IB01x --- 4.1 --- Introduction to fermentation technology

After you have gathered information about the stoichiometry and the process reaction you need to think about what can happen in a large scale fermenter. At this stage transport phenomena become critical. If the broth becomes crowded with microbes and the transport paths are long, then the flow of gas and liquid will become difficult. A good analogue is found in traffic jams. During rush hour many cars want to move in the same direction. But traffic gets stuck because the transport of cars reaches a flow limit.

You will all have experienced this in traffic, but inside an industrial bioreactor, the same things happen! Later this week we will see that, typically, the overall rate of reaction is limited by at least 1 out of 4 different potential transport limitations. One is liquid mixing: the liquid feedstock is pumped into the fermenter and is mixed in a liquid that is already in motion through the action of gas or an impeller. Far away from the inlet point the concentration of feedstock is much lower than close to this inlet point. That means that cells far away have difficulties to get enough feedstock, compared to cells that are close to the inlet. And those cells, in contrast, may suffer from too high feedstock concentrations. The second important transport limitation in large scale operations is oxygen transfer. Oxygen dissolves very poorly in water, but is essential for most microorganisms to function. Therefore, a constant gas inflow is required that provides the gas transfer. The third potential transport limitation is related to the oxygen problem. This bottleneck is the removal of CO_2, one of the products of the process reaction. Oxygen will be replaced by carbon dioxide in the gas bubbles. If not removed properly, CO_2 can become toxic for the microorganisms. The fourth important transport limitation is cooling. You could consider the fermentation of glucose into a product with the help of oxygen like a controlled combustion. During combustion, a lot of heat is produced and this heat has to be removed from the bioreactor. Cooling via the fermenter wall is usually not sufficient for large scale processes and will create problems in temperature control. Therefore, other solutions are needed.

Apart from transport there are more design questions for the fermentation process. The next step would be selecting the best type of fermenter. Bioreactors typically come in different shapes and sizes. Specific processes require other designs. For example in wastewater treatment the upflow anaerobic sludge blanket reactor is used. Other examples of bioreactors are the single-stage fluid bed, the multi-stage fluid bed and the packed bed column. However, we will focus on the three dominant fermenter types which are the stirred tank reactor, the bubble column and the air lift loop reactor. We can call these the principal working horses for fermentation processes.

Once the type of fermenter has been selected, one needs to define the best operation mode. For example, you can provide all feedstock and nutrients from the start in the fermenter and wait until the conversion is completed: this is called a batch process, which is common in traditional fermentation industries. It is very simple and convenient but also has limitations in terms of efficiency: there is relatively much down-time and, moreover, the cells are not in the optimal state to make product. The second option is continuous fermentation. From a process point of view this is the optimal mode of operation, because one can maintain the process and the microbe's environment is always at the optimal state. Also you make optimal use of the hours that are available to run the process. However, a drawback is that microbes may not remain productive for a very long time. And often you see that the whole conversion becomes less efficient after one or two weeks and the process has to be stopped and restarted. There is an intermediate solution called the fed-batch. This is the dominant mode of industrial fermentation. You start with a batch type process and after a while when there is enough biomass you start feeding the substrate. With this operation mode one can create a nearly optimal environment for the microorganism to make product and end the operation after a desired time. These three types of operation are the most important and will also be treated later on this week.

We have now introduced the basic elements of fermentation design. Transport issues are in the end determining how much product you can make in a fermenter. There are different degrees of freedom in the choice of fermenter type and operation. But there are more issues that need to be considered for the final design. These relate to properties of the microorganism (for example the morphology), choices of feedstock that you have and product toxicity. In conclusion: these elements in addition to the process reaction and stoichiometry determine how to make a full scale design.

In a proper design of a biotechnological process, there are four major steps:

1. First, you make the large scale design behind your desk. Weight with experiments and try to envision how the process will be.
2. Secondly sort out how the process can be studied in the lab; do experiments at low cost with different fermenters in parallel and relatively fast. This is also known as scale-down of the full process.
3. If the scale-down is up and running one can try to change the design and find an optimal operation for the fermentation process.
4. Once this third step is completed you can continue to the final step which is to implement the findings from the lab into the large scale fermenter and to operate that in the best sustainable way.

This is the core of what we will be doing this week. We will use the example of 1,3-propanediol to work on a realistic case. When you master this, it will be possible to apply the same approach to the process in your own research and development or scale-up and implementation project.

See you in the next unit!