enzymes, amino acids, some antibiotics and ethanol. High value products are often made with more sanitary (and expensive) equipment design, due to the high cost of losing a batch compared to equipment value.

Sanitary design principles: wetted parts

The following principles apply to sanitary design for the wetted parts of agitators and similar process equipment:

1) Avoid trapped pockets that do not drain freely
2) Avoid horizontal surfaces where material can build up.
3) Pay attention to polishing procedures for in-tank surfaces. Proper polishing removes material by cutting with sharp abrasive. Burnishing may actually create a more attractive finish, but it bends over the surface metal, making thorough cleaning difficult. Dull abrasive will create a burnished finish.
4) Electropolish may make cleaning easier, but sometimes increases measured roughness. It will almost always increase measured roughness on a burnished finish, as it preferentially dissolves sharp peaks, and will open up cavities “buried” by burnishing.

Figures 1 and 2 illustrate the difference between a properly polished finish made using fresh, sharp abrasive, and a burnished finish made using dull abrasive.

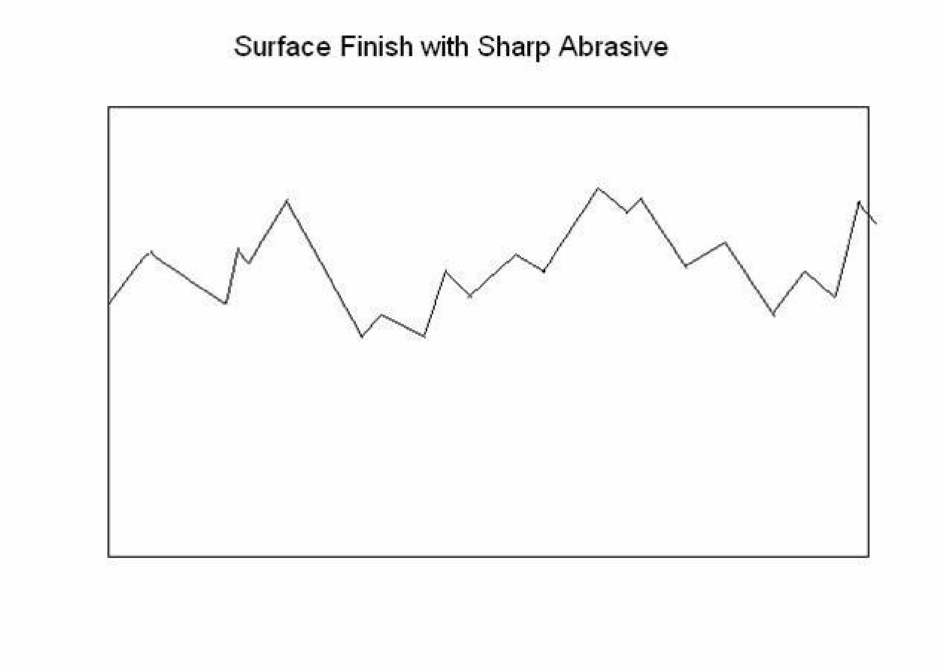


Figure 1: Polished surface

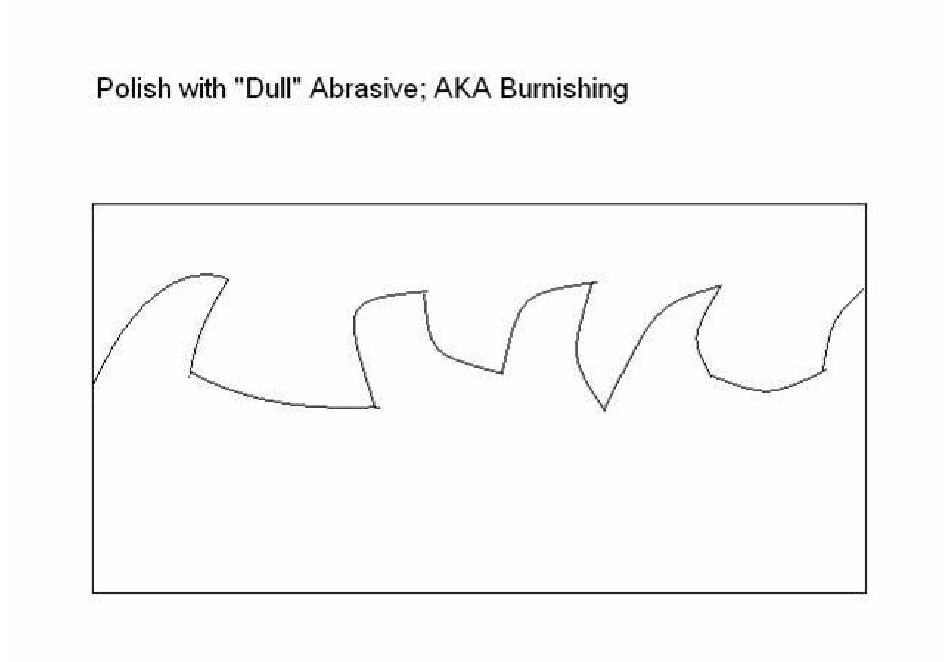


Figure 2: Burnished surface

Surface finish

Surface finish is often described by roughness and lay.

Roughness is typically measured in either micro-inches or microns. The instrument used to measure roughness is called a profilometer. Most profilometers measure the arithmetic average, or RA, though sometimes end users prefer to specify root mean square roughness, or RMS. A good rule of thumb is that the RMS value of roughness is about 10% higher than the RA value measured on the same surface. For sanitary design, most users will specify an RA value of <32 microinches or <8 microns.

Lay refers to the direction of the scratches left by the polishing operation. Profilometers should measure across the lay. Generally, there are two kinds of lay: unidirectional and random. Unidirectional lay is preferred, as it is easier to clean.

The polishing method used determines the lay. Methods which produce a unidirectional lay include belt sander, flapper wheels on a lathe, detail grinders and most hand polishing. Random lays are produced by such devices as rotary or orbital sanders. Sometimes a random lay looks better but a unidirectional lay cleans better.

Agitator shafts are easy to polish using flapper wheels on lathes. This produces a unidirectional lay. However, the lay is circumferential about the shaft. It would be better if it were longitudinal, I.E., parallel with the shaft axis, so that fluid might drain more easily. At present, there does not seem to be an economical method for producing a longitudinal lay on agitator shafting.

Sanitary design: wetted parts construction details

Standard wetted parts construction on agitators consists of bolted blades, typically mounted on a hub with a clearance fit on the shaft, driven by a key. Such designs have many ways to trap material, yet are acceptable for some processes. Many times, agitator shafts are supplied in more than one piece. The sections are connected by in-tank couplings, which are bolted together as standard, and may be attached to each shaft half by such techniques as welding, shrink fit, taper bore or taper pin construction. These may be very difficult to sterilize quickly. Steady bearings have many crevices as well.

The most sanitary wetted parts design is all-welded construction. It can be had for a small premium over bolted construction. However, making changes is quite difficult, and installation may be very difficult. Sometimes a removable top head on the tank is required, or an oversize agitator mounting flange. Another way to handle this problem is to ship the impeller and shaft assembly to the vessel fabricator and have it placed in the vessel prior to welding the heads on. A third way is to weld the impeller blades on at the jobsite. If bolted construction is used, adequate sterilization time must be allowed for. *Avoid acorn nuts!* These may look pretty but they trap material in a way that is impossible to clean and lengthens sterilization time.

Various ways have been devised to allow increased sanitary design while still using bolted construction, sometimes without exposed fasteners. In general, these methods are more expensive than either standard bolted or welded construction.

One example of sanitary impeller design is the Chemineer Smoothline™ method of construction (Figure 3, photocredit Chemineer, Inc.) This design has internal threading so that the impeller can pass though a vessel opening equal to the blade width, and when assembled, the internal threads are sealed from the process contents by gaskets or o-rings.

Figure 3: Smoothline™ impeller

In-tank couplings can trap substantial amounts of material between their halves and thereby extend sterilization time. Such time can be shortened by sealing off the inner part of the coupling by an o-ring or gasket just inside the bolt circle, as shown in figure 4. (Illustration by Benz Technology International, Inc.)

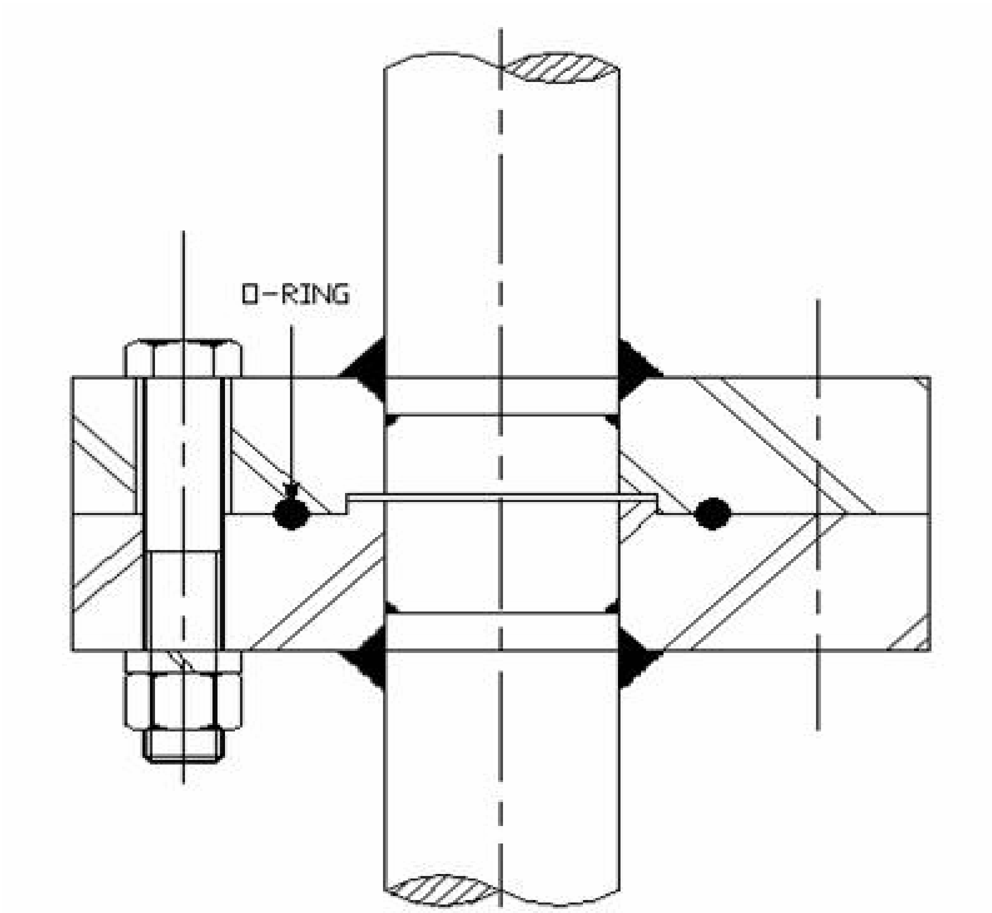


Figure 4: Sterilizable in-tank coupling

This design still has some pockets around the bolts, and has a horizontal surface on top of the coupling where material can accumulate. Figure 5 (illustration by Benz Technology International, Inc.) shows a “sanitary” in-tank coupling, which is more expensive. It has no exposed threads. The bolts are blind tapped using a self-locking thread form (e.g., Spiralok^{TM}), and are sealed at the bottom coupling half by an o-ring in a chamfered bolt hole or a gasket mounted on a stainless washer, such as the Parker-Hannefin Stat-O-Seal^{TM}. The top of the coupling is sloped to facilitate drainage, and the two coupling halves are sealed at the coupling O.D. by a gasket or O-ring.

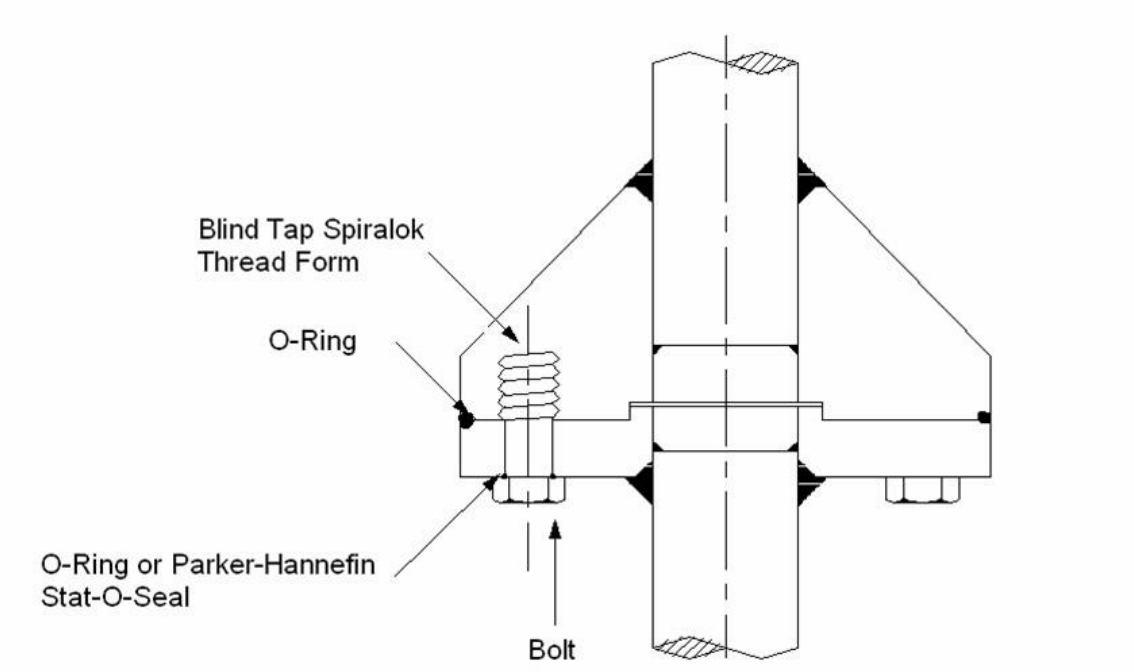


Figure 5: Sanitary in-tank coupling

Steady bearings are impossible to make truly sanitary. However, it is possible to make maximum use of sloped surfaces and minimize exposed fasteners. Sterilization can be enhanced by addition of a steam port in the annular area between the shaft and the bushing, as shown in figure 6 (illustration by Benz Technology International, Inc.).

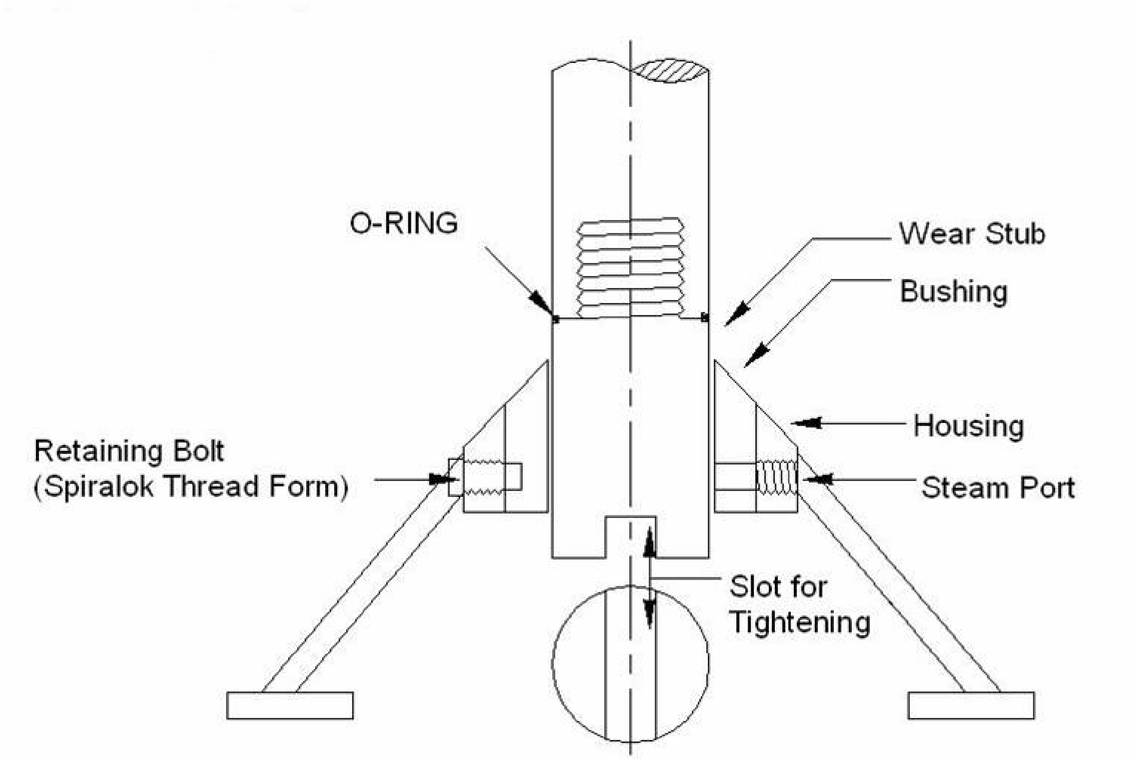


Figure 6: "Sanitary" steady bearing

Sanitary design principles: shaft seals

Most agitators used in pharmaceutical and bioprocessing applications have some sort of shaft seal where the shaft enters the tank, though some applications have none and just use open top tanks. The shaft seal may be called upon to serve several functions, such as maintain a sterile barrier between the inside and outside of the tank, contain hazardous compounds or organisms, or prevent product contamination from outside the tank. Some designs also prevent wear particles from the seal from entering the tank. Several common seal types will be illustrated, with comments on their performance. All seal types can be sterilized by addition of a steam port in an appropriate location.

Figure 7 (illustration by Benz Technology International, Inc.) shows compression packing with a steam port. It is basically a throttling device: fluid or vapor can leak in either direction. If a steam port is used, nothing will enter or leave the vessel in a living state. Compression packing is inexpensive and easy to maintain, though it must be adjusted and replaced more often than with some other seal types. It is adjusted by tightening the nuts at the top of the gland plate. Food grade materials (GRAS) are often used for food and bioprocessing applications.

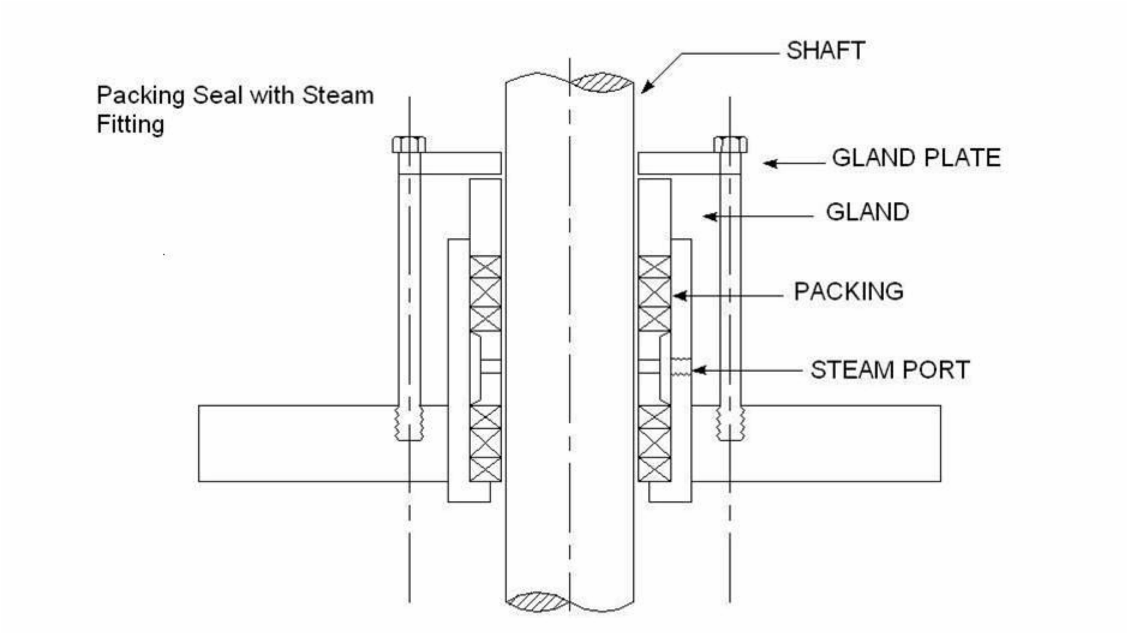


Figure 7: Compression packing seal with steam port

The next two figures illustrate single mechanical seals (Crane 75FS; photocredit John Crane, Inc.) that are split for ease of maintenance. They are shown horizontally, though most agitators are vertically mounted. A single seal is still a throttling device, just as packing is. However, it leaks far less. The second figure adds a debris well (also called carbon catcher) which prevents wear particles from entering the product, plus a steam port. Mechanical seals last much longer than packing, but are more expensive to replace. Dry running mechanical seals (not shown) come in two varieties: contacting and non-contacting. The contacting varieties have a somewhat lower life expectancy than the wet running seals. Non-contacting dry seals can have a very long life.

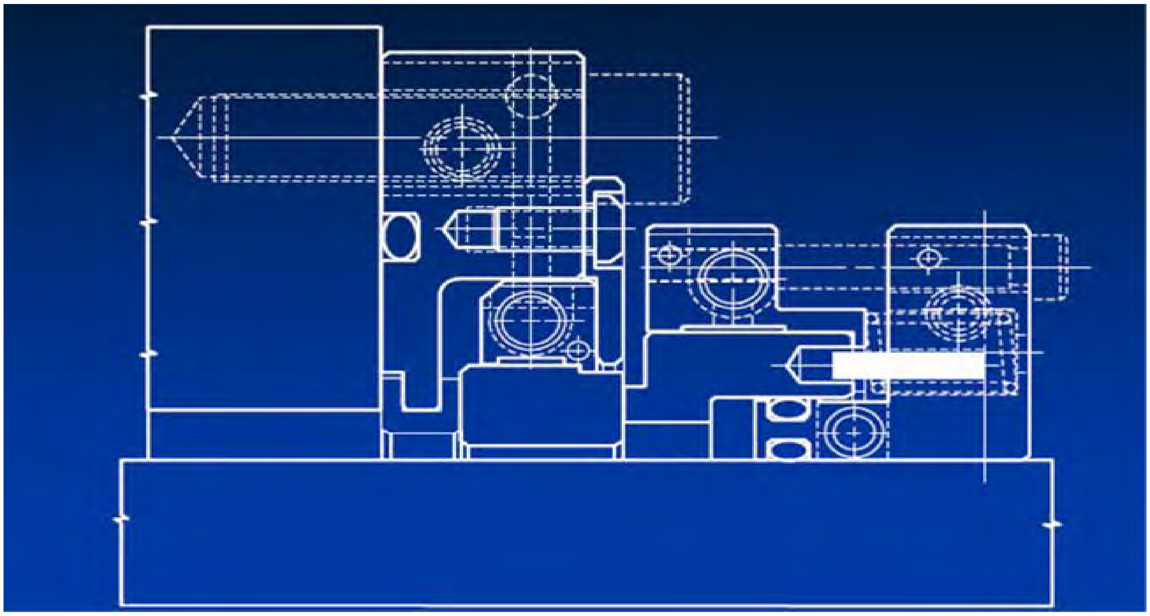


Figure 8: Split single mechanical seal (Crane 75FS)

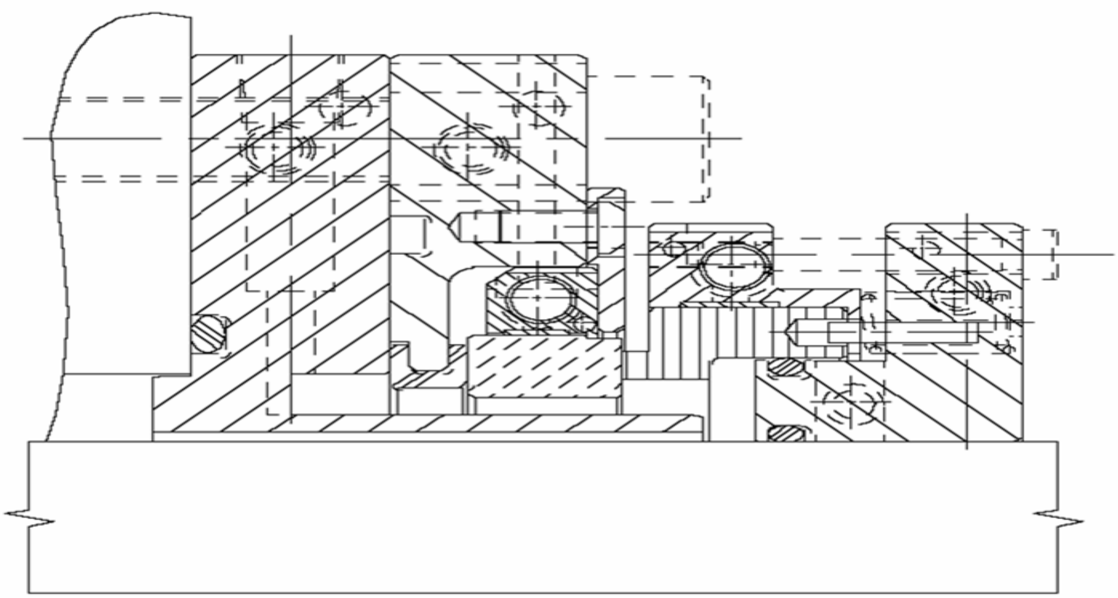


Figure 9: Split single seal with debris well, steam port (Crane 75FS)

Single seals are also available in non-split configuration. When used, the agitator design requires extra parts to facilitate seal change without removing the entire unit from the tank. This may make the initial unit cost higher. However, seal replacement costs are less and the designs are slightly cleaner. Figures 10 and 11 (Photocredit John Crane, Inc.) illustrate typical seals without and with debris wells.

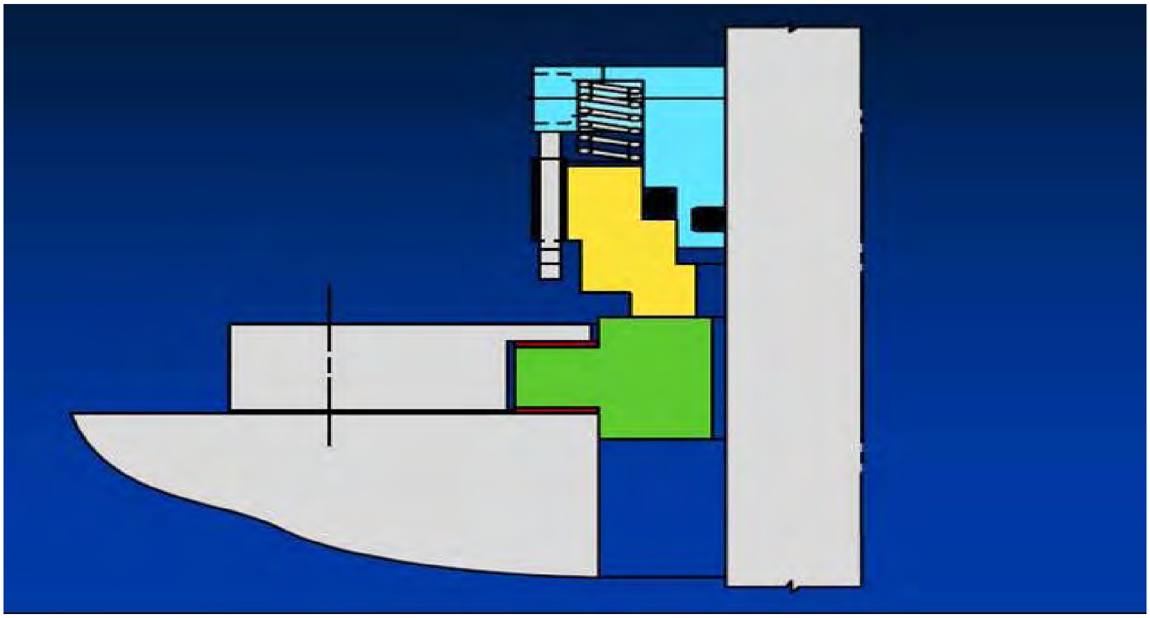


Figure 10: Single mechanical seal without debris well (Crane type 32)

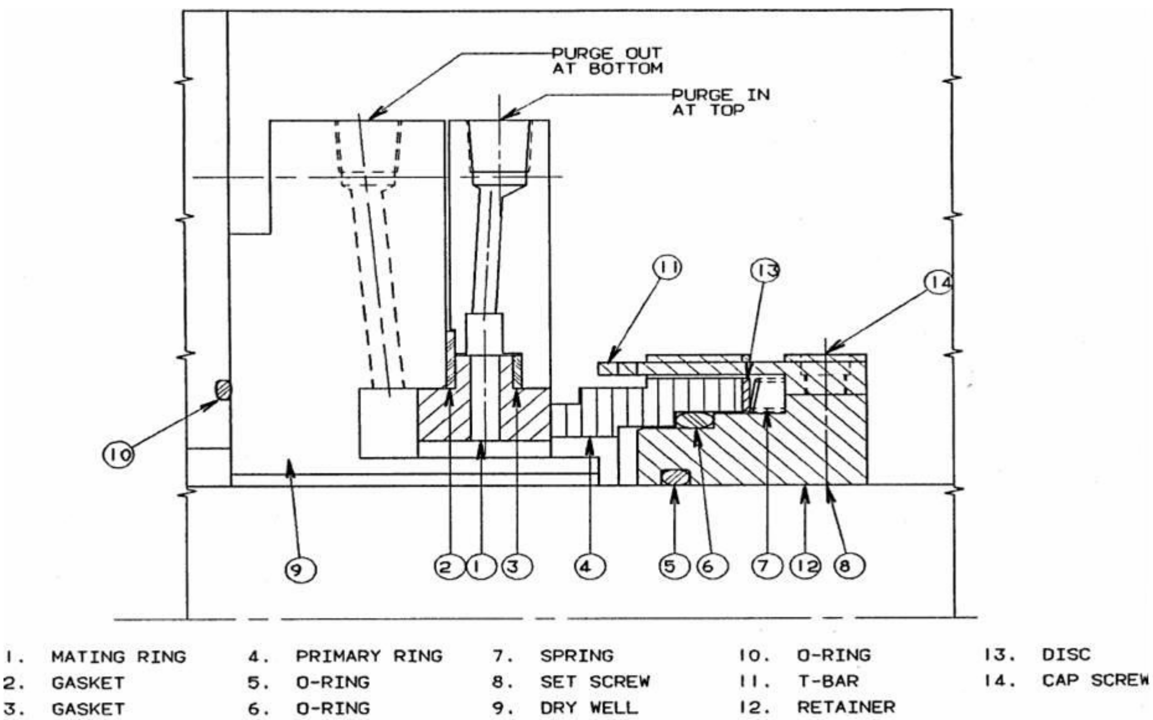


Figure 11: Single seal with debris well (Crane type 32)

When absolute containment is desired, yet a seal still must be used, there is no substitute for a double pressurized mechanical seal. These use a barrier fluid (which can be a liquid or gas) between two single seals, pressurized above tank pressure. That way, the barrier fluid leaks into the tank and out of the outer seal.

Tank contents cannot escape. Neither can anything enter the tank from outside. Often such seals may be mandated by local authorities when highly toxic, flammable or pathogenic materials are in the tank. Sometimes a seal shutoff (not shown) may be required to permit seal change without fully depressurizing or cleaning the tank. Such seals are commonly mounted in a cartridge for ease of maintenance. The cartridge may be made by the seal manufacturer or the equipment manufacturer. The cartridge may or may not have a debris well.

Figure 12 (photocredit John Crane, Inc.) shows a double mechanical seal (Crane 8B1V) in a Chemineer style HTN cartridge, manufactured by Chemineer, Inc.

Figure 13 (photocredit John Crane, Inc.) shows a double seal (Crane 7700) in a John Crane cartridge, equipped with a debris well and a stem port in the gland (not shown.)

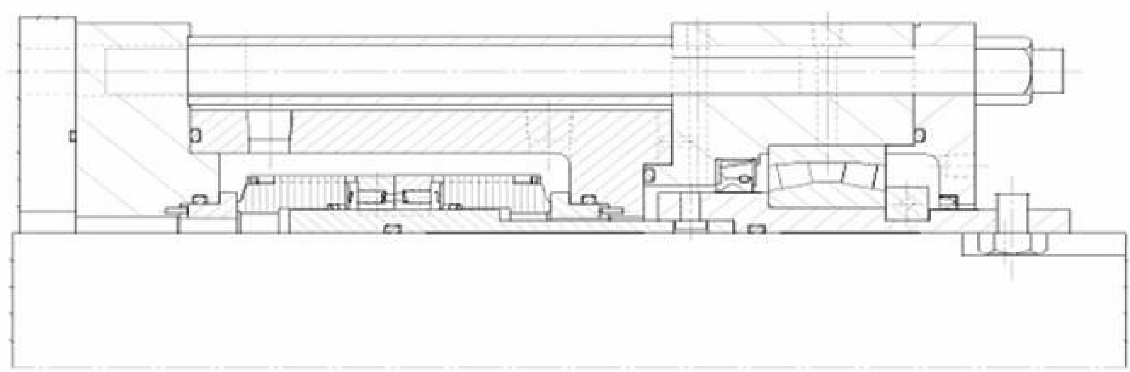


Figure 12: Double mechanical seal (Crane 8B1V in Chemineer HTN cartridge)

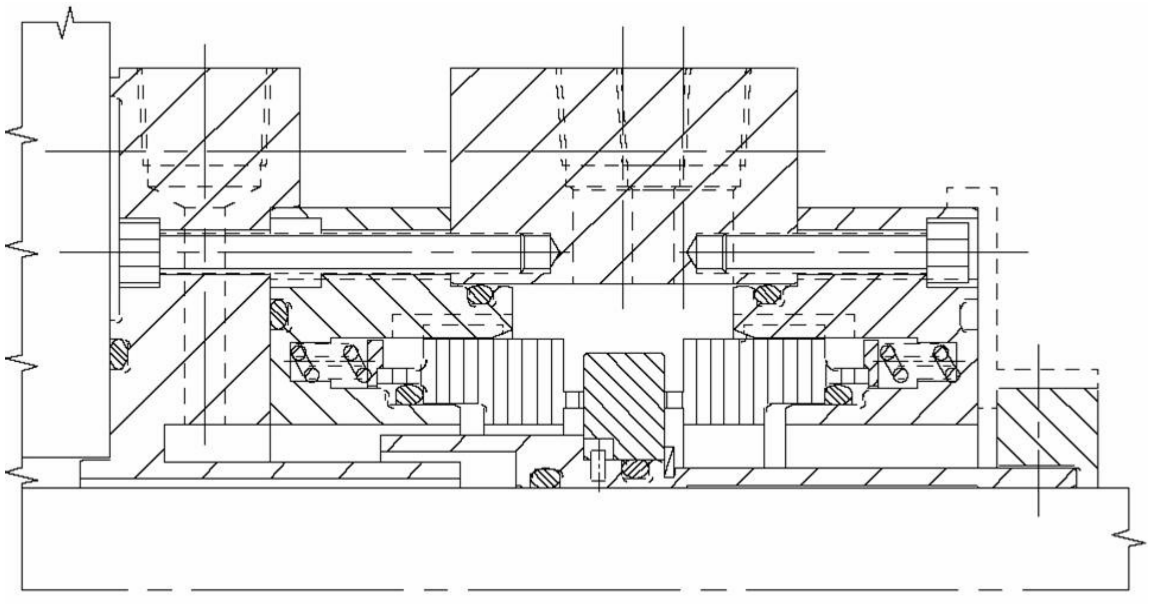


Figure 13: Double mechanical seal with steam port and debris well (Crane 7700)

In addition to the relatively standard types of double seals shown above, some manufacturers offer special proprietary seal designs for sanitary purposes. These have fewer horizontal surfaces and crevices. They also have more exposure to in-tank spray balls and steam. One such seal is the Ekato ESD 44 (photocredit by Ekato, Inc.), shown in figure 14.

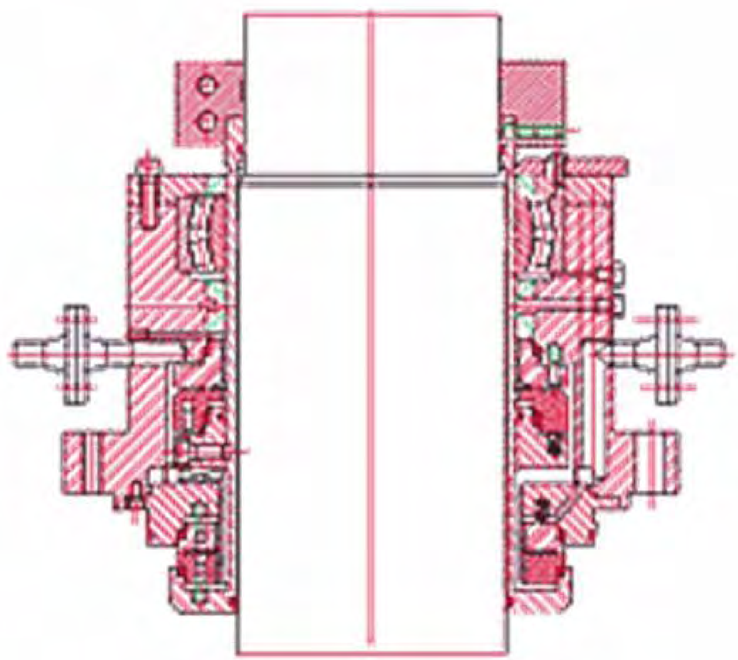


Figure 14: Proprietary sanitary double seal (Ekato ESD 44)

Some applications cannot tolerate any seals at all, yet must contain pressure and isolate the tank contents. These applications are conventionally handled by magnetic drive agitators, which do not have a shaft penetrating the tank. Instead, the shaft is supported by in-tank bearings, which are generally of a GRAS material such as PTFE or ceramics. The shaft is driven by a magnet outside the tank wall, and has a sealed magnet inside to transmit the power. Wear particles from the in-tank shaft support will enter the product. Such products are available both in top entering and bottom entering configuration. A bottom entering unit is illustrated in figure 15 (photocredit MagnaSafe, Inc.) In the future, we may see drives that support the shaft by magnetic levitation. Though such products are on the market now, their use is still quite rare.

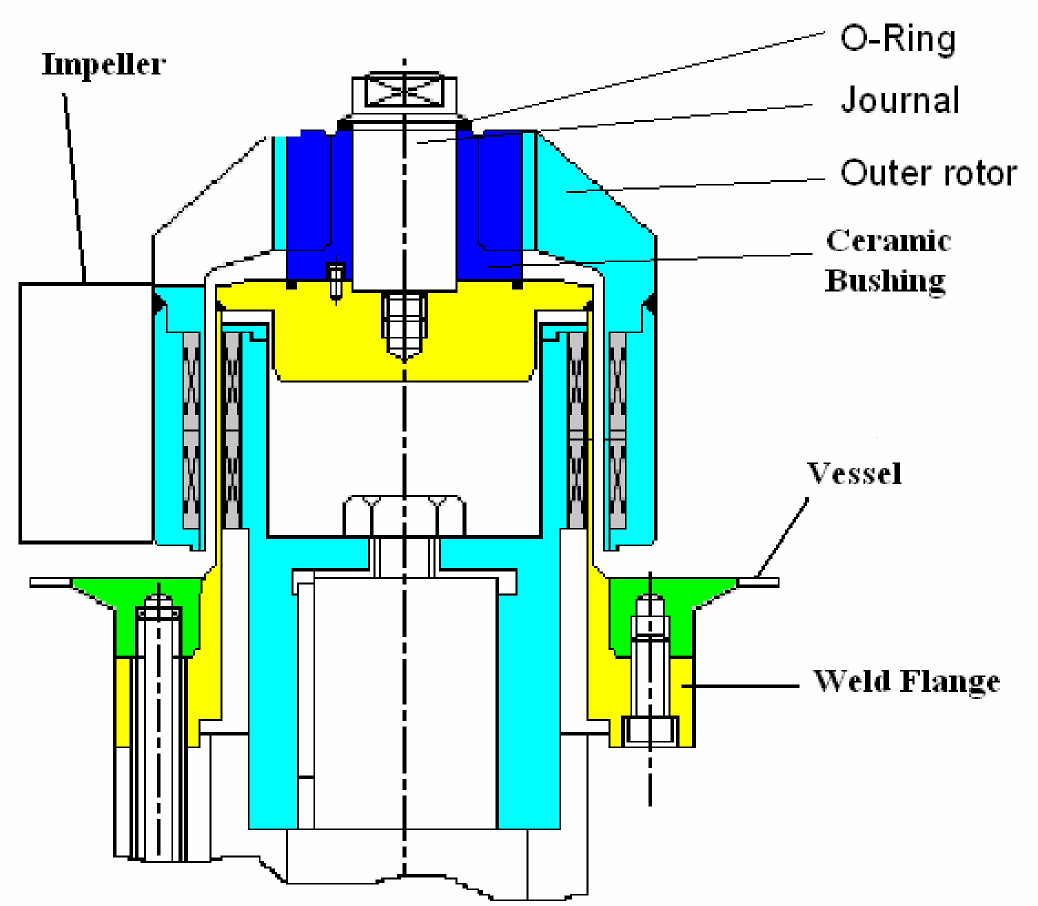


Figure 15: Bottom entering magnetic drive agitator (MagnaSafe)

In addition to the material presented here, there are other sources of equipment sanitary guidelines. One excellent source is the ASME Bioprocessing Equipment Guidelines. Another is the seminars offered by ISPE (International Society for Pharmaceutical Engineering).

Chapter 7: Fermenter Pilot Plant Protocol

In this chapter, we will explore concepts of how to conduct pilot plant research in fermentation in a way which maximizes its usefulness for agitation system design. Unfortunately, this is not the way most fermentation pilot plant research is conducted. However, this situation is completely understandable, as the people charged with conducting such research are rarely responsible for designing the production plant, much less designing the agitation system. Instead, they mainly study the microbiology system and the conditions which are optimal for product production. This creates a number of problems for agitation scale-up:

- Extremely high levels of agitation are often used that are not attainable in production equipment
- Generally, power/volume is much higher in the small scale than in the large scale
- Generally, superficial gas velocity is much lower than full scale

Pilot versus full scale variable range

Most full scale fermenters have a P/V in the range of 1-3 W/kg. Pilot P/V is often 5-10 W/kg or even more.

Full scale superficial gas velocity (U_s) is generally in the range of 0.03 to 0.09 M/s. In the pilot scale, it is usually less than 0.01.

Many full scale fermenters operate with a VVM (Volume of gas per Volume of liquid per Minute) rate in the range of 0.5 to 1.5. Pilot VVM rates would often need to be more than 10 to match full scale superficial gas velocity, which it would need to do to validate mass transfer correlations.

As an example, we provide table 1, which illustrates values of P/V and U_s as a function of scale, based on a “typical” OTR of 200 mmol/l-h and an “average” mass transfer coefficient correlation.

Scale	Vol, l	U_s, m/s	P/V, w/l	VVM
Pilot	1	0.0065	9.8	3
	5	0.009	7.1	2.5
	20	0.011	6.1	2
	100	0.015	4.5	1.6
	300	0.019	3.9	1.4
Production	5K	0.032	2.4	0.96
	20K	0.044	1.8	0.85
	150K	0.064	1.3	0.68
	350K	0.074	1.1	0.62
	1000K	0.091	0.88	0.57

Table 1: Pilot/Full scale range example

We can clearly see that the major variables used to correlate mass transfer coefficients are different in magnitude as a function of scale, at equal mass transfer rate. Because such correlations are not perfect, it is not wise to extrapolate them much beyond the range of variables for which they have been studied. That means that to get good $k_l a$ correlations from a pilot study, it is necessary to conduct runs at conditions which bracket the anticipated range full scale. In practice this means using less agitation and more air in the pilot scale than is customary. Impeller flooding must be checked and avoided. The pilot air supply and sparging system may need modification to accommodate the rather significant increase in airflow required.

For example, let us suppose we wished to pilot the 150Kl production scale listed in table 1. Table 2 shows the values of P/V and U_s that would be required in various pilot scales.

Vol, l	U_s, m/s	P/V, w/l	VVM
1	0.064	1.3	30
5	0.064	1.3	17.8
20	0.064	1.3	11.3
100	0.064	1.3	6.7
300	0.064	1.3	4.67

Table 2: Pilot conditions to model 150Kl production unit

We can see that the VVM rate can get quite high in the pilot scale! Many pilot fermenters do not come equipped with sufficient air supplies to allow this. Yet if the resulting correlations are to be used with confidence to design full scale equipment, they must be modified to bracket the full scale conditions.

Here are the steps to a good pilot plant protocol:

- Start with an estimated $k_l a$ correlation
- Estimate the full scale design (Chapter 8 details this procedure)
- Calculate pilot airflow, agitation speed to match full scale P/V, U_s
- Design pilot runs to take data above and below the direct scale down
- Fit a correlation to the new data

More detail follows on each bullet point.

Start with estimated correlation

If pilot data are available, use them for developing the correlation even if the data range does not match full scale conditions. It is still likely to be more representative than generalized air-water correlations from the literature. However, if no data or correlations are available from the pilot plant, use published correlations for similar systems if available, or even air/water correlations if not. For example, for a waterlike broth, an "average" relationship is:

$k_l a = 0.95\,(P/V)^{0.6}(U_s)^{0.6}$ (units of watts, kg, meters and seconds)

If viscosity is greater than 1, adjust by viscosity in cP raised to the -0.5 exponent, but do not use this for severely viscous or non-Newtonian broths such as xanthan gum.

Estimate full scale design

1) Start with a known peak value of OUR (Oxygen Uptake Rate). Assume that the OTR (Oxygen Transfer Rate) must match it.
2) Set airflow rate based on assuming 50% oxygen transfer. (This is based on the author's personal observation that this condition is often close to optimum in terms of minimizing power consumption)
3) Perform a mass balance and determine driving force.
4) Solve the kla correlation for agitator power
5) Now a rough value is known for both P/V and U_s in the full scale design

Design pilot runs

1) Calculate airflow based on the same superficial gas velocity as full scale.
2) Calculate agitator speed to give the same power/volume as full scale.

3) Lay out a grid of values of airflow that covers a range of at least 0.5 to 2 times the scaled down airflow.
4) Lay out a grid of agitator speeds that goes at least from 0.75 to 1.3 times the scaled down agitator speed. (This gives a range of 0.5 to 2 times the power/volume)
5) Check for flooding; avoid flooded runs. If most of the runs seem likely to be flooded, consider upgrading the lower impeller to a concave style if the OEM impeller is a Rushton.

Check for flooding

Limit the aeration number, Q_g/ND^3 to $C(N^2D/g)(D/T)^{3.5}$, where C = 30 for a Rushton turbine, 70 for a CD-6 or 180 degree concave, and 170 for a BT-6. Recent work suggests these numbers may be conservative for concave turbines at higher Froude numbers. For viscous fluids, the differences among impellers are more pronounced, though all have their capacity reduced. Consult an expert for help if needed. Also, use visual observation if the plot fermenter is made of glass or other transparent material, or has generously large full length view ports.

Comments on required OTR

Some runs, especially those combining low rpm with low airflow, may not allow sufficient OTR for the organisms to thrive. However, data from these conditions are still needed for accurate full scale design. There are several techniques to cope with this problem:

- Reduce the net biomass to reduce the OUR requirement. This can sometimes be done by scheduling the low OTR runs in the early stage of fermentation.
- Increase back pressure at equal *actual* airflow, while taking care not to inhibit CO_2 disengagement to the point of toxicity
- Use oxygen enriched feed gas to increase the driving force at low mass transfer coefficient conditions.

Fit model to new pilot conditions

Many mathematical models have been proposed to fit kla data. Some are quite complex. The most common form, which will be used throughout this course, is:

$$k_la = A(P/V)^B(U_s)^C$$

Typically, this form will fit the data +/- 30% in fermenter broth, though it often fits tap water within a 5% error band. The experimental error probably has more to do with variations of trace substances in a living system than with the form of the correlation. Changes in viscosity, surface tension, suspended solids content and ionic strength can all affect the relationship. Other correlations usually have similar error bands.

Once the model has been established, use it to establish agitator power and airflow, using the procedures in Chapter 8. Allow ample safety factors for error or future process changes.

Chapter 8: Full Scale Power, Airflow Design Optimization

In previous chapters, we discussed the principles of mass transfer and how to conduct pilot experiments so as to get the necessary data for agitated gas-liquid mass transfer relationships. In this chapter we will begin the process of designing the full scale equipment by selecting the agitator power and airflow. Later chapters will deal with agitator speed and impeller systems.

Principles of full scale design

As noted previously for liquid motion problems, different combinations of agitator power, shaft speed and impeller system can yield the same results. Similarly, there are equivalent combinations of agitator power and airflow that can yield the same mass transfer potential in a gas-liquid system. When the power draw of the agitator and the power draw of the compressor are added together, the sum represents the principal power costs associated with mass transfer. In this course, we will not discuss other energy costs, such as solid or liquid transport power, heating or cooling costs, etc. These are not significantly adjustable by changes in agitation or airflow.

The sum of agitator power plus compressor power goes through a minimum for a given mass transfer potential, as a function of airflow. We wish to calculate what that minimum is so as to minimize power costs. Safety factors should be applied to the final answer. This is not only because there may be error in the correlations, but because the process may change. For example, if the productivity of the strain of microorganisms used increases an average of 5% per year due either to selective breeding or genetic modification, in 10 years the required OTR will go up 63% and the agitator power needed will typically more than double, based on typical exponents in the $k_l a$ correlation. So, it is reasonable to apply a safety factor of 2 or more.

The final design should also take into account variable gas flow, shear, liquid blending and CO_2 concentration at the outlet. Sometimes the CO_2 concentration at the outlet limits the overall design.

Figure 1 illustrates the concept of total power going through a minimum. Note that the minimum is relatively broad; we don’t have to hit it exactly to do a reasonably good design. Also, note that for this illustration the compressor power curve is a straight line. This is the case in a new installation where system pressure drop is set by design, and components will be sized accordingly. On an existing piping system, it will be a curve.

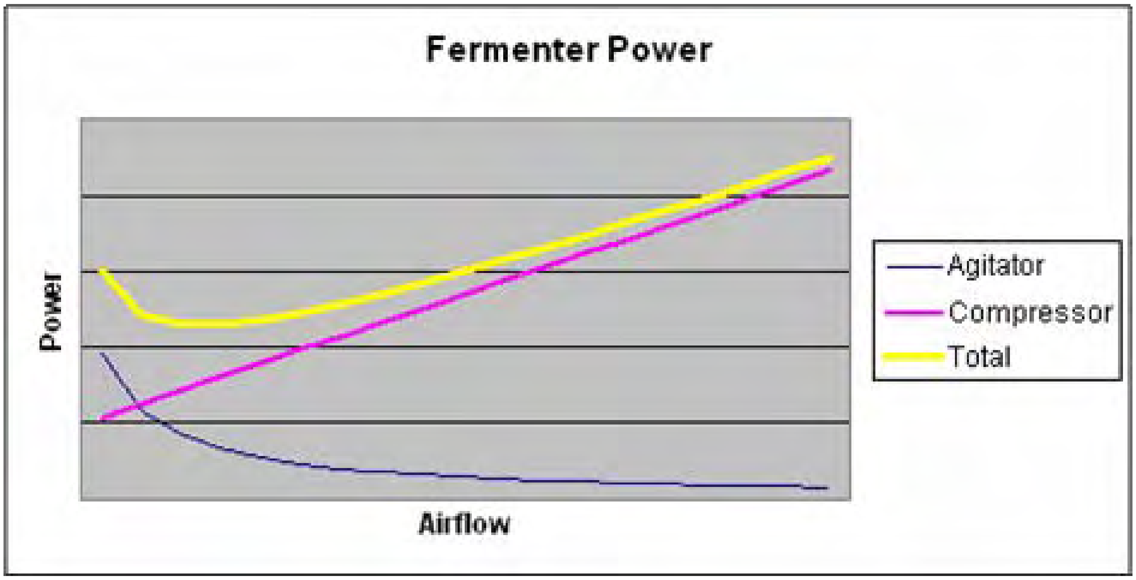


Figure 1: Power Optimization Concept

Unfortunately, not all designs make use of full data or the procedures available to optimize. Yet facilities must be built and equipment must be selected. So, this course will also deal with those cases.

There are 3 common cases for design:

1) No data (optimization of power not possible)
2) Limited pilot or production data (difficult to minimize power)
3) Full data from a properly designed pilot program (required to enable full optimization of power)

We will deal with each of these cases in turn.

No data

With no data, a plant may still be built if the fermentation is at least similar to some that have been done by others or in the same plant. Flexibility in both operation and performance expectations by management are desirable. A reasonable template may be made by dividing fermentations into 3 categories: easy, average and difficult. These categories are roughly equivalent to mass transfer rates of 3000, 5500 and 10000 mg/l-h, respectively. Based on waterlike materials with high ionic strength (little coalescence), table 1 has been prepared. It can be used as a guide when nothing else is available. It can also serve as a check on existing designs or those calculated by scale-up or calculation from full data.

Volume, M^3	"Easy" OTR≈3000 mg/l-h P (kW)/U_s (M/s)	"Average" OTR≈5500 mg/l-h P (kW)/U_s (M/s)	" Difficult" OTR≈10000 mg/l-h P (kW)/U_s (M/s)
20	25/0.025	45/0.045	75/0.085
40	45/0.025	75/0.050	188/0.090
80	75/0.030	150/0.060	300/0.110
160	150/0.035	300/0.060	560/0.120
320	260/0.040	560/0.070	1000/0.140
640	560/0.045	1100/0.080	1900/0.160

Table 1: Power/Gas Velocity Guidelines with No Data

In the above table, suggested combinations of motor power and superficial gas velocity are given as a function of working volume and classification of fermentation. For example, a fermenter of "average" OTR requirements with a working volume of 80 cubic meters (about 21,000 gallons) would need about 150 kW (200 Hp) motor size and a superficial gas velocity of about 0.06 M/s (roughly 0.2 ft/s).

Limited pilot or operating data

For this case, it is normal to use scale-up methods. A traditional method is to scale up on the basis of equal agitator power/volume and equal VVM (volume of gas per volume of liquid per minute). This will certainly work but will usually be oversized, as we will show below.

When the airflow is scaled on the basis of equal VVM, the superficial velocity will increase if the tank geometry is even remotely similar upon scale-up. This increases the value of $k_l a$. In addition, the driving force for mass transfer will increase due to the higher absolute pressure at the bottom of the tank (increased liquid head). The net result is an increase in potential OTR.

If the scale range is not too large, using equal superficial gas velocity and equal P/V is sufficient. The $k_l a$ value will be the same. The decrease in concentration driving force due to increased molar depletion will roughly be compensated for by the increased pressure driving force at the tank bottom. However, the VVM rate cannot be allowed to fall below stoichiometric levels, or, in practice, below about 125% of the theoretical transfer requirement.

Full data: ideal design method

Naturally, when designing anything, it is always best to have all the data necessary. That is what we mean by full data. Only with full data is it possible to minimize power and optimize the design. What are these data?

Here is a minimum list:

- "Good" $k_l a$ data (based on pilot studies in actual broth, under conditions similar to those expected full scale)
- Known peak OUR (Oxygen Uptake Rate)
- Known saturation data or Henry's law constants
- Known minimum DO (Dissolved Oxygen) levels required
- Known rate of CO_2 generation per mole of oxygen consumed

Design steps

When full data are known, there are specific steps which must be followed to optimize the design. These will be listed below.

1) Begin with the peak OUR. Assume that the peak OTR (Oxygen Transfer Rate) must equal it.
2) For the first iteration, assume an airflow at least 20% higher than the minimum rate for stoichiometric conversion, I.E., that required at 100% consumption of available oxygen. (At 100%, the required agitator power would be infinite)
3) Perform mass balance calculations to determine exit gas concentrations, accounting for CO_2 generation as well as oxygen depletion. (Changes in water vapor concentration are usually neglected.)
4) Based on saturation data or Henry's law constants, calculate saturation concentrations, C_{sat}, at the bottom and top of the fermenter.
5) For calculation purposes, set the actual DO at the top of the fermenter equal to the minimum required DO.
6) Set the actual DO at the bottom of the fermenter to that at the top multiplied by the factor in table 2, which follows these steps. (This is a rough guideline; more on this later).
7) Calculate the log mean driving force
8) Based on the known driving force and the OTR required, calculate $k_l a$ as shown: $k_l a$ = OTR/driving force
9) Based on the $k_l a$ expression derived from a well executed pilot program, calculate required agitator invested power/volume. For example, using the form of equation that is most common, $P/V = (k_l a/(A^*(U_s)^C)^{1/B}$; $P = P/V^*V$
10) Calculate agitator motor power by assuming 95% mechanical efficiency of the gear drive and shaft seal: $P_{agit} = P/0.95$
11) Based on the airflow, inlet and outlet pressure and compressor efficiency, calculate compressor power consumption. For air, we can use the

following: P_c (kW) = 5.97 (inlet pressure, atm)*(inlet flow, M^3/min)*((pressure ratio)$^{0.283}$-1)/efficiency

12) Add compressor power to agitator power to get total power, P_{tot}
13) Repeat at incrementally higher airflow rates until the combined power reaches a minimum. If applicable, check to be sure CO_2 outlet concentration or partial pressure is not too high.
14) Apply safety factors and judgment to the above optimum design, both on motor power and airflow.
15) Final motor size must account for power draw at minimum airflow, especially if a fixed speed motor is used.
16) The impeller system and shaft speed used affect shear, blending, heat transfer and power drop due to gassing. These issues must be considered, and will be covered in chapter 9.

Volume M3	20	40	80	160	320	640
DO ratio, Bottom /top	1.1	1.2	1.3	1.5	2	3

Table 2: DO ratio estimation

The above table is a guideline based on very limited data. It is reasonable for well designed impeller systems in a combination of axial and radial types. The DO ratio is much worse when an all-radial design is used. In the future, we may be able to combine CFD techniques with oxygen consumption models to predict the DO distribution more accurately.

Example Problem: data

The following data apply to the example problem, which is of the “full data” variety:

- Working liquid volume: 114 M^3 (30,100 gallons)
- Tank diameter: 3.66 M
- Ungassed liquid level: 10.97 M (vessel has a dished bottom)
- Density: 1.0 g/cc or 1000 kg/M^3
- Temperature: 38C
- Oxygen saturation data: at 1 atm (absolute) and 21% oxygen, C_{sat} = 7.0 mg/l
- CO_2 evolution rate: 0.95 moles per mole of oxygen consumed

- Peak oxygen uptake rate (OUR): 2000 mg/l-h
- Minimum DO requirement: 2 mg/l
- Tank back pressure: 0.68 atm = 10 psig = 0.69 bar-g
- Line losses for air flow (design): 2.04 atm = 30 psig = 2.07 bar-g
- Compressor efficiency: 70%
- $k_l a$ constants: A= 0.02, B = 0.6, C = 0.6 using units of 1/s, W/M^3 and M/s
- Operation is at sea level, so the background pressure is 1 atm.

Problem solution, step by step:

1) Assume peak oxygen transfer rate (OTR) equals peak oxygen uptake rate (OUR) = 2000 mg/l-h

2) For this problem, rather than doing all the iterations, we will demonstrate the steps all the way through one iteration. We will begin at roughly 2 times the stoichiometric ratio required so that the answer will be reasonable. To do this, we will calculate the total OTR so that a material balance can be done: Total OTR = 2000 mg/l-h*114 M^3 * 1000l/M^3 * (1 gmol O_2)/32000 mg = 7125 gmol O_2/h. We note from the appendix that 1 nM^3 of air at 1 atm and 0C contains 44.6 g-mol, which at 21% oxygen contains 9.366 gmol of oxygen. The stoichiometric airflow required is thus (7125 gmol/h)/(9.366 gmol O_2/nM^3) = 760.7 nM^3/h. Doubling this would give a figure of 1521. We will round this to 1500 nM^3/h for this problem. If we were doing all the iterations to find the minimum power, we would start at about 913 nM^3/h, or about 20% more than the minimum stoichiometric amount.

3) Perform the mass balance. Changing to a per minute basis to make the numbers easier to manage, we have an inlet air stream of 1500/*60 = 25 nM^3/min. The molar flow is 25 nM^3/min.*44.6gmol/nM^3 = 1115 gmol/minute. This consists of 234.2 gmol/min of oxygen at 21% and 880.8 gmol/min of “other”. We will make the assumption that the other constituents remain unchanged and are present in the outlet gas. The oxygen consumed equals 7125 gmol/h divided by 60, or 118.8 gmol/min. Therefore, the outlet oxygen flow equals 234.2-118.8 or 115.4 gmol/min. CO_2 is generated at the rate of 0.95 moles per oxygen consumed; 0.95*118.8 = 112.8 gmol/min. The “other” components are still present at 880.8 gmol/min. The total outlet flow is thus 880.8 + 115.4 + 112.8 = 1109 gmol/min. Oxygen concentration equals 115.4/1109 = 0.104, or 10.4%. In volumetric terms, the outlet airflow is 1109/44.6 = 24.9 nM^3/min. Mean airflow averaged at the top and bottom of the fermenter is 24.95 nM^3/min. Adjusted for temperature (38C) and local absolute pressure at the middle of the liquid height (1.21 atm), the actual average volumetric flow is 12.85 M^3/min. The mean superficial gas velocity based on the tank diameter is thus 0.0204 M/s.

4) Calculate C_{sat} at the inlet and outlet based on adjustments for pressure and changes in composition. Since the saturation data were given based on air at 21% oxygen at 1 atm, we do not need to use Henry’s law, but can ratio directly.

At the inlet, we are still at 21% oxygen, so we can ratio by absolute pressure. At the inlet, the absolute pressure = 1 + 0.68 (back pressure) + 1.06 (liquid head) = 2.74 atm absolute. Thus, C_{sat} = 2.74*7 = 19.18 mg/l. At the outlet, the pressure is 1+ 0.68 = 1.68 atm abs. The composition has changed, so we must ratio by the pressure change and the composition change: C_{sat} = 7*1.68*(10.4%/21%) = 5.82 mg/l.

5). Set the DO at the top to the minimum required. By problem statement, this is 2 mg/l.

6) Set the DO at the bottom higher using table 2. To be slightly conservative, we will use the ratio from 160 M^3, which is 1.5. Thus, the estimated bottom DO is 1.5*2, or 3 mg/l. This is a reasonable estimate based on using an impeller system which mixes well, such as an axial/radial combination.

7) Calculate the log mean driving force:
(ΔC(top)-ΔC(bottom))/ln((ΔC(top))/(ΔC(bottom))) = ((5.82-2)-(19.18-3))/ln((5.82-2)/19.18-3)) = 8.56 mg/l. In this formula, ΔC is understood to mean the local driving force, C_{sat}-C.

8) Based on driving force and OTR, calculate the required value of $k_l a$:
$k_l a$ = OTR/driving force = (2000mg/l-h)/8.56 mg/l = 233.6/h or 0.0649/s.

9) Calculate required P/V from the applicable correlation. In this problem, P/V = $(k_l a/(A*(U_s)^C)^{1/B}$ = $(0.0649/(0.02*(0.0204)^{0.6})^{1/0.6}$ = 349 W/M^3; P = P/V*V = 349*114 = 39800 W = 39.8 kW = 53.4 Hp.

10) Calculate motor power draw assuming 95% mechanical efficiency of the gear drive/seal combination: P_{agit} = P/0.95 = 39.8/0.95 = 41.9 kW.

11) Based on the airflow, inlet and outlet pressure and compressor efficiency, calculate compressor motor power consumption. For this problem we will assume that the ambient air temperature at the compressor inlet is 20C; therefore, the actual compressor inlet airflow is 26.83 M^3/min. P = 5.97(inlet pressure, atm)(inlet flow, M^3/min)((pressure ratio)$^{0.283}$-1). The pressure ratio, including the line losses, is 4.78. (Discharge pressure = 2.04 +1 +0.68 + 1.06 = 4.78 atm abs). Therefore, P = 5.97(1)(26.83)((4.78)$^{0.283}$-1) = 89.2 kW. At 70% efficiency, P_c = 89.2/0.7 = 127.4 kW.

12) Add compressor power to agitator power to get the total: P_{tot} = P_{agit} + P_c = 41.9 + 127.4 = 169.3 kW.

13) The complete procedure would be to repeat all of the above at incrementally higher airflows, usually starting about 20% above the minimum stoichiometric value, until the total power is minimized. An additional constraint is sometimes

required relative to the partial pressure of CO_2 in the outlet gas (total absolute pressure at the outlet times mole fraction CO_2).

14) Apply safety factors to both airflow and motor power, based on judgment, possible correlation error and allowance for future process changes. For example, if the process life is expected to be at least 10 years and the microbiologists are expected to improve the strains used by an average increase in OUR of 5% per year, the agitator power and airflow would each need to increase by at least 50% to accommodate this.

15) Final motor size must account for actual power draw at minimum airflow, especially if a fixed speed motor is used. Variable speed makes this less of an issue. Impeller selection affects this logic, as will be seen in chapter 9.

16) Impeller selection will affect other things, as will be detailed in chapter 9.

State of design completion

Up to now, we have learned to select various combinations of agitator power and airflow so as to minimize power consumption for a given mass transfer rate. We have learned to eliminate combinations which give too much carbon dioxide in the exhaust gas.

We still need to define the impeller system and shaft speed used to invest the power. We also need to examine the effects of variable airflow and OTR requirements on the design outcome.

Chapter 9: Fermenter Impeller System Design

The design of fermenter agitators is not complete until the impeller system is selected. The impellers must be viewed as a system because there can be more than one type of impeller used on the same shaft, and the power allocated to each one can influence overall results. The impeller size affects the required shaft speed to draw the target power and several other important results as well. Several distinct steps are involved in the design and selection of the impeller system and shaft speed. We will go through each of those steps in turn.

Impeller system design steps

1) Choose type(s) of impellers
2) Choose design conditions for sizing
3) Choose quantity of impellers
4) Choose power input for each impeller for those conditions
5) Choose shaft speed
6) Size impellers
7) Look at options for other process conditions: fixed speed, variable speed, multispeed motors, etc.

Choose type(s) of impellers

A quick review of chapter 1 indicates there are 3 main categories of impeller types: axial flow, radial flow and mixed flow. Axial flow can be further subdivided into high solidity and low solidity. We will discuss each type in turn, beginning with axial flow, high solidity.

Solidity is defined as the fraction of the circle swept by the impeller that is occluded by the impeller in plan view. Most high solidity impellers have a solidity of 0.8 or more. Most low solidity impellers have a solidity of less than 0.2. There are few impellers on the market with intermediate solidities.

Examples of high solidity impellers include the Chemineer MaxFlo series impellers such as shown in Figure 1 (photo by Chemineer, Inc.), and Lightnin A-315. Such impellers can disperse gas at low to intermediate gas flow rates without the use of a lower radial impeller. They provide intermediate flow performance between pitched blade turbines or other mixed flow turbines and low solidity hydrofoils. They can be very mechanically unstable when directly gassed and operated in down pumping mode. Stability is improved considerably in up-pumping mode. (Vibration velocity is reduced about 50%).

Figure 1: MaxFlo High Solidity Impeller

Low solidity axial flow impellers, such as the Chemineer HE-3 (figure 2, photo by Chemineer, Inc.), the Lightnin A-310, and many others on the market today, are among the best impellers for flow controlled applications. They are unable to directly disperse more than a small amount of gas effectively, but if they are placed above a lower radial impeller which pre-disperses the gas, they can be very effective. They must draw enough of the total power to assure gas does not re-coalesce in the upper part of the tank. Most early process performance problems with axial/radial impeller combinations have been shown to be caused by improper power distribution. When properly applied, such impellers give very good blending and heat transfer performance and ample gas dispersion performance.

Figure 2: HE-3 low solidity axial flow impeller

Radial flow impellers have been traditionally used for gas dispersion in fermenters. In fact, they were first developed around the time of the commercialization of penicillin. They are characterized by a staged flow pattern, wherein the primary flow direction is normal to the shaft axis. They produce fine bubbles in the discharge area, which may coalesce when they travel outside the impeller zone. Radial impellers vary widely in terms of power draw, gas handling characteristics and the tendency to unload when gassed. Some common radial impellers are described in more detail below.

The Rushton or D-6 impeller typically has 6 blades at a 90 degree angle, mounted to a disc. The blades are typically 1/5 of the impeller diameter in height and ¼ of its diameter in length. The disc is typically 2/3 of the impeller diameter. The ungassed power number is about 5.5. The ratio of gassed to ungassed power (P_g/P_u) under highly gassed conditions such as typically found in large scale fermenters is about 0.4. For comparison purposes, the relative gas handling capacity is 1.0. An illustration by Chemineer is given in figure 3.

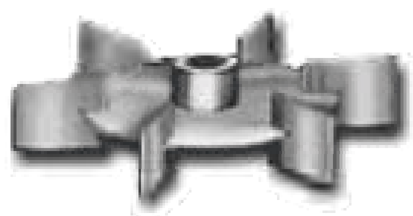


Figure 3: Rushton turbine (D-6)

Another radial turbine in widespread use is the concave radial design based on the work of John Smith and others, called the CD-6 by Chemineer, Inc., who provided the illustration in figure 4. Its ungassed power number is about 3.2 and its typical ratio of gassed to ungassed power is about 0.65. Compared to the Rushton turbine, its gas handling capacity before flooding is about 2.4, a substantial increase.

Figure 4: CD-6 or modified "Smith" turbine

Ekato Corporation offers a product called the Phasejet, which has deeper concavity than a CD-6. Little quantitative data has been published about this impeller. The author estimates that its power number is about 1.8. No data are publicly available with regard to gas handling capacity. The ratio of gassed to ungassed power is about 0.8 under highly gassed conditions. The illustration in figure 5 was provided by Ekato, and is a photograph of an actual impeller. The U.S. patent illustration is different; it shows a conical disc rather than a flat one, and the disc has serrated edges. It is presumed this version is intended for use with a pipe sparger rather than a sparge ring.

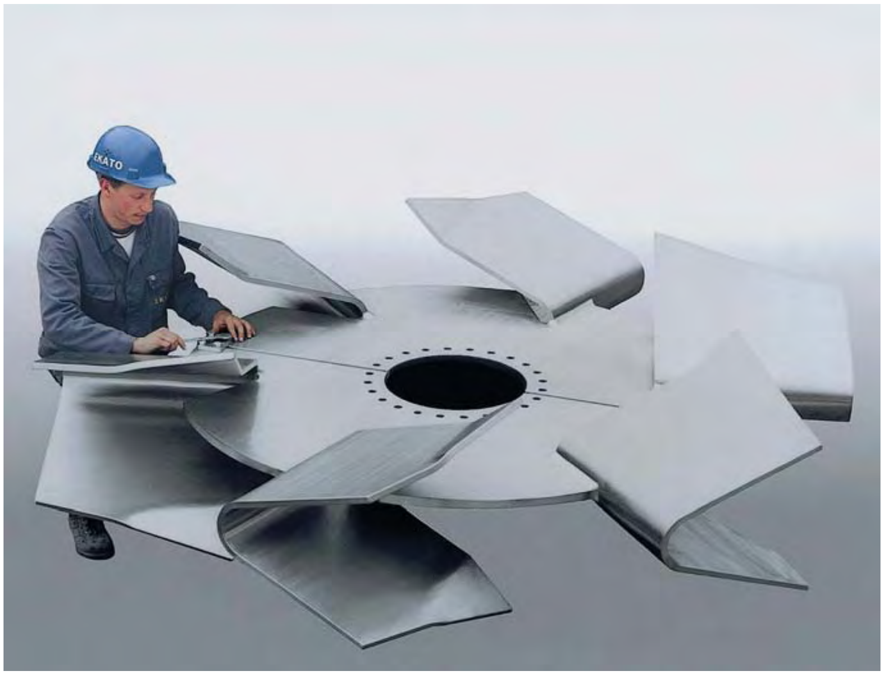


Figure 5: Ekato Phasejet

These three radial impellers shown are all symmetric with respect to the plane of the disc. In the late 1990s Chemineer introduced a unique impeller called the BT-6, which is asymmetric. The blade shape is different above and below the disc, and there is an overhang of the upper blade half The reason is that the gas is rising due to gravity, so an overhanging blade was though to be helpful to capture the gas. The blade shape was designed to minimize or eliminate gas pockets. Its ungassed power number is about 2.4. Its high-flow ratio of gassed to ungassed power is about 0.84, or about the same as the change in apparent density due to gas holdup, indicating the gas pockets are not present. Its relative gas handling capacity is about 5.4, which is probably the greatest of anything currently on the market. This design is illustrated in figure 6. (Photo by Chemineer, Inc.)

Other proprietary impellers not shown herein include the Middleton impeller, owned by ICI, and the Scaba SRGT.

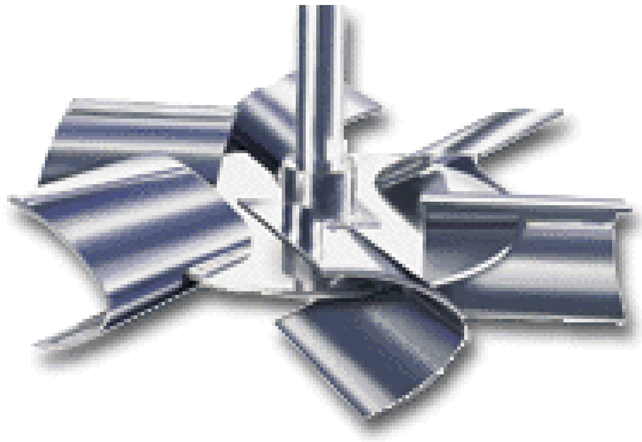


Figure 6: Chemineer BT-6

Mixed flow impellers discharge somewhere between axial and radial. One kind is pitched blade turbines with a blade angle above the stall angle. The most common variety has 4 blades mounted at a 45 degree angle, with an actual blade width 20% of the impeller diameter. When diameter is based on the flat-to-flat dimension (as opposed to the swept circle or diagonal), the typical power number is 1.37. This impeller, called the P-4 by Chemineer, is illustrated in figure 7 (Illustration by Chemineer, Inc.).

Another variety of mixed flow impeller has an inner section pitched to pump one way and an outer section pitched to pump the other way. (No illustration available). In practice, these create a very chaotic flow pattern which is roughly mixed flow, with more radial component than a pitched blade turbine.

In general, mixed flow impellers are poor at gas dispersion, often causing coalescence of gas pre-dispersed by a lower radial impeller and larger bubbles on the discharge side than on the entry side. They are also inferior to hydrofoils in terms of blending and solids suspension. They are therefore not frequently used in fermenters. However, they are very useful at creating a surface vortex, which can be used to incorporate dry powders or to entrain gas from the head space.

Figure 7: Pitched blade turbine (mixed flow)

Choose Design Conditions

Normally, the impellers are designed to fully load the selected motor at conditions of peak OTR, which is also normally at the peak airflow. As a reminder, the equation for impeller power draw is:

$P = N_P \rho N^3 D^5 (P_g/P_u)$,

where the term in parentheses is called the gassing factor, and depends on impeller type, D/T, aeration number and Froude number.

The power split allocated to each impeller depends on the system of impellers used. It is critical to distribute the power in such a way as to strike a balance between taking advantage of the higher driving force in the bottom while avoiding coalescence at the top and the attendant low DO that results.

Since most systems will have variable airflow, which changes the gassing factor, the effect on power draw must be addressed. Some options include oversizing the motor, using variable speed drive, or multispeed motors.

Not only does each impeller have a gassing factor, the impeller system has a combined gassing factor. This affects how the mass transfer and power draw react to changes in airflow.

Mass transfer depends on gassed power, not motor power. Therefore, if motor size alone is specified, an impeller system which unloads the least (that is, has the highest value of gassing factor) will draw the most power at peak airflow conditions, and therefore will provide the highest mass transfer potential in a variable airflow system.

If gassed power is specified at peak airflow, the impeller system with the highest gassing factor will not increase in power draw as much at reduced airflow, so it can use a smaller motor to handle minimum airflow, or less reduction in shaft speed. That allows it to have more mass transfer potential at reduced shaft speed and airflow, since most variable speed drives and multispeed motors are constant torque devices, rather than constant power. They cannot deliver as much power at reduced shaft speed.

Detailed gassing factor curves are not available here, though many have been published for the Rushton turbine. However, it is instructive to reiterate the gassing factors for some common impellers used for gas dispersion, at conditions typical of those in large fermenters:

Rushton: 0.4
180 degree concave: 0.65
Chemineer BT-6; 0.84
Ekato Phasejet: 0.8
Narrow hydrofoils: 0.75
Wide hydrofoils: 0.76

Flooding check

To avoid flooding, limit the Aeration number, Q_g/ND^3, to a value of $K(N^2D/g)(D/T)^{3.5}$, where K is 30 for a D-6 or Rushton turbine, 70 for a 180 degree concave turbine, and 170 for the Chemineer BT-6. There is some evidence that the coefficient becomes larger for concave turbines at higher Froude numbers, so this correlation may be conservative. Flooding definitions and correlations are unavailable for axial turbines used as lower impellers.

Impeller system concepts

This section includes concepts of impeller types, size and shaft speed. It must be viewed as a system, as the total result is more than just the sum of individual results.

Large-scale fermentation began in the 1940s with the commercialization of penicillin. At the time, the full scale process used multiple Rushton turbines. This practice was prevalent until the late 1970s. However, as commodity fermenters were designed with ever increasing capacity, the problems of DO gradient began to be noticed. In the 1980s, people began experimenting with axial/radial hybrid systems, reasoning that after the lower radial impeller dispersed the gas, the upper impellers need only blend the liquid. Some of these hybrids were quite successful. Others failed completely. Those that failed generally had almost all of the power invested in the bottom turbine, allowing coalescence near the top and very low DO in the upper parts of the tank.

Today, axial/radial systems are the industry standard. Some plants even use all-axial impellers, which blend even better but have lower gas handling capacity and sometimes lower mass transfer.

Another modern issue is up-pumping versus down pumping. Though it may seem counter intuitive, up-pumping axial impellers above a lower radial impeller have a shorter *gassed* blend time than a down pumping plus radial system. (They have a longer *ungassed* blend time, however, as would be expected by looking at the intuitive flow pattern.) Apparently, fighting the gas flow instead of working with it harms the blending results.

Up-pumping also results in 50-60% lower vibration velocity. This reduces wear on seals and steady bearings, and may even allow a smaller shaft in some cases. However, it increases the downward load on the shaft support bearings, and this must be taken into account.

The gassing factor is usually slightly higher up-pumping, which can provide higher mass transfer capability or a smaller motor.

A major benefit of up-pumping impellers is a smaller tendency to generate foam, and even an ability to re-incorporate foam that has been formed, if the upper impeller is covered by about 0.5 to 1.0 impeller diameters. One can understand this by examining which is a more effective hand position for splashing someone at the beach: pitched down or pitched up. Pitching one's hand down will create a much larger splash. Reducing foam generation can mean there is less need for antifoam. This author has seen cases where antifoam usage dropped 50% or more, not only saving the cost of expensive chemicals but also providing a higher $k_l a$ value.

The hybrid axial/radial system can also be compared to an all-axial system, which is often up-pumping. In general, the hybrid system has a higher system $k_l a$, especially if the all-axial system has the sparging done outside the impeller diameter. The hybrid system can handle more gas. It has greater mechanical stability, particularly when compared to all-axial down-pumping systems, which may have very high side loads. The hybrid system may create more shear and smaller local bubbles, which may be a disadvantage in some fermentations, such as cell cultures. The hybrid system has a longer gassed blend time than an all-axial, up-pumping system, and therefore may have a greater DO gradient. If the lower radial turbine used in the hybrid is one of the concave turbines, the hybrid system will have a higher system gassing factor.

Choose quantity of impellers

The zone of influence of an impeller depends on impeller type, position in the tank and viscosity. Upper impellers have a smaller incremental influence than the lower impellers. The table below gives guidelines for the Z/T ratio each impeller can handle, for axial and radial turbines.

Viscosity, cp	Z/T impeller # 1 (Radial)	Z/T increment Radial/Axial
<500	0.8	0.6/1.0
500-5000	0.6	0.5/0.8

Table 1: Impeller quantity guidelines

Comparison of three impeller systems in a simulated fermentation

To better illustrate the concept of viewing impellers as a system, we will compare three popular impeller systems in a simulated fermentation. Each system is well designed for its type.

The gas flow varies with time, as is typical of batch fermentations. The agitator starts out at half speed during the inoculation and lag phase, then switches to full speed at 10 hours, when the growth phase takes off. The gas flow profile is illustrated in Figure 8.

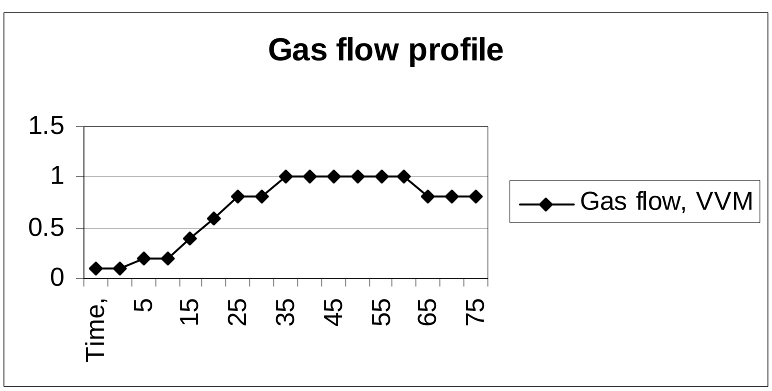


Figure 8: Simulated fermenter gas flow profile

The impeller systems to be simulated are as follows.
System 1: (3) Rushton or D-6
System 2: (2) Down pumping low solidity axial above a 180 degree concave radial turbine

System 3: (2) Up-pumping high solidity axial above a Chemineer BT-6 radial turbine

All three systems are sized to draw 250 kW gassed power upon going up to full speed at 10 hours, at the minimum gas flow required at this condition (0.25 VVM). As gas flow increases with time until 70 hours into the batch, all impeller systems draw less power than they did at 10 hours. However, the degree with which they decrease in power draw varies, with system 1 dropping the most, followed by systems 2 and 3. This power draw curve is illustrated in figure 9.

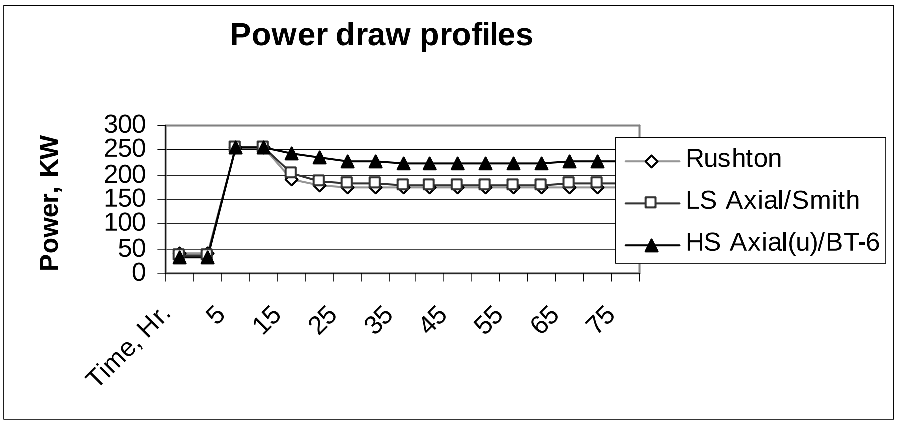


Figure 9: Impeller system power draw profiles

The change in power draw is accompanied by a change in mass transfer coefficient, as illustrated in figure 10.

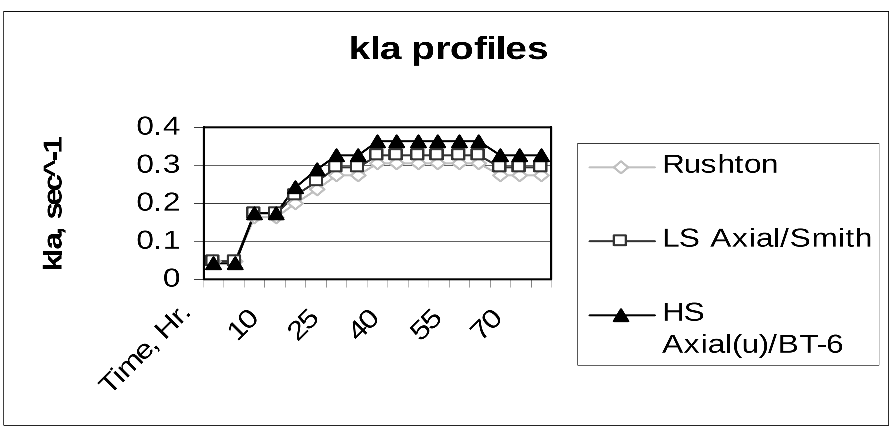


Figure 10: k_la profiles

Under peak airflow conditions, the 3 impeller systems differ in mass transfer potential. System 3 has about 20% more mass transfer potential than system 1. System 2 has about 8% more than system 1. Potentially these differences could result in higher rate of production or higher product titer.

Choosing shaft speed

Shaft speed has major effects on both process performance and cost of the equipment, as we shall see.

For a given power input, impeller size required varies according to shaft speed, with larger impellers being required at lower shaft speed. The D/T ratio also affects power draw characteristics.

As D/T increases (and shaft speed decreases) with constant power input, several things happen. Some are good, some not. Here are a few of the most important effects.

- Impeller pumping increases ($Q \approx C(D/T)^{1.9}$)
- Blend time decreases slightly; typically no more than a 10% change within the useful D/T ratio of about 0.25 to 0.5
- Process side heat transfer coefficient increases ($h \approx C(D/T)^{0.95 \text{ to } 1.05}$). This is good. However, it is generally better to manipulate heat transfer by surface area or temperature driving force than to design the agitator for a given heat transfer coefficient
- Tip speed decreases (tip speed $\approx C(D/T)^{\approx -0.67}$; this may be good for shear sensitive organisms (though gas bubble bursting is more important), but may be bad if organisms clump together and might work better if the clumps are broken apart
- Gas handling capacity increases ($Q_{g,\, max} \approx C(D/T)^{0.4}$)
- Shaft speed decreases ($N \approx C(D/T)^{-0.6}$)
- Wear on seals and steady bearings generally decreases due to the lower shaft speed
- Torque = P/N, so torque increases
- Agitator cost $\approx C(\text{torque})^{0.6 \text{ to } 0.8}$
- So, Higher D/T, lower rpm *costs more!*
- Power drop with gas flow increases; I.E., P_g/P_u decreases, which impacts motor size or mass transfer potential

The above bullets illustrate that the effects of low rpm, high D/T can be good or bad. The last bullet point is so important that we will present examples illustrating such effects. We will compare systems consisting of dual upper high solidity impellers above a lower 180 degree concave radial turbine. They will be compared at two D/T ratios: 0.3 and 0.5. The fermenter is one of 5M diameter, 200 M^3 working volume. The temperature is 40C, the specific gravity is 1.02 and the viscosity is 5 cP. It is assumed the fluid has high ionic strength and is mostly non-coalescing.

We will examine power draw and mass transfer coefficient for each at airflow rates of 0.1, 0.3, 0.5 and 0.7 VVM.

We will look at two different examples. For example 1, the motor power is fixed at 420 kW and the impellers are sized to draw 90% of the motor power maximum at the minimum airflow rate of 0.1 VVM. For example 2, the impeller power is set at 350 kW at the maximum airflow of 0.7 VVM, but the motor size is determined by using a maximum of 90% loading at the minimum airflow of 0.1 VVM.

The results for example 1 are summarized in table 2.

D/T=0.3			D/T=0.5	
VVM	P, kW	$k_l a$, 1/s	P, kW	$k_l a$, 1/s
0.1	379	0.172	378	0.173
0.3	355	0.29	308	0.271
0.5	339	0.365	278	0.33
0.7	328	0.424	270	0.385

Table 2: Example 1 power, $k_l a$ with motor fixed at 420 kW

Observations: Though both systems start out with the same power draw at 0.1 VVM, the one with the larger impellers drops more as airflow increases, culminating in about a 10% mass transfer advantage for the smaller system at peak airflow conditions. The smaller system also costs only 40-50% as much as the larger one.

Example 2 is summarized in Table 3

D/T=0.3			D/T=0.5	
VVM	P, kW	$k_l a$, 1/s	P, kW	$k_l a$, 1/s
0.1	403	0.177	487	0.197
0.3	378	0.298	398	0.307
0.5	362	0.377	360	0.375
0.7	350	0.438	350	0.438

Table 3: Summary of example 2 with gassed power set at 350 kW at 0.7 VVM

Observations: Setting the gassed power at peak airflow conditions is the most logical way to ensure proper mass transfer design. However, attention must also be paid to what happens at low gas flow. If we require a fixed speed motor, the larger D/T design requires a 550 kW motor, whereas the smaller D/T design needs only a 450 kW motor. If we decide to use only a 450 kW motor for the larger D/T, then we must maintain a minimum airflow of 0.3 VVM to avoid overload, which uses more compressor power. Either way, the larger D/T system ends up using more power. In addition, the 550 kW, large D/T design costs about 2-3 times as much as the 450kW small D/T system. Even at 450 kW, the larger D/T system costs about 1.5 to 2 times as much.

Of course, instead of using a fixed speed motor, we could use a multispeed motor or a variable speed drive. This would allow either system to be set at a 450 kW motor size, though the larger D/T design would still cost 1.5 to 2 times as much. However, since multispeed motors and variable speed drives are usually constant torque devices rather then constant power, less power is available at reduced shaft speed. ($P_{available}/P_{motor} = N_{operating}/N_{full\ speed}$). This means that the higher D/T design would have to be slowed down more as a percentage to avoid overload than the small D/T design, and would have less mass transfer potential in the off-peak part of the process.

We can also illustrate these concepts graphically, as shown in figures 11 and 12.

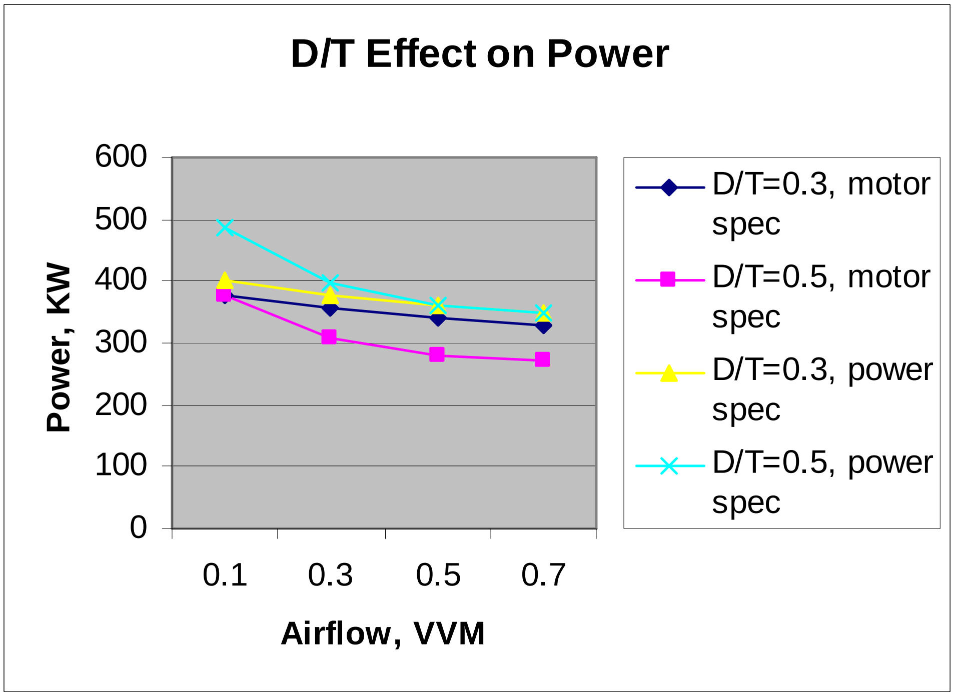


Figure 11: D/T effect on power draw

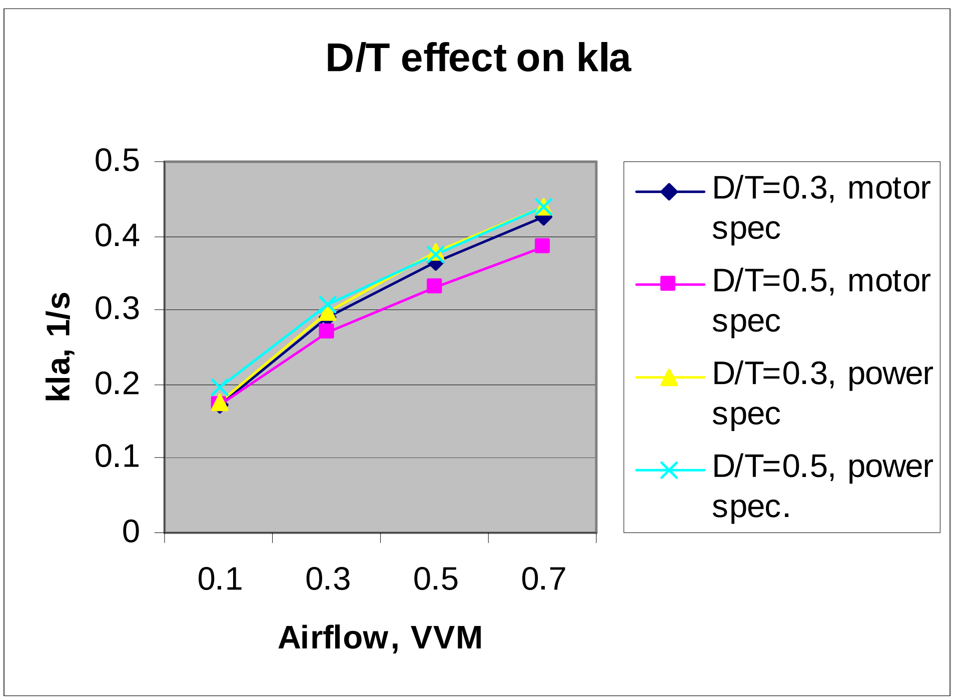


Figure 12: D/T effect on $k_l a$

Conclusions about D/T, shaft speed

Large D/T, low rpm designs have several advantages in terms of blending, shear and heat transfer. However, they have disadvantages in terms of power and mass transfer in a variable airflow environment. Often, a smaller D/T design can outperform a larger D/T design and even costs less. Imagine that!

Options for other process conditions

As mentioned in the observations for example 2, if variable speed is used, motor size can be chosen for peak airflow, regardless of impeller type. However, systems with higher gassing factors will allow investing higher power at lower shaft speed and airflow, because speed will not have to be reduced as much to avoid overloading. The motor relationship, once again, is ($P_{available}/P_{motor} = N_{operating}/N_{full\ speed}$).

For example, if one impeller system changes from a gassing factor of 0.6 to 0.8 at lower airflow, its speed would have to be reduced by 13% and its power draw would also have to be reduced by 13%. If another system changes from a gassing factor of 0.8 to 0.9 under the same conditions, its speed would have to be reduced by 6%, and its power draw would likewise have to be reduced by 6%, giving it an 8% advantage in power draw at reduced airflow and about 5% higher mass transfer potential.

In lieu of variable speed, two-speed motors are sometimes used. The can prevent overload at reduced or even zero airflow. Of course, they are not as flexible as variable speed drive.

Viscous effects

Most of the preceding discussion about D/T was aimed at low viscosity fermentations. Viscosity has several effects on the results. Heat transfer coefficients depend on viscosity to about the -0.33 exponent. Mass transfer coefficients depend about to the -0.3 to -0.5 exponent. Larger D/T ratios improve gas handling and blending in viscous fermentations, which is important because both get worse with increasing viscosity. In fact, blending can be more important than mass transfer at high viscosities. This observation has led some to use all-axial impellers in viscous gum fermentations, which are shear thinning and often have apparent viscosities at the impeller exceeding 2000 cP.

Impeller system design conclusions

Impeller system design follows several steps geared toward a balance of blending, heat transfer, shear and mass transfer. Different types and sizes of impeller systems can vary widely in terms of blending and mass transfer performance, especially under variable airflow conditions. Size and shaft speed not only affect performance but have a major effect on capital and operating costs. Variable speed drives or multispeed motors allow more flexibility in both operation and choice of impeller system.

For most low viscosity fermentations, the current best impeller practice is to use relatively small D/T impellers (typically about 0.3 +/-0.05) at relatively high shaft speed. The best practice impeller system is generally a lower deeply concave radial turbine with up-pumping high solidity impellers above.

For higher viscosities, the best practice is to use as large an impeller diameter as needed to provide adequate blending and minimize DO gradients, with consideration given to all-axial designs for extreme cases.

Chapter 10: Cell Culture Bioreactor Design Issues

Cell culture bioreactors are basically aerobic fermenters using specialized cells as opposed to complete organisms such as bacteria or yeasts. They are characterized by much longer fermentation times than bacterial fermentations and have much lower oxygen demand. Their rate of production is much lower than normal fermentations. Their main reason for use is to make products such as specialized proteins that have proven difficult or impossible to make any other way.

Such bioreactors have similar design issues to other fermenters plus a few of their own. These include:

- Mass transfer
- Shear damage
- Mixing
- Sensitivity to contamination

Each of these will be covered in turn.

Mass transfer design

The same general principles apply as in any aerobic fermentation. The key for creating the proper design is to have a broth-specific correlation relating the mass transfer coefficient to agitation and air flow parameters. If no such correlation is available, a generic correlation or scale-up techniques may be used.

There are two different ways that air is introduced into an agitated cell culture reactor: sparging directly into the impeller, or sparging in a way such that sparged gas does not come into direct contact with the impeller. The mass transfer approaches and calculations are different for these two cases. Also, indirect sparging results in lower mass transfer potential for a given airflow rate.

For the case of air being sparged through the agitator impeller, both airflow and agitation affect mass transfer. The form of equation used to correlate $k_l a$ in normal fermenters probably works just as well here, though the range of variables is different and therefore the constants may be different:

$$k_l a = A(P/V)^B (U_s)^C$$

The constants can be fitted empirically as described in Chapter 6, or, since the agitator will be operated with a variable speed drive, it is reasonable to use the common “average” correlation with A= 0.95 and B = C = 0.6 (units for the correlation are 1/s, W/kg and M/s). Since OUR is small, generous safety factors are reasonable. As always, flooding should be checked.

For the case where air is sparged outside of the impeller, the $k_l a$ value will be lower and likely independent of agitation. In that case, $k_l a$ will tend to be a function of the superficial gas velocity only. However, if the agitation is strong enough to pull gas rising near the wall back into the impeller zone, agitator power will have an effect and should be included in the correlation. This indirect method of sparging produces a larger mean bubble size, in addition to lower $k_l a$ values.

Mass transfer design by calculation

If $k_l a$ correlations are available, whether directly or indirectly sparged, the design calculation steps are the same. Beginning with a mass balance, follow the steps listed in Chapter 7 for fermenter design. This will yield various combinations of power and airflow for a given OTR requirement, or just a required air flow rate for most indirectly sparged designs.

Mass transfer design by scale-up

Without any kind of $k_l a$ correlation, it is still possible to design by scaling up successful small scale cell culture bioreactors. Various authors have suggested various strategies, one of which we will comment on here.

One such strategy is to scale the airflow on the basis of equal VVM and the agitation on the basis of equal tip speed. The two methods of sparging previously described affect the validity of this approach.

For the case of direct impeller sparging, equal VVM and equal tip speed will give equal $k_l a$ if and only if the exponents B and C are the same. This is because P/V goes down and U_s goes up by an equal ratio, based on geometric similarity. If the exponents differ, the results can be way off. If the vessels are not geometrically similar, the results will also be off.

Driving force increases upon scale-up, so this rule will be conservative when the exponents B and C are the same.

Impeller flooding becomes increasingly likely as the scale ratio becomes larger using this rule, so flooding must be checked, and agitation increased if necessary.

When the gas is sparged indirectly, agitator P/V may not have an effect, so the $k_l a$ value will depend on U_s, which increases upon scale-up using equal VVM. Since the driving force also increases, this rule is extremely conservative for the indirect sparge case.

Equal agitator P/V and equal superficial gas velocity will work reasonably well in most cases. However, use of correlations is better than most scale-up techniques.

A Simplified Approach to Design

Because agitation is not very critical for these bioreactors, it is possible to use a simplified design template that will work in the majority of cases. Basically, it consists of designing the agitator for liquid blending only, ignoring mass transfer, and letting the air sparge handle mass transfer.

The agitator design would normally be based on a scale of agitation of 2-4, with variable speed drive. It will usually have impellers that are near 50% of the tank diameter, for reasons we will discuss later.

The air sparge will typically be near 80% of the tank diameter, so that the air bubbles will usually not go through the impeller, and the rising air bubbles will add to the liquid mixing created by the down-pumping action of the agitator impellers. A typical range for airflow is about 0.01 to 0.05 VVM, much less than for normal aerobic fermenters. Likewise, the superficial gas velocity will be in the range of 0.01-0.03 M/s. The airflow can be set based on known $k_l a$ correlations or just made high enough to be fairly certain it will be adequate.

Shear Damage

Plant and animal cells from multicellular organisms are far less robust against mechanical damage, such as that caused by shear forces, than bacterial or yeast cells. As a result, process engineers have traditionally tried to minimize shear in cell culture bioreactors.

The two main sources for shear stresses are agitator turbulence and rupturing of gas bubbles at the liquid surface. Work by Dr. Jeff Chalmers (Ohio State University) and others strongly suggests that the vast majority of shear damage comes from the rupturing of gas bubbles, not from agitator shear. One might therefore be tempted to ignore agitator shear effects. However, agitator design can affect bubble size distribution and therefore may indirectly affect shear damage.

We will look at both sources of shear and examine how we can minimize them.

Turbulence theory suggests that there is a scale of turbulence or eddy size, and that particles smaller than this scale are not likely to undergo shear damage. Individual cells are very small, and likely are smaller than the scale of turbulence created by agitation. Cells affixed to microcarrier supports may be more susceptible to shear and collision damage, as the supports are much larger than individual cells. An estimate of turbulence scale was proposed by Kolmogoroff:

$\lambda_K = ((\mu/\rho)^3/\varepsilon_T)^{0.25}$

where λ_K is the length scale of turbulence and ε is local power dissipation rate per unit mass. The local power dissipation rate is difficult to calculate, as it may be orders of magnitude higher than the mean throughout the vessel.

Professor Chalmers has studied the shear effects extensively, with and without air sparge. He has found that most unsupported cells will not undergo shear damage at local power dissipation rates less than 10,000 kW/M^3.

Microcarrier supported cells are more sensitive. Based on typical support sizes, the eddy scale should be more than 200 microns. Professor Chalmers has studied shear damage on supported cells. He found that the threshold of damage was around 10 kW/M^3, about 1000 times as sensitive as unsupported cells.

Because eddy size depends on local power dissipation rate, agitator designs which have more uniform power dissipation rates throughout the vessel are favored over those that have extremely high local power dissipation. In practice, this means using axial flow impellers of large diameter, and more than the customary number per tank.

Given the dependence of eddy size on local power dissipation, it is important to find a way to calculate the local power dissipation rate. Probably the only feasible way today is with Computational Fluid Dynamics (CFD). Current CFD codes allow calculation of such figures for single phase media within about 10% error, as long as the mesh size is small enough, particularly around impeller discharge zones. For gas-liquid systems, the accuracy may be less. Many codes do not include the gas power in the overall computation. This could create a serious error for a conventional fermentation. However, the gas flow is very low in a cell culture bioreactor, so the errors may not be as serious.

Minimizing agitator shear

Although direct agitator shear may not be important, the steps we can take to minimize it also will reduce local P/V variation and improve bubble size distribution. Direct agitator shear principally depends on impeller tip speed. Within a given impeller type and scale of agitation, or even a constant power input, we can minimize tip speed by using large D/T and more impellers. We can also reduce tip speed by favoring impellers with a higher power number. We will comment more on impeller design later in this chapter.

Minimizing bubble rupture shear

Most shear damage is caused by the rupture of bubbles smaller than 5 mm diameter. Also, the more bubbles rupturing the more shear damage will occur. Therefore, we want to have only bubbles larger than 5 mm diameter, and as few of them as possible. However, mass transfer is enhanced by both smaller bubbles and more of them. So, mass transfer requirements conflict with shear requirements. The best way to handle both needs is to create as uniform a bubble size distribution as possible, so that we can get the job done with minimal shear damage for the mass transfer rate needed.

Bubble size distribution, it turns out, directly relates to local P/V. So, the measures we take to make the local P/V as uniform as possible to avoid too many pockets of small scale eddies also benefit us in the creation of a uniform bubble size distribution. For a given power input, a large D/T distributes that power more uniformly than a small D/T, creating a more uniform bubble size distribution. Adding more impellers also does this. Sparging near the walls with a large ring sparger creates large bubbles of fairly uniform size, although $k_l a$ will be lower than with direct sparging into the impeller.

Some CFD codes can be used to compare bubble size distribution and volume fraction. While the actual numbers may have error approaching 30%, they can still be used to compare different systems.

As previously noted, reducing the number of bubbles also reduces shear damage. If we are already creating a fairly uniform bubble size distribution but want to reduce shear damage even further, we must increase the driving force for oxygen transfer. One way to do this is to enrich the feed gas with oxygen. Another way is to increase back pressure. However, care must be taken to avoid CO_2 poisoning of the cells

Other methods to reduce bubble shear

We can reduce bubble rupture frequency by reducing surface area of the liquid. This means using a tall thin vessel instead of a square batch. However, this results in poorer blending, higher tip speed and more trouble with CO_2 disengagement. A reasonable compromise in tank geometry would be to use a Z/T ratio of 1.5, with 3 impellers.

Certain surfactants, such as Pluronic F68, cellulose gums, serum and PVA have been shown to reduce cell attachment to bubbles. Thus cell damage by bubble rupture is reduced. However, all surfactants have negative effects on mass transfer.

Need for a variable speed drive.

Because of the inherent conflict between mixing and mass transfer versus shear damage, variable speed drives have come to be viewed as essential. They allow adjustment of power and shear. In conjunction with variable airflow, they afford considerable freedom in fine-tuning the process. Simple conventional fermentations may be able to get by without variable speed.

Mixing to minimize gradients

In this section we look at the effects of different impeller styles, and how to create maximum blending at minimum shear. We also give simple formulae to calculate blend times.

Impeller styles

Though it may seem odd, all common types of impellers have been successfully used in cell culture bioreactors. This even includes Rushtons and other gas dispersion impellers. However, in keeping with the principals of maximum mixing for the power and minimizing shear, and also favoring uniform power distribution, most new reactors use some form of axial flow impeller. The two most common kinds are marine impellers and high solidity axial hydrofoils, although low solidity hydrofoils have also been used.

Figure 1 shows a common marine impeller. (Photo by Chemineer, Inc.)

Figure 1: Marine Impeller

Such impellers are used primarily in small vessels. Because they are castings, they are usually not available in large sizes, and their weight would be an issue if they were. They also have small pits due to being castings, and this may be a sanitary issue.

Figure 2 shows a typical high solidity hydrofoil (photocredit Chemineer, Inc.)

Figure 2: High Solidity Hydrofoil

These types of impellers are fabricated, so they can be made in any size. Their power number (0.7-1.0) is higher than that of a marine impeller (0.3-0.4), so their tip speed is lower for a given power input. They also handle gas better. Generally, they are the preferred impeller style for cell culture bioreactors.

Maximum mixing, minimum shear design template

For maximum mixing at minimum shear, the following principles apply:

1) High power number hydrofoil for minimum tip speed
2) Large D/T (about 0.5)
3) Multiple impellers

These principles not only minimize agitator shear, they minimize shear damage due to bubble rupture, by producing a more uniform power distribution and hence a more uniform, bubble size distribution.

So, the following template applies in most cases:

1) D/T =0.5
2) High solidity hydrofoil impellers
3) Two impellers per square batch (number of impellers = 2Z/T; round up)
4) Scale of agitation 2-4
5) Large ring sparger as long as mass transfer needs can be met
6) Vessel Z/T about 1.5

This design template will usually give tip speeds of 0.5-2 M/s. Some cell cultures have been run at up to 8M/s.

Blend time prediction

Basis: single impeller, Z/T = 1, D/T = 0.3-0.5.

For a marine impeller, the blend time to 99% uniformity may be calculated as follows:

$\theta_{99}*N = 16.7(D/T)^{-1.65}$

Similarly, for a high solidity hydrofoil, we have:

$\theta_{99}*N = 11.3(D/T)^{-1.62}$

The effect of gassing is not accounted for, but gas will actually aid in blending when a large ring sparger is used.

For our recommended design template, with two impellers per square batch, multiply the blend time by about 0.5 to 0.7. For Z/T other than 1, multiply by $(Z/T)^{0.44}$.

Sensitivity to contamination

Because of the much slower metabolism of cells used in cell cultures compared to bacteria or viruses, they can be easily overrun by an infection. Sanitary design is paramount to assure aseptic operation.

The most sanitary agitator design is an all-welded and polished construction. However, an all-welded design with a D/T of 0.5 may require a removable top head, which is not only expensive but introduces a potential contamination source: the flat ledge just inside the I.D. of the head gasket, which is hard to clean. Sometimes this can be avoided by welding the impellers inside the tank, either at the jobsite or at the vessel fabricator's shop. Another way is to install the welded impeller and shaft assembly before the vessel heads have been welded on.

Certain special construction features can allow in-tank assembly of parts with no exposed fasteners. An example of this is the Smoothline™ impeller construction shown in figure 3. (Photocredit Chemineer, Inc.)

Figure 3: Smoothline™ impeller

Current state-of-the-art for cell culture agitator design

Summarizing, the following seem to be best practice guidelines:

1) D/T = 0.5
2) Z/T = 1.5
3) 2 impellers per square batch; 3 impellers at Z/T = 1.5
4) Scale of agitation 2-4 unless more power is needed for mass transfer
5) Variable speed drive
6) Sparge air using large sparger outside impeller unless mass transfer requires direct sparging
7) Consider oxygen enrichment for difficult cultures
8) Employ sanitary design

Chapter 11: Use of CFD in Fermenter Design

CFD, or Computational Fluid Dynamics, is a tool that has been used for modeling fluid transport phenomena in many industries. Basically, it solves the equations of motion and continuity over a large number of "cells" in the flow fields of interest. Some computational models can be used not only for fluid flow, but heat and mass transfer, chemical reaction, etc. The use of CFD in agitator design and fermentation is continuing to grow, and the examples presented here are by no means exhaustive. This chapter presents some of the uses of which the author is aware. Relax and enjoy the pretty pictures!

Acknowledgments

All tank sketch and CFD plots in this section were downloaded from the site www.bakker.org, and are used with the permission of the author, Dr. André Bakker of Ansys (formerly Fluent, Inc.) The plots of k_la, etc. were prepared using proprietary software called GHOST! (Gas HOldup Simulation Tool!) owned by Chemineer, Inc.

How can CFD be used in agitator design?

Although many more uses for CFD in agitator design are constantly being developed, here are a few of the most commonly applied uses.

- Overall flow velocity distribution can be studied, within about 5% error
- Flow around object such as coils and baffles can be studied
- Impeller turbulence
- Eddy dissipation
- Prediction of impeller power
- Local power dissipation
- With special code, multiphase phenomena can be studied
- Chemical reaction conversion, product distribution can be modeled with addition of suitable kinetics equations
- Local bubble size (useful for cell culture)

One of the most common uses is an overall velocity plot, as shown in figure 1:

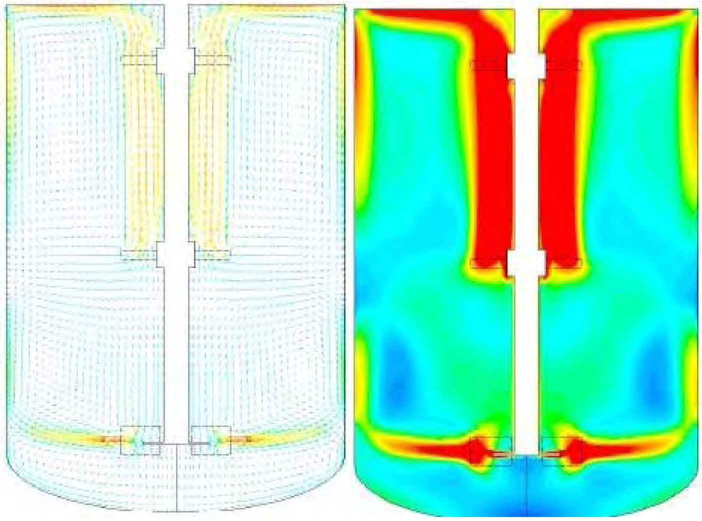


Figure 1: Vector and raster velocity plots

The vector plot on the left shows magnitude and direction of axial and radial velocity, as a time average. The raster plot on the right shows magnitude only, but includes the tangential component. Both plots are of the same system, which consists of upper up-pumping axial impellers above a lower radial impeller.

Figure 2 shows more detailed velocity and vortex information around a pitched blade turbine.

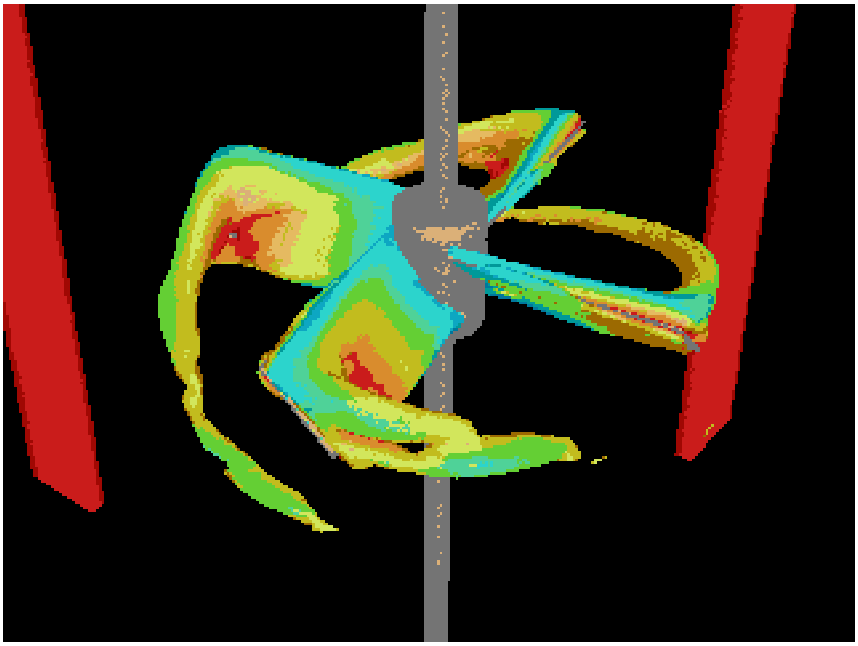


Figure 2: Velocity around pitched blade turbine, showing vortices

Similarly, figure 3 shows vortices around a Rushton turbine

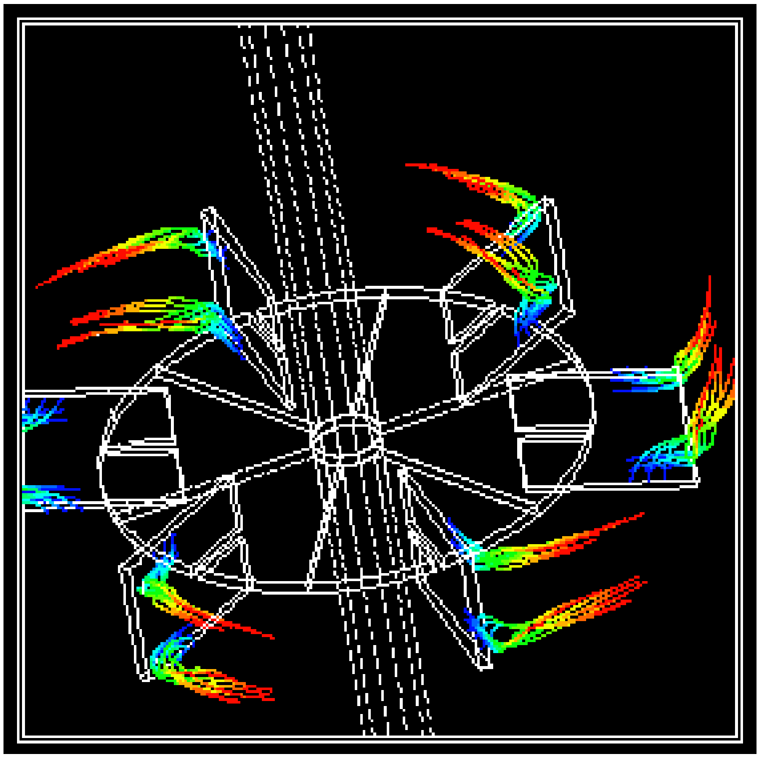


Figure 3: Vortices trailing Rushton turbine blades

Below is a still shot from an animation of vortices on a Rushton turbine. The original animation showed how the vortex formation was somewhat chaotic, and how the vortex trails lengthened and shortened with time, varying in energy content as well.

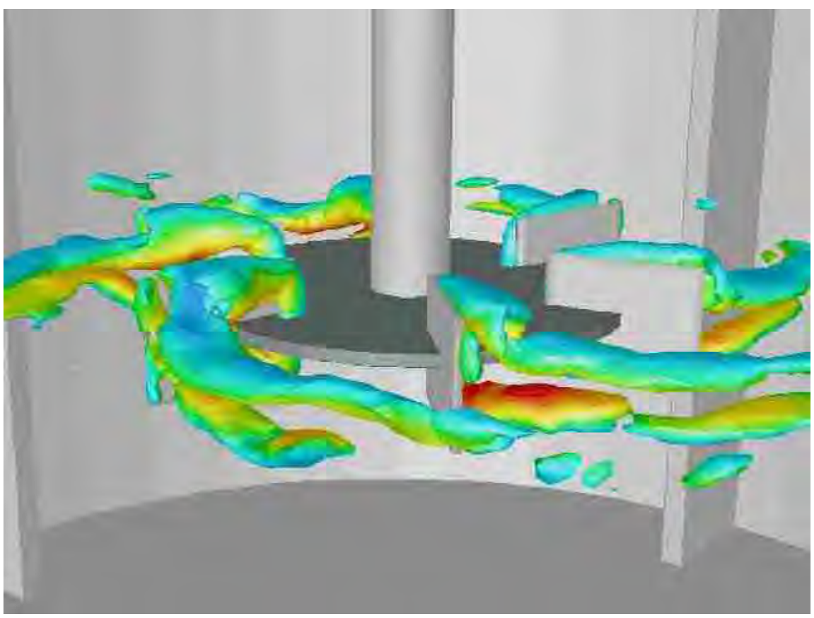


Figure 4: Still shot from a Rushton vortex animation

In addition to velocity information, the blending process can be simulated. The next several figures simulate the blending process of red and blue colors in an initially segregated tank, over a time interval of 0-20 seconds.

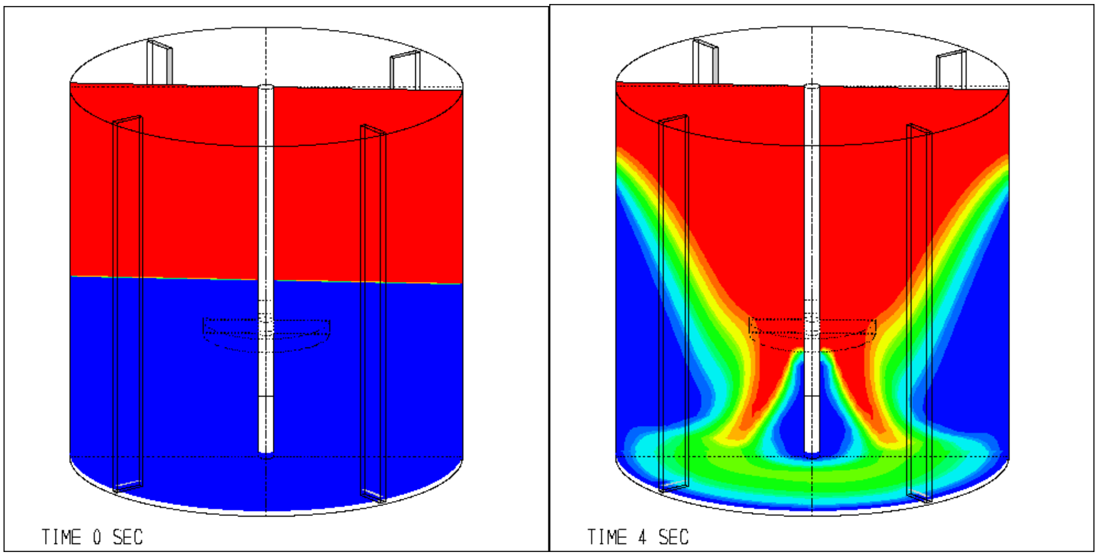


Figure 4: Blending Simulation at 0 and 4 seconds

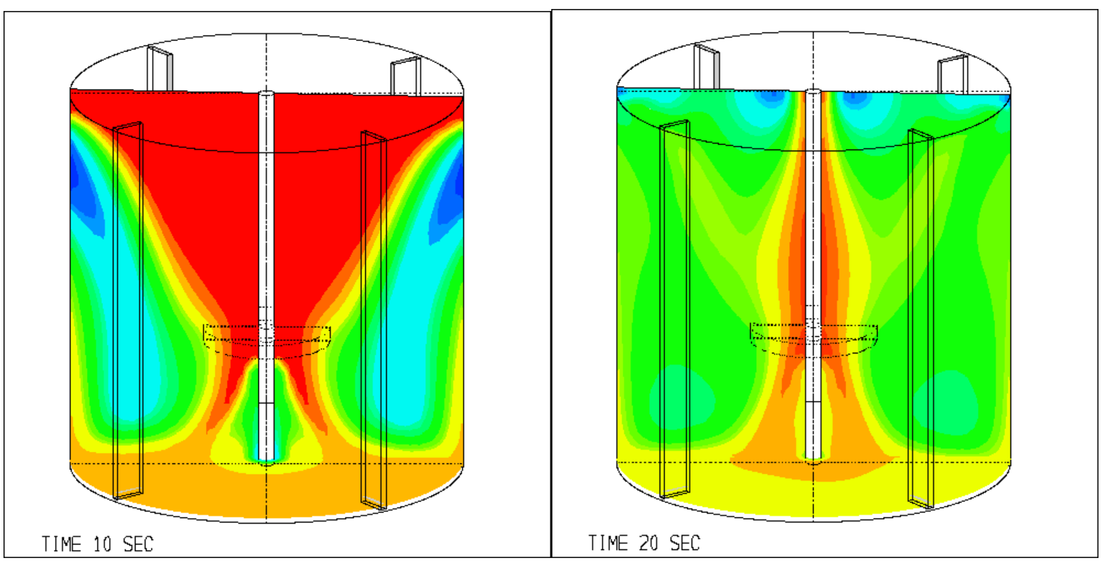


Figure 5: Blending Simulation at 10 and 20 seconds

These types of simulations can show where the last region of the tank to be blended is. Sometimes the results are surprising, such as the 20 second shot above, which shows an unblended region along the agitator shaft. In fermentation, they can suggest where low DO areas may exist, and where the best points to add reagents may be.

Particle path trajectories can be modeled by using random turbulence models. Figure 5 shows possible trajectories. The streaks show the trajectory, and the color is coded to speed along the trajectory. In all models, red represents a high magnitude and blue represents a low magnitude.

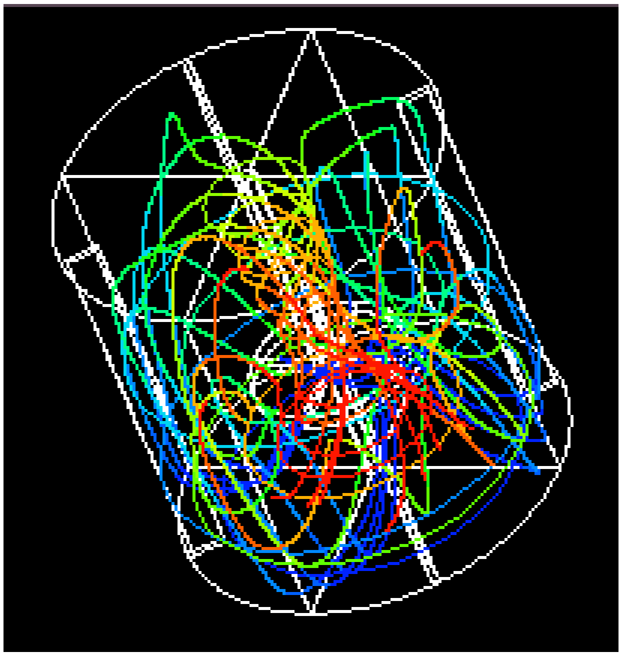


Figure 6: Particle path streaks

Simulation of a chemical reaction

In this simulation, a radial turbine is used to mix materials that create a competitive/consecutive reaction:

$A+B \rightarrow R$; $R+B \rightarrow S$

In this sequence, it is desired to maximize formation of product R. First, we will look at the vector plot of the tank and impeller system. The radial impeller produces two mixing zones and creates strong but highly localized mixing near the impeller discharge.

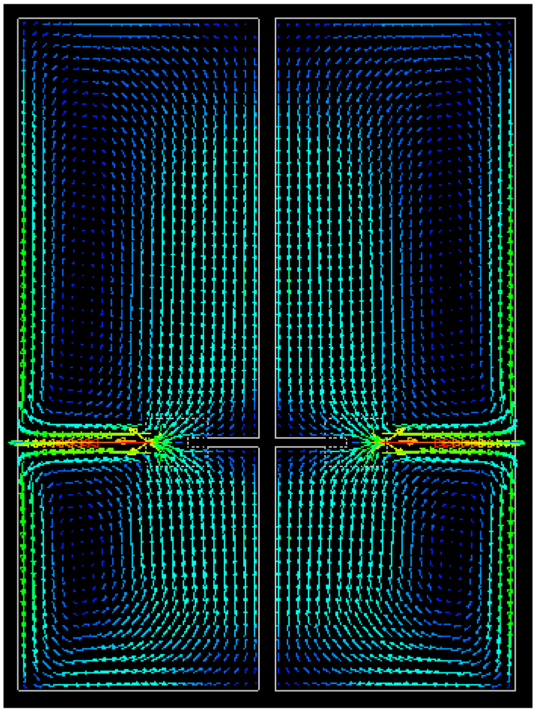


Figure 7: Vector plot of reaction system

Next, we will look at concentration profiles of A, R and S at time intervals from 0 to 20 seconds. In all cases, the visualization panels represent the right half of the tank, and within each slide, the concentrations are of A, R and 3 times S, going from left to right. At time = 0, we can see the point of injection of B just above the impeller.

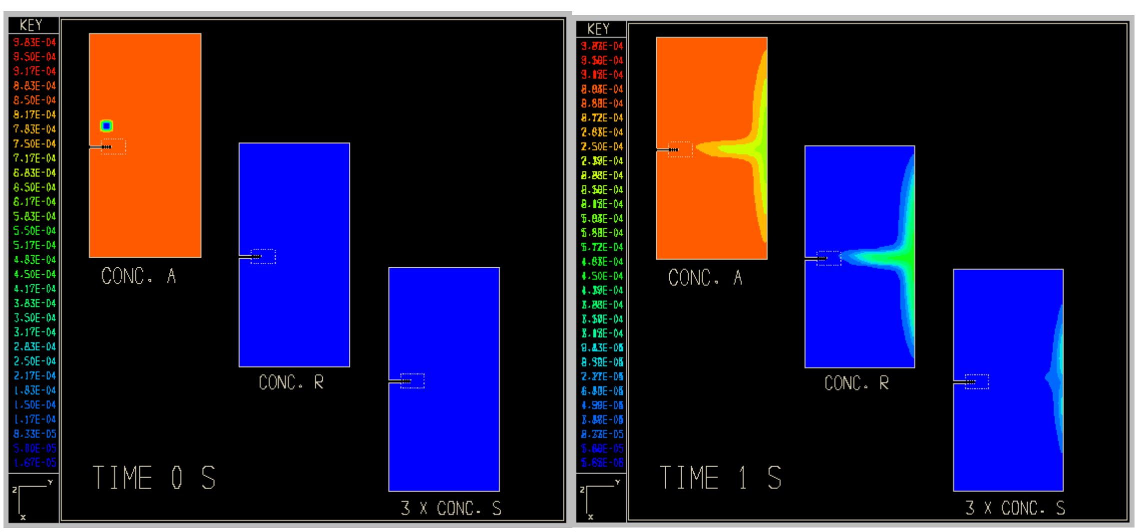


Figure 8: Reaction simulation at 0 and 1 seconds

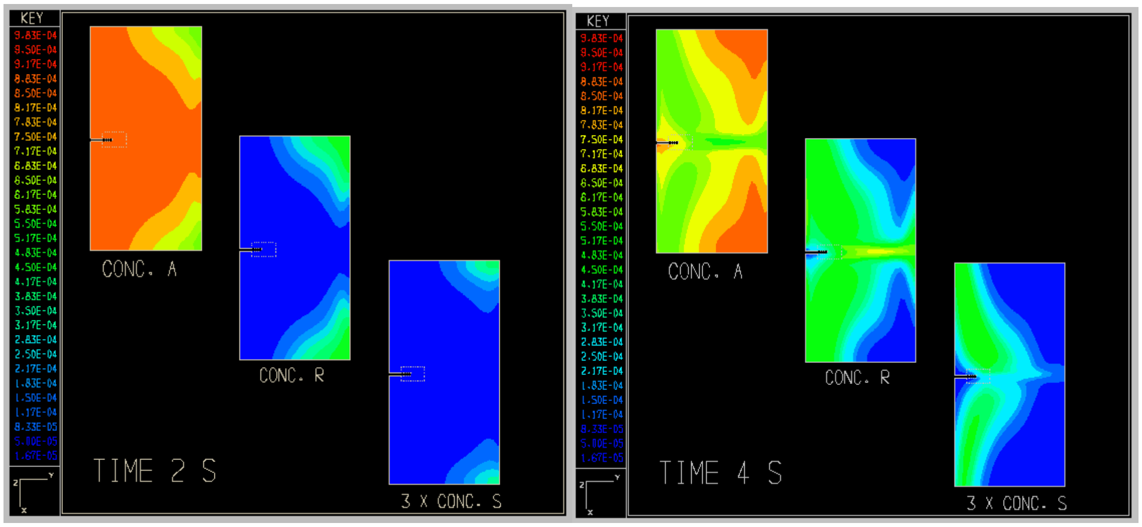


Figure 9: Reaction simulations at 2 and 4 seconds

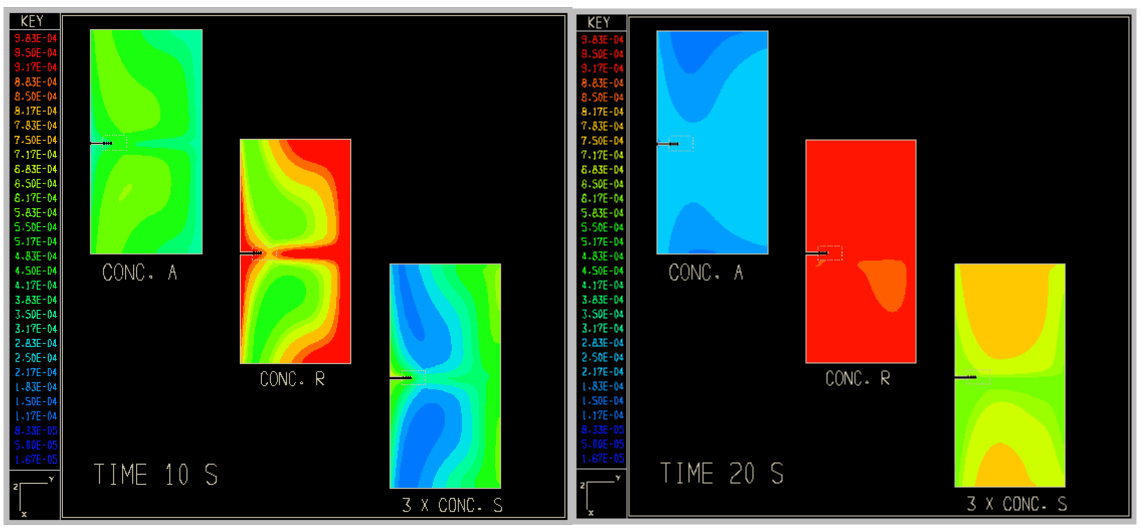


Figure 10: Reaction simulations at 10 and 20 seconds

Modeling of a large production fermenter

Several things can be modeled for large production fermenters. The example we will use to illustrate some of them is an actual unit of 750 kW motor size. A large number of these are presently in operation. The impeller system consists of (3) narrow blade hydrofoils in down pumping configuration above a lower 180 degree concave turbine. The tank has 12 groups of vertical tube bundles used both for heat transfer and as anti-swirl baffling. One of the purposes of the modeling was to be sure there would be good flow between these bundles.

Figure 11 shows rough layouts of the impeller system and bundles, in both elevation and plan views.

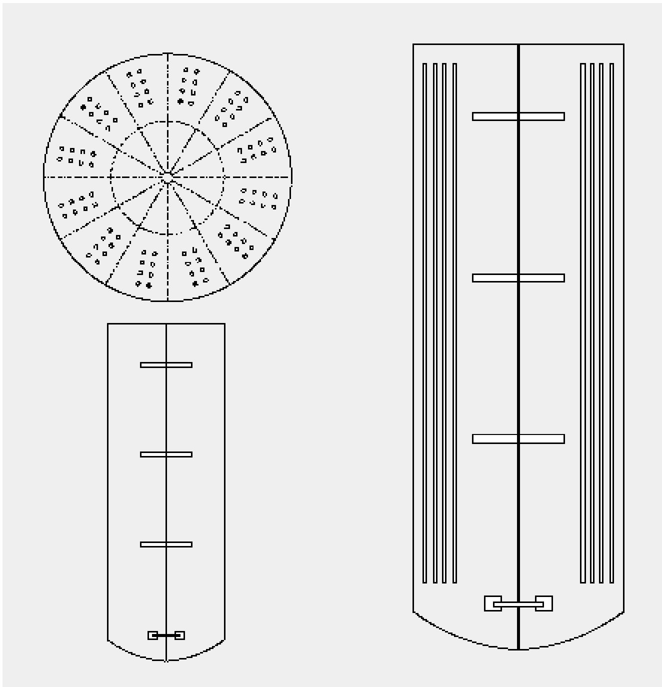


Figure 11: Large fermenter layout

To simulate flow between coils, a raster plot was prepared looking at velocities at several coil elevations, going from top to bottom and left to right.

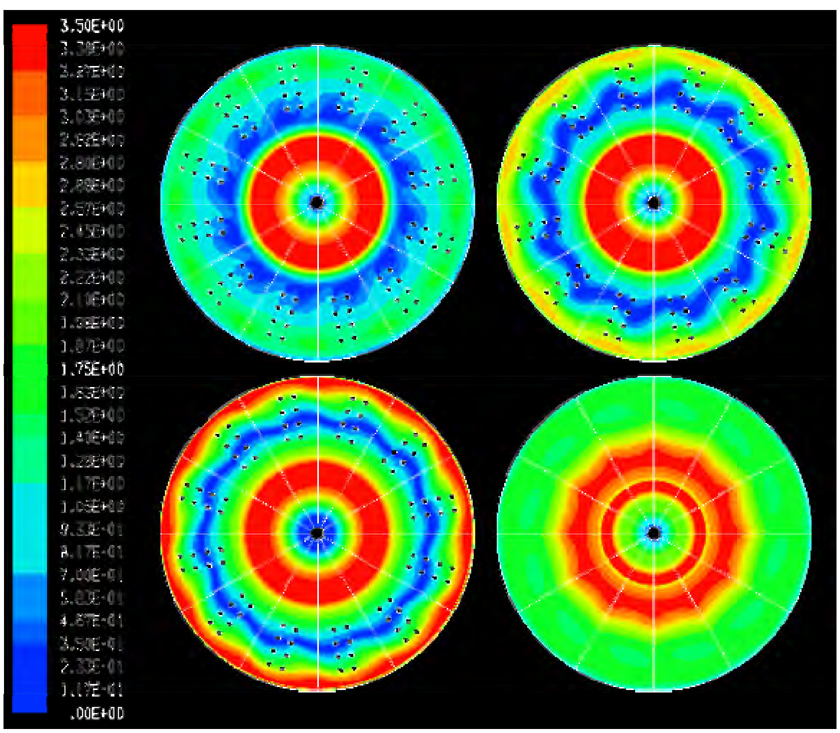


Figure 12: Flow between coils

In addition to flow phenomena, gas volume fraction (holdup), 3 times $k_l a$ and 10 times bubble size were plotted on one illustration. As expected, volume fraction and mass transfer coefficient were much higher near the impellers than near the walls, and bubble size was much smaller near the impellers. About 80-90% of the mass transfer occurs in less than 20% of the tank volume, so good liquid mixing is required to spread the dissolved oxygen throughout the tank. Adding an oxygen consumption model to the mixing and mass transfer models could produce a localized DO plot, which could be very useful.

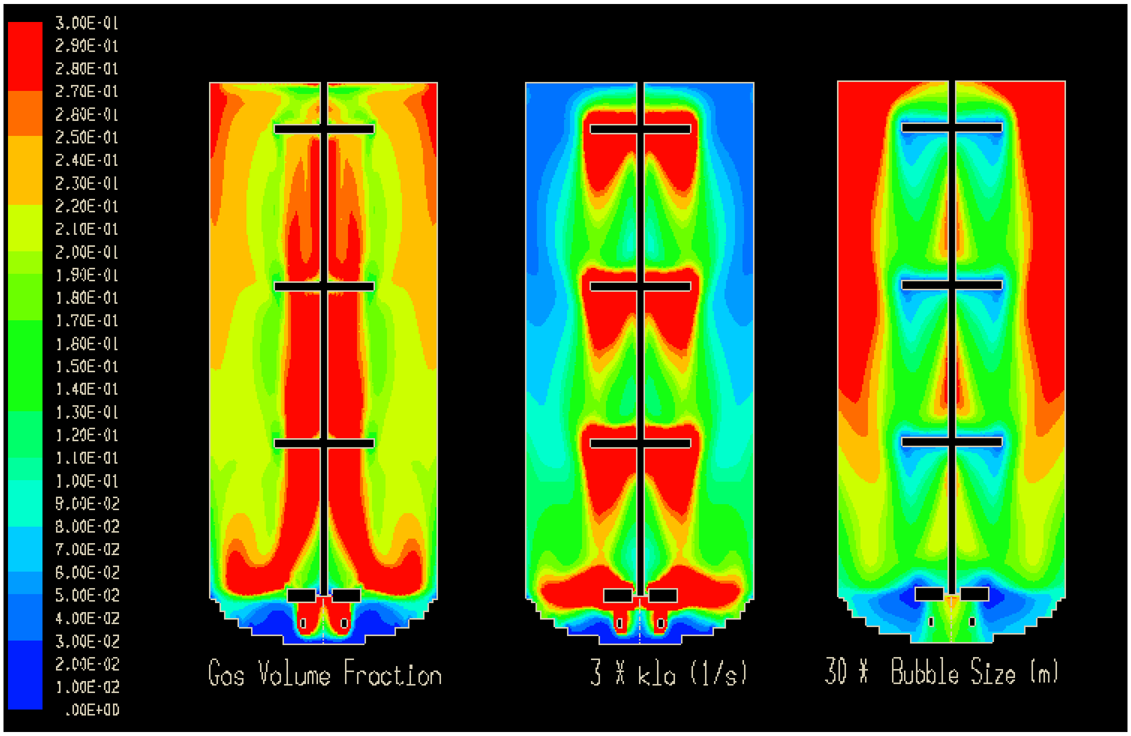
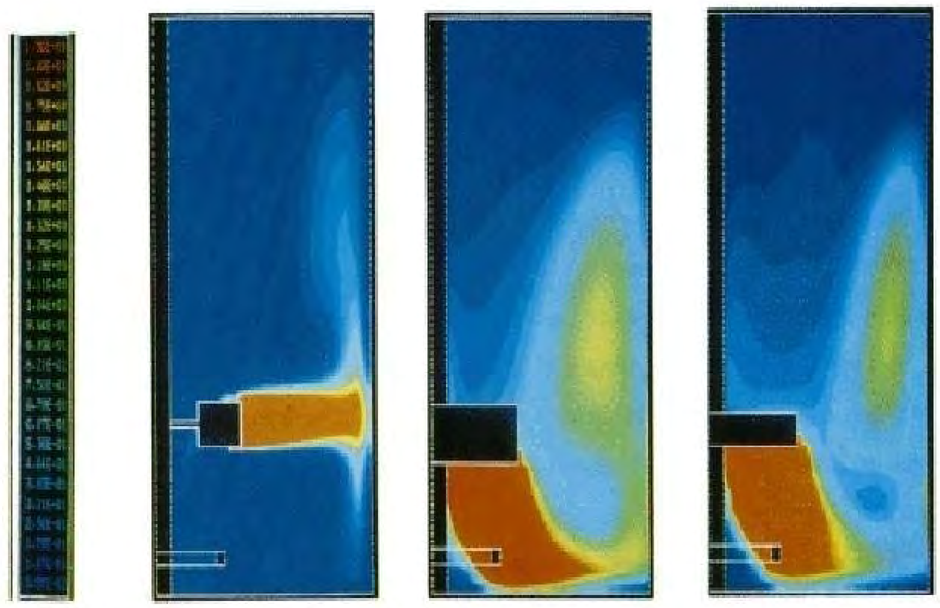


Figure 13: Volume fraction, 3*k_la, 10* bubble size

As mentioned in Chapter 10, local power dissipation can be of interest for cell culture bioreactors. Figure 14 compares the local power dissipation of a Rushton turbine, a Lightnin A-315 high solidity hydrofoil turbine, and a pitched blade turbine, from left to right. These are all at the same total power input.

One can readily see that the Rushton dissipates its power in a highly localized fashion. The high solidity hydrofoil spreads out the power over a much larger tank volume. The pitched blade turbine is similar to the hydrofoil, but spreads the power over a somewhat smaller volume.

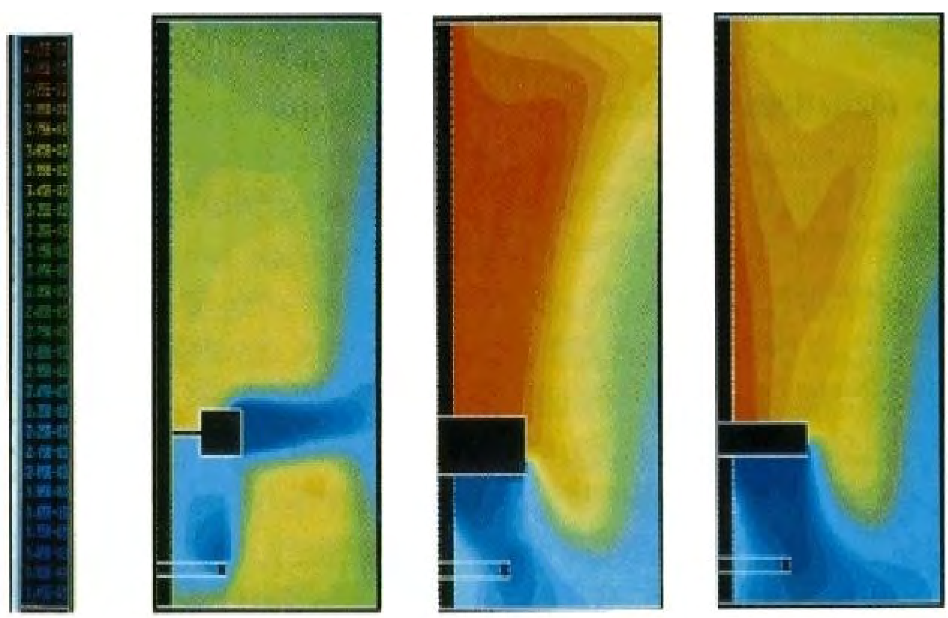
The conclusion is that the local eddy size is smallest for the Rushton, followed by the pitched blade turbine, then the hydrofoil.



Local power dissipation: Rushton, A-315, Pitched blade turbine

Figure 14: local power dissipation

Also of interest both in normal fermentations and in cell culture is bubble size distribution. The same impellers used in figure 14 are looked at in figure 15, but with gas present. Bubble size distribution is shown.



Local bubble size distribution: Rushton, A-315, Pitched Blade Turbine

Figure 15: Local bubble size

One can see that the Rushton creates finer bubbles at the liquid surface, leading to more shear damage when they rupture. The axial and mixed flow impellers keep most of the fine bubbles near the tank bottom, and appear to have a more uniform size distribution. Note that the down-pumping high solidity hydrofoil has a zone of large bubbles near the shaft, leading to mechanical instability and large bubble eruptions near the center of the tank. That is why up-pumping is often used in highly aerated fermenters.

Summary

CFD simulations can be used to tell us many things about what is happening in an agitated tank. Velocity simulations are quite accurate, typically being within 5% of experimental data. More complex multiphase simulations may have larger errors and should be used primarily to compare different systems.

Reaction simulations are becoming more accurate. Although beyond the reach of the average user, it is theoretically possible to combine several models to predict DO distribution, which can be very useful to avoid cell death, change in metabolism or bad product distribution.

Chapter 12: Fermenter Agitator Design Conclusions

One thing should have become evident by now: fermenter design is complex, even without looking at the microbiology or biochemistry. Just examining the physical aspects of agitator design, we have established a need to address the following phenomena:

- Mass transfer
- Heat transfer
- Blending
- Solids suspension
- Shear
- Sanitary design
- Mechanical design and interactions
- Agitator power draw
- Compressor power draw
- Minimization of power consumption
- Capital cost
- Maintenance cost

We have not even touched on shaft seal design, which could easily be a chapter or two in itself.

Seldom are the data sufficient for best practice design. Often design engineers fall into the “do as done before” trap without investigating improvements in agitation technology. Sometimes crude scale-up rules are used, leading to oversized equipment. The emphasis is usually on microbiology, which it often should be, but neglect of sound design principles for agitation does cost money in the long run. Good pilot protocol allows more accurate, economical design.

Both process and mechanical design are important. Proper process design assures that the product can be made at the right rate and yield. Energy cost can be minimized.

While this course did not cover mechanical design, fermenter agitators must dissipate a lot of power, and have the potential to require considerable maintenance if not properly designed. Poor reliability costs more in downtime and product loss than any possible capital cost savings. Poor design can also result in problems with the vessel and ancillary equipment.

What’s in the future?

Though no one can absolutely predict the future, here are a few safe bets:

- Better numerical simulations (CFD), with kinetic and consumption models, at an affordable price and capable of being used by non-expert operators

- Better mechanical technology, consisting of more commonplace use of FEA (Finite Element Analysis) and better definition of mechanical forces created by agitation equipment
- Better understanding of the fundamental mechanisms of mixing and its effect on the process, leading to improved impeller designs and power distribution

Now, on to your test for PDHs or CEUs!

Appendix for Agitator Design Courses

Table of contents

Table 1
Scale of Agitation versus Fluid Property Differences

Scale of Agitation	Maximum Δ S.G.	Maximum Viscosity Ratio
2	0.1	100
6	0.6	10,000
10	1.0	25000

Table 2
Geometry Guidelines

Impeller Type	Reynolds Number	Z/T, first impeller	Z/T increment
Hydrofoil	>1000	1.4	1.1
Hydrofoil	300-1000	1.1	0.9
Pitched Blade	>800	1.2	1.0
Pitched Blade	100-800	0.8	0.7
Radial	>300	0.8	0.7
Radial	50-300	0.6	0.5

Table 3 Various Heat transfer correlations

Correlation for Jacketed Heat Transfer to Side Wall
$N_{Nu}=K(N_{Re})^{(2/3)}(N_{Pr})^{(1/3)}(\mu/\mu_w)^{0.14}(T/Z)^{0.15}$
K= 0.74 for Rushton
K=0.31 for narrow hydrofoil
K=0.45 for pitched blade
K≈0.4 for wide hydrofoil (author’s estimate)

Correlation for Jacketed Heat Transfer to Vessel Bottom
$N_{Nu}=K(N_{Re})^{(2/3)}(N_{Pr})^{(1/3)}(\mu/\mu_w)^{0.14}$
K=0.50 for Rushton
K=1.08 for pitched blade
K=0.90 for narrow hydrofoil
K≈1.0 for wide hydrofoil (author’s estimate)

Helical Coil Correlation
Defining Nusselt number as $h_c d_t/k$,
$N_{Nu} = K(N_{Re})^{0.67}(N_{Pr})^{0.37}(D/T)^{0.1}(d_t/T)^{0.5}$

K = 0.17 for pitched or radial turbines
K = 0.14 for narrow hydrofoils
K ≈ 0.15 for wide hydrofoils (author’s estimate)

Vertical Tube Correlation

Defining Nusselt number as $h_c d_t/k$,

$N_{Nu} = K(N_{Re})^{0.65}(N_{Pr})^{0.3}(D/T)^{0.33}(2/n_b)^{0.2}(\mu/\mu_w)^{0.14}$

n_b = number of baffle bundles

K = 0.09 for pitched or radial turbines

K = 0.074 for narrow hydrofoils

K ≈ 0.08 for wide hydrofoils (author's estimate)

Table 4a

Generic Power Numbers at D/T=0.25

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.73	2.28	2.14	5.5	3.6
200	0.53	1.78	1.75	5.5	3.2
300	0.47	1.56	1.6	5.5	3.2
500	0.41	1.3	1.46	5.5	3.2
800	0.38	1.14	1.38	5.5	3.2
1200	0.36	1.09	1.37	5.5	3.2
3000	0.33	1.06	1.37	5.5	3.2
10000	0.33	1.06	1.37	5.5	3.2

Table 4b

Generic power numbers at D/T= 0.30

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.71	2.24	2.14	5.5	3.6
200	0.52	1.75	1.75	5.5	3.2
300	.45	1.53	1.60	5.5	3.2
500	0.39	1.29	1.46	5.5	3.2
800	0.37	1.12	1.38	5.5	3.2
1200	0.34	1.08	1.37	5.5	3.2
3000	0.32	1.05	1.37	5.5	3.2
10000	0.32	1.05	1.37	5.5	3.2

Table 4c
Generic power numbers at D/T= 0.40

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.69	2.15	2.14	5.5	3.6
200	0.49	1.69	1.75	5.5	3.2
300	0.42	1.48	1.60	5.5	3.2
500	0.37	1.24	1.46	5.5	3.2
800	0.34	1.09	1.38	5.5	3.2
1200	0.32	1.05	1.37	5.5	3.2
3000	0.3	1.0	1.37	5.5	3.2
10000	0.29	1.0	1.37	5.5	3.2

Table 4d
Generic power numbers at D/T= 0.50

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.68	2.11	2.14	5.5	3.6
200	0.46	1.65	1.72	5.4	3.15
300	0.40	1.45	1.60	5.5	3.2
500	0.35	1.23	1.46	5.5	3.2
800	0.32	1.08	1.38	5.5	3.2
1200	0.30	1.03	1.37	5.5	3.2
3000	0.28	0.98	1.37	5.5	3.2
10000	0.27	0.98	1.37	5.5	3.2

Table 5a
Generic pumping numbers at D/T= 0.25

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.33	0.44	0.45	0.70	0.68
200	0.34	0.54	0.55	0.72	0.7
300	0.36	0.58	0.60	0.72	0.7
500	0.38	0.64	0.66	0.72	0.7
800	0.43	0.67	0.70	0.72	0.7
1200	0.45	0.71	0.74	0.72	0.7
3000	0.51	0.77	0.82	0.72	0.7
10000	0.57	0.8	0.88	0.72	0.7

Table 5b
Generic pumping numbers at D/T= 0.30

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.31	0.41	0.42	0.70	0.68
200	0.33	0.48	0.50	0.72	0.7
300	0.35	0.51	0.54	0.72	0.7
500	0.36	0.57	0.61	0.72	0.7
800	0.42	0.60	0.65	0.72	0.7
1200	0.44	0.62	0.67	0.72	0.7
3000	0.47	0.69	0.75	0.72	0.7
10000	0.55	0.73	0.80	0.72	0.7

Table 5c
Generic pumping numbers at D/T= 0.40

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.30	0.36	0.37	0.70	0.68
200	0.32	0.43	0.45	0.72	0.7
300	0.34	0.45	0.48	0.72	0.7
500	0.36	0.51	0.54	0.72	0.7
800	0.41	0.54	0.57	0.72	0.7
1200	0.43	0.57	0.60	0.72	0.7
3000	0.45	0.62	0.66	0.72	0.7
10000	0.53	0.63	0.68	0.72	0.7

Table 5d
Generic pumping numbers at D/T= 0.50

Reynolds Number	Narrow Hydrofoil	Wide Hydrofoil	Pitched Blade	Rushton 6-Blade	180 Degree Concave
100	0.30	0.35	0.36	0.70	0.68
200	0.32	0.40	0.41	0.72	0.7
300	0.34	0.43	0.44	0.72	0.7
500	0.35	0.46	0.47	0.72	0.7
800	0.39	0.48	0.50	0.72	0.7
1200	0.41	0.50	0.52	0.72	0.7
3000	0.44	0.55	0.57	0.72	0.7
10000	0.51	0.56	0.6	0.72	0.7

Table 6a
Gassing factors for radial turbines

$P_g/P_u = 1-(a*\mu-b)*\tanh(c*N_a)(N_{Fr})^d$, where μ is in cp and a,b,c and d are as follows:

Impeller Style	a	b	c	d
Rushton 6-blade	-0.000715	0.723	25.54	0.25
180 degree concave 6-blade	-0.000115	0.440	12.077	0.37

Table 6b
Gassing factors of high solidity impellers at low gas flow rates, down pumping, D/T=0.4

Aeration number, N_a→ Froude number, N_{Fr}↓	0.01	0.02	0.03	0.04	0.05
0.3	0.97	0.96	0.98	1.02	1.04
0.6	0.95	0.87	0.86	0.85	0.84
0.9	0.94	0.85	0.82	0.79	0.77

Table 6c
Gassing factors at high air rates, typical:

Rushton, 0.4
180 degree concave, 0.65
Chemineer BT-6, 0.84
Ekato Phasejet 0.8
Narrow hydrofoils, 0.76
Wide hydrofoils, 0.77

Note: for other conditions and impeller styles, consult the equipment manufacturer.

Table 7
Flooding correlation for radial turbines

$Q_g/ND^3(\max) = K(N_{Fr})(D/T)^{3.5}$; K=30 for Rushton, 70 for 180 degree concave, and 170 for BT-6; all have 6 blades and w/D=0.2

Table 8
DO ratio estimating

Volume, M^3	20	40	80	160	320	640
DO ratio, bottom/top	1.1	1.2	1.3	1.5	2.0	3.0