Alfa Laval in brief

Alfa Laval is a leading global provider of specialized products and engineered solutions. Our equipment, systems and services are dedicated to helping customers to optimize the performance of their processes. Time and time again.

We help our customers to heat, cool, separate and transport products such as oil, water, chemicals, beverages, foodstuffs, starch and pharmaceuticals.

Our worldwide organization works closely with customers in almost 100 countries to help them stay ahead.

How to contact Alfa Laval

Up-to-date Alfa Laval contact details for all countries are always available on our website at www.alfalaval.com

Cell cultures require a gentle touch

Alfa Laval’s gentle hollow spindle design technology
Cell culture

An ongoing revolution inside Life Science

Drug production based on cell culture is quickly growing in scale and turning into an established production method for complex protein based drugs. Benefits of cell cultures as a host are well documented, but these valuable mammalian cells must be treated with a gentle touch throughout their productive life, during fermentation and even more so in the subsequent harvesting stage.

Liquid-filled bowl - hermetic
Whole milk was fed under pressure by a pump through the spindle into the bottom of the bowl. The seal between the stationary inlet pipe and the rotating spindle consisted of a U-shaped rubber gasket which had its wear surface towards the spindle reinforced with fabric. The milk entered the bowl via the central chamber at its bottom, from where it was distributed in the disc stack in the usual way. Since it did not have a hole through its centre its diameter was considerably reduced when compared to machines with top feed. As a result of the overall design, the entire free space in the bowl was filled with liquid.

Improved performance
Besides delivering cream and skim milk free from foam, the hermetic separator was found to possess several other advantages. The most important one was that its clean skimming capability was better than that of any other separator. Two factors brought about this improvement in performance. Firstly, the milk was accelerated very gently in the long hollow spindle, minimizing the splitting of fat globules. Secondly, the Alfa-discs were given a smaller inner radius, increasing their separation area in a given bowl volume.

Culturefuge 100 separation system.
It is the smallest unit in Alfa Laval’s Culturefuge range and suitable for fermentors in the range of 200 - 2,000 litres.

Culturefuge 400 separation system.
It is the largest unit in Alfa Laval’s Culturefuge range and suitable for fermentors in the range of 2,000 - 20,000 litres.

Experience and unmatched performance
Alfa Laval has supplied a large number of cell culture harvest separators for pilot and production scale, and the trend is clear. Cell culture processing is now spreading globally from the market leaders in the USA, and production sizes increases.

Another strong trend is the increasing awareness of gentle separation and the benefits of the Alfa Laval hollow spindle design, largely driven by the good operating experience from industry leaders. Performance details are normal- ly confidential, but in general terms, the gentle touch of a Culturefuge separator has shown very low increases of LDH levels, high centrate clarity numbers wherever installed in pilot or production facilities.

Cell culture separation performance can vary greatly depending on many factors, including e.g. CHO cell viability, fermentation time, hold time, sparge, feed delivery method i.e. pump or fermentor pressure, piping set up etc. However, the typical production rates seen for the Culturefuge 100 is in the range of 0.5-1.0 m³/h, and 6-10 m³/h for the larger Culturefuge 400.

“What is all knowledge except recorded experience, and a product of history?”

Thomas Carlyle (1795 - 1881), Scottish historian
Other gentle acceleration designs

If it is not practical to use a hollow spindle hermetic inlet, other less efficient techniques are possible. The aim is to have a liquid level inside the centrifugal separator inlet at as little an inner radius as possible. Further the unavoidable energy dissipation during acceleration must be distributed over largest possible volume, in order to reduce shear forces. One design that allows smoother inlet conditions and reduced air entrainment is the disc inlet, a patented Alfa Laval concept used in a wide range of biotech separators outside the Culturefuge range.

Many studies highlight the need for gentleness

In a mathematical model for feed zone breakage of shear sensitive particles in centrifugal separators, the breakage was found to be independent of flow rate. In a study by Boychyn et al. simulated the flow field in the acceleration zone of a traditional centrifuge, using computational fluid dynamics (CFD). In this study two cases are compared, one classic with air present in the feed zone, and one gentle liquid filled, i.e. with no air present.

This modeling technique confirms that during acceleration with air present, the maximum energy dissipation rate expressed as W/kg is up to two times higher than in air free acceleration. This higher energy dissipation leads to a considerably higher particle breakage in the protein precipitate suspension and consequently a less successful clarification.

In a later study by Boychyn, a similar CFD tool has been used to model the acceleration forces in the acceleration zone of a multichamber bowl. In this work the group could make good predictions of centrifuge performance.

Finally, there is a comparative study by the same research group on a Cell Culture case processed in two small production/pilot scale disc/stack centrifuges. One separator had a classic non-filled acceleration zone and the other a hollow spindle hermetic inlet for gently accelerating the feed. In other respects (area equivalent, rpm etc), the machines were identical. The group found a 2.5-fold increase in throughput for the same clarification performance when processing thru a hollow spindle type centrifuge.
Alfa Laval’s involvement in cell culture processing goes back to the beginnings of cell culture as a production platform. Working with industry leaders in the development of large scale cell culture fermentations, we soon found that the cell culture characteristics called for extremely gentle separator designs such as the hollow spindle. The current design can be traced back to designs originally developed over 50 years ago for use in the dairy industry. In this application, the gentle touch was used to prevent fat particles in milk from shearing apart during acceleration.

Now, many many decades later, the same base technology is a corner stone in the modern cell culture processing. Alfa Laval has used the experience from the several thousand of hollow spindle separator installations, and combined the latest knowhow and developments to meet the modern and demanding Life Science industry requirements on automation, hygiene and documentation.

The history of the remarkable hollow spindle design of centrifugal separator goes much further back in time, and is worth sharing.

Separation under pressure - the revival of an old idea
Around 1930 Alfa Laval’s drawing office decided to study the feasibility of a separator with liquid discharge under pressure. But, it was beer, not milk, that they had in mind. The opinion was that there should be a good market for beer purification separators if the process could take place without air admission and under pressure high enough to prevent the loss of carbon dioxide. Another large separator producer had unsuccessfully tried to launch such a machine in 1925.

The only rational way in which to achieve the bowl neck. Thus an experimental machine for clarifying beer was built but also tested on milk as it was felt that the machine might solve the milk froth problem. It was found to function well and it discharged milk free from froth. The machine was then modified to have two outlets so that it could be used as a cream separator and subsequently tested in a dairy at Upsala, Sweden, for a period of nearly one year. The outcome was so good that Alfa Laval decided to manufacture a number of these new separators and introduce them at the 1933 Deutche Landwirtschaftliche Gesellschaft exhibition in Berlin. This was the birth of the so-called hermetic separator which radically changed dairy and brewery technology. Its inventors were Nore Bergner, Per Staaff and chief engineer Olof Lindgren.

The design of the hollow spindle hermetic separator
Compared with earlier models, the hollow spindle hermetic separator had an entirely new appearance. The frame was designed so that the inlet parts for whole milk at the bottom of the machine were readily accessible. Neither the traditional two-piece bowl spindle, existing on the 1920 ball-bearing separator, nor the newer Baltic type spindle could be used.

As a consequence, the hermetic separator had to have an entirely new design of spindle. The solution was an adaptation of that from the largest yeast separator, the OVK 5 from 1929. At the top end of the spindle, just beneath the bowl, the flexible top bearing - a radial ball bearing - supported the weight of the bowl, and at the bottom end, a spherical ball bearing allowed for the precision movement of the spindle.

Mammalian cells are fragile organisms. Although relatively easy to separate in a centrifugal disc stack separator, the challenge is to do so with a gentle touch. Acceleration of the protein rich feed material is completed in a fraction of a second and must be in a manner that does not destroy the shear sensitive cell wall membranes and release undesired intracellular proteins into the broth. If additional cell lysis during acceleration can be avoided, the capacity of the separator can be dramatically increased while still preserving the separation result.

Furthermore the downstream purification of the target proteins becomes much easier and equipment smaller, generating significant savings.

The importance of the hollow spindle
The gentlest acceleration possible in a centrifugal disc stack separator is found in the hollow spindle hermetic design in the Cultufuge product range, designed for cell culture harvesting. The hollow spindle design allows gentle acceleration, effectively reducing the acceleration forces experienced by the cells.

In addition, the use of a hollow spindle also provides the opportunity to completely eliminate an air-liquid interface within the centrifuge, creating a truly hermetic design. This air-liquid interface where it exists, has been proven to be a source of foaming and in turn protein degradation.

As a bonus, the hollow spindle design also allows centrate discharge at small radius. This in turn reduces both power consumption and the temperature pick up to a minimum during separation.

Unfortunately the term ‘hermetic’ is sometimes a source of confusion. Hermetic in its true meaning implies no air ingress or air free conditions. Air free conditions in centrifugal separators can be achieved in various ways, e.g. water seals (often called hydrohermetic), and do not necessarily relate to gentle acceleration of feed.