IB01x - 4.6 - Mixing

This unit will deal with the last of the four most important limiting transport steps in large-scale bioreactors and that is related to liquid mixing.

In this unit we will estimate the magnitude and impact of mixing in different bioreactor concepts.

I will explain that mixing starts with identifying the different liquid flow patterns and related flow regimes.

This is key for understanding mixing. Mixing can be quantified through the 95% mixing time, which can also be made dimensionless in the form of a mixing number. I will show that in a minute.

The bubble column basically shows two different liquid flow patterns depending on how much gas is supplied. There is a switch between these two flow patterns at superficial gas velocities of about 4 – 8 centimeters per second. Below that value then the flow of bubbles is quite ordered, and this is called the homogeneous flow regime. Above this limit then the flow is chaotic and characterized by large circulation loops; this is called the heterogeneous flow regime. You can easily calculate that at lab scale the superficial gas velocity is usually low, generating a homogeneous regime, with slow mixing. However, in large industrial reactors you will usually have the heterogeneous regime, which is characterized by relatively fast mixing. It is important to understand this for scale-up.

For stirred tanks there are many different impeller designs, and you can encounter most of them in industrial practice. They have a strong effect on the liquid flow pattern, although this in the end depends on the balance between the energy input from the impellers and the gas.

In a stirred tank 5 different flow regimes can be encountered, depending on the ratio of gas and impeller power input. The pattern on the left hand side is observed when there is a lot of gas energy compared to impeller energy. This regime is called flooding. On the right hand side is the other extreme when energy input via the impeller is much higher than from the gas, causing complete gas recirculation. In between, there are intermediate patterns indicating how the gas and liquid circulate under these conditions.

Another phenomenon when dealing with impellers in stirred tank reactors is that cavities develop behind the blades. The cavities are responsible for the initial movement of the liquid, and also dispersion of the gas. Some vortex structures will be created at the edges of the blades. If you supply more gas to the impeller, then the cavity sizes increase. At fixed impeller speed, the cavities cause a drastic drop of the power input via the impeller, sometimes down to 40% of the unaerated conditions. This has a major impact on the flow patterns and mixing time in large scale stirred tank reactors.

In industrial practice, there are usually more than one, often 3 or 4, impellers present in the fermenter. What is the impact of the number of impellers on mixing? Intuitively, one may think that mixing gets better with multiple impellers. However, this is often not the case as demonstrated in these lab experiments.

On the left side is a fermenter with 3 radially pumping impellers.

After injection of a tracer, the liquid slowly decolorizes.

We clearly see a slow progress. Many impellers, especially the radially pumping impellers but also the axially pumping variants, create zones of liquid circulation on top of each other, between which there is little exchange of liquid. Such zoning effect will result in poor mixing. On the right hand side the same fermenter is shown, with also the same impeller speed, but now gas is added. The supply of sufficient gas is a good solution to promote good liquid exchange between the zones, despite the reduced power input due to the formation of cavities.

In large fermenters the liquid circulation is even more slow. The computer simulation shows that it can easily take one minute before the contents are almost completely mixed. An often used measure to quantify mixing, is the 95% mixing time, which is the time after which everywhere in the reactor the concentration of the supplied material is within 5% of the final value.

Experimental data on mixing should be interpreted with the flow regimes in mind. This graph compiles a series of test data from a 30,000 litre fermenter with a fixed impeller configuration. Looking at all data together, obtained with different impeller speeds and gas flow rates and gas velocities, mixing times are about 10 - 30 seconds, and the results are not clear at first sight. . However, looking at the unaerated data we observe a falling profile: at higher stirrer speed, mixing time goes down so mixing is faster. This makes sense. But why is mixing worse under aeration at high impeller speeds, and better at low impeller speeds?

Well, this is related to the flow regimes : in the green circle we have impeller loading with more or less complete gas recirculation.

Due to a lower aerated power input the mixing time is higher: mixing is worse. In contrast, at low impeller speeds, in the red circle, the gas is not sufficiently dispersed and here the impeller is flooded. There are long axial loops that promote liquid mixing, so mixing is good. However, mass transfer will usually be quite poor and this regime should therefore be avoided.

The energy input, geometry and fermenter size have a further impact on the mixing time. In order to take this all into account, it is useful to make the mixing time dimensionless, using the total power input and reactor diameter, in the form of the mixing number,N_{mix}. For details I refer to the recent book chapter by van't Riet and van der Lans, who introduced this concept. Just like for the 95% mixing time, a low number means: fast mixing, and a high number: slow mixing.

This is a powerful equation, as it can be applied to all main reactor configurations: STR, BC and ALR. The mixing number is constant for specified geometries and flow regimes and one of the main conclusions is that it appears to be strongly dependent on the aspect ratio, that is the reactor height divided by diameter.

Comparing experimental data from many studies results in this universal overview of the mixing number as a function of the aspect ratio. Lower aspect ratios give a low mixing number and are more favourable for good mixing. Typically, the mixing number for stirred tanks increases dramatically, from about 16 to 500, when the aspect ratio increases from 1 to 5. For bubble columns, at aspect ratios below 3 the mixing number is constant at around 16, while above 3 the same dependency on the aspect ratio is found as in a stirred tank. Comparing with the stirred tank, it is clear that mixing in a bubble column is faster for most aspect ratios. The third reactor type is the airlift loop reactor and there a more or less constant mixing number is found at all aspect ratios between 2 and 10.

This means that only at very high aspect ratios this reactor type has advantages for mixing and that at intermediate levels it is similar to the STR, but still worse than bubble column mixing. However, the ALR can have other advantages, as shown earlier.

At the optimal specific growth rate of 0.0245 h-1, we can make the following analysis.

The tank diameter of 10.7 meter has been estimated in the previous unit. The power input from the gas is calculated from the average gas flow rate, and using the logarithmic pressure ratio from bottom to top, 1.41 W/kg is found.

The dimensionless mixing number for the BC with aspect ratio 2.34, is found to be 16. As a result, the 95% mixing time is calculated 69 seconds. Broth circulation data can be easily derived from this mixing time and we find an average circulation time of 17 s, which is a quarter of the mixing time, as a rule of thumb. And a circulation velocity of 1.5 m/s and circulation rate of 132 m^3/s.

The consequence of this poor mixing is that substrate concentration gradients will develop in the bioreactor, and the cells shuttle between high and low values. Close to the glucose inlet point, the estimated value is more than 5 times higher than close to the exit of the reactor.This can have a negative impact on the metabolic state of the cells, and result in a poor performance of the process.
And that completes this unit on mixing.