LAMBDA MINIFOR

Laboratory Fermenter-Bioreactor

OVERVIEW AND BENEFITS

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TABLE OF CONTENTS

Overview and Benefits

Many different types of laboratory fermentors and bioreactors are used worldwide, but the selection of a good quality bioreactor is not easy. Some advantageous parameters found in one product are cancelled out by other drawbacks within the same system. We have put all the innovations together and released the new LAMBDA MINIFOR bioreactor, which satisfies most requirements of modern biotech laboratories.

You can find the answers about our bioreactor solutions on www.bioreactors.eu :

20 reasons why your cells will love it... and you, too!

1. EXTREMELY COMPACT BIOREACTOR SYSTEM

- Covers the whole laboratory-scale culture volume range from 35 ml to over 5 liters
- Much more compact than any bioreactor system on the market
- Minimum bioreactor foot print - comparable to the size of a sheet of paper (A4)
- Minimized instrument dimensions - several times smaller than existing systems
- Weight of only 7,5 kg - no other bioreactor system can be carried by a child
- Despite of its compact size the bioreactor grants perfect access from all sides!

more about... Extremely compact bioreactor system

The construction of very compact instruments is a time consuming and expensive task, which no one will make just for the fun of construction engineers.
The main reason for minimizing instrument dimensions is because laboratory bench space is among the most expensive surfaces known. It counts much in terms of productivity, if it is possible to place just one bioreactor or four of them on the same laboratory bench surface...

Therefore, LAMBDA made a major effort to construct the most compact reactor available which despite of its compactness allows for excellent access to the fermentation vessel from all sides. (see also Optimized vessel design for additional information on the culture vessels, which very much contribute to this enhanced accessibility.)

Instead of piling up equipment into towers aside the reaction vessel (which is commonly done in other existing bioreactor systems), the key idea was to put all components just below the fermentation vessel. In this way, both, the bioreactor's foot print and its dimensions are strongly reduced. The sealed, water tight control unit serves at the same time as a stable holder for vessels of all volumes.

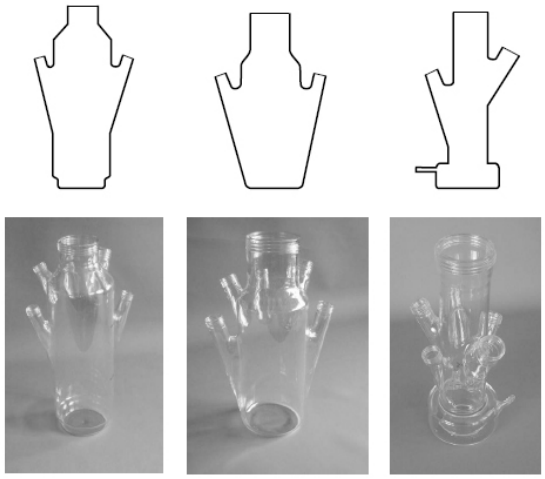
Additionally, many cables, connections, tubing as well as the heating source disappear inside the control unit. This makes the bioreactor vessel environment much less complex and the work with the LAMBDA MINIFOR bioreactor/fermenter much more convenient. It spares also a lot of work doing all the connections for each experiment (setup and dismantling time). (Have you ever seen a picture of a fully connected bioreactor on leaflets of any bioreactor producer? You can guess why not…)

Traditional bioreactor setup

Compact MINIFOR bioreactor system

Much effort was also invested to keep a perfect overview of all parts of the bioreactor (see also maximal accessibility and visibility).

2. OPTIMIZED VESSEL DESIGN



- The very expensive, clumsy and complex to set up traditional metal head plates were completely eliminated (see Elimination of expensive head plates) and replaced by new threaded glass vessels, which make ports manipulation as easy as screwing a cap on a bottle!
- The LAMBDA fermentation vessel has one central neck with large threads for fast and reliable fixing of the agitating and aeration system. This can be easily done just with one hand.
- Eight additional threaded necks are distributed around the side of the vessel (7 small necks and 1 larger neck for quadruple sampling and addition ports) - all well accessible from all sides
- Multiple ports and other implemented solutions make the MINIFOR configuration equivalent to **16** classical ports.
- The side necks are made tight by special elastic stoppers, which have very long contact surface and multiple seals to prevent any contamination. These stoppers are permanent and may be used a great many times. Therefore, operating and maintenance costs are extremely low. The stoppers are easily kept in place by threaded caps.

- Several interchangeable vessel types allow growing cultures in volumes from 35 ml to over 5 liters with just one single instrument. Our standard vessel is of 1 liter total volume. It allows getting high quality results at minimal costs.

- The autoclavable whole-glass vessels are single-walled (jacketed vessels are not needed in the MINIFOR bioreactor system, see revolutionary radiation heating), but if needed, jacketed vessels can also be supplied.

- A big advantage is that the costs of passing to vessels of other volumes are much lower than in traditional systems using head plates. Therefore, the users are not forced to select unpractical, unnecessarily large volume vessels, because they think to eliminate future high costs for additional larger vessels.

more about… Optimized vessel design

The selection of simple, inexpensive and easy-to-use bottle-like bioreactor vessels would never be feasible without the introduction of several innovations:

- The novel non rotational mixing does not generate a central eddy (vortex) and therefore no baffles are required anymore. As a consequence, there is no need to provide a large central vessel opening otherwise indispensable just for the installation of these baffles! The central opening can therefore be of much smaller diameter and such a central neck can be closed easily and at low cost just by using a threaded cap. During the same closing movement the elastic sterility membrane is brought into position. This elastic membrane closes physically the vessel from its outer environment and at the same time enables the up and down agitation movement. The very time consuming preparation and mounting of traditional head plates has been eliminated!

- The revolutionary radiation heating eliminates completely the need for jacketed vessels and generates natural convection even without any stirring! This allows us to use single-walled vessels which considerably increase heat transfer during sterilization and cooling. The sterilization procedure is faster and thermal decomposition of medium components is strongly reduced. Radiation heating through the bottom of the vessel allows an easy use of culture vessels of different volumes. As there is no changing of heating jackets (heating blankets), head plates, electrodes (probes), the cost of passing from one vessel volume to another is considerably reduced compared to all other systems on the market.

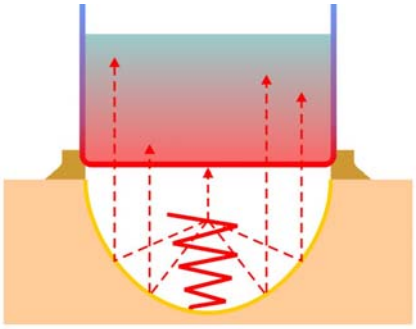
- The threaded side necks allow unhindered access to all ports. Multi-seal permanent stoppers are easy-to-use and eliminate sealing problems due to the well known flattening of o-rings with the resulting loss of sterility and high run to run costs (operation costs). The ports for the probes are located in such a way that the same probes can be used in any vessel volume. This makes a considerable economy when compared with bioreactors of other producers.

- With the exception of inexpensive lateral vessel holders and stirring axis all other parts can be reused when working with different fermentation vessel sizes.

- Multiple ports and additional solutions increase the effective port number of the MINIFOR fermenter-bioreactor, so that its configuration corresponds to 16 classical ports. This is more than enough for the vast majority of fermentation and cell culture requirements. Moreover, the ports can be configured freely by the user according to the application needs.

- The use of large needles (cannulaes) passing through silicon stoppers allows an easy and low cost adjustment to the process by the user. It is not necessary to buy special and expensive parts and accessories.

3. REVOLUTIONARY RADIATION HEATING



- The vessel is heated from underneath by infrared radiation generated by a spiral heater of high heating power but very low heat capacity.
- Heat rays are concentrated by the gilded parabolic reflector with 98 % efficiency onto the bottom of the vessel, where about 50% is absorbed by the glass and about 50% is absorbed directly by medium. The result is an extremely soft heating without any hot spots, not even at lowest medium levels.
- Natural thermal convection takes place even without any mixing of the culture.
- Due to the low heat capacity of metals (corresponding to heat capacity of one ml of water!), the precise dosing of the supplied heat allows a very accurate control of the temperature in the medium
- This novel heating system is also very convenient, because cables, tubing, connectors, the necessity of heating blankets or jacketed vessels and circulating water supplies are completely eliminated
- This new system outperforms all other heating systems

more about... Revolutionary radiation heating

Why are today's best and most expensive bioreactors always equipped with jacketed vessels and thermal circulating bathes?

Such equipment is very expensive, voluminous, not practical and has many other serious problems. Just to mention a few: a very high heat capacity, a low heat transfer during sterilization either with water filled in the jacket or without any water and the consequential longer sterilization times resulting in increased degradation of medium; long cooling-down times; the need for cooling water supplies with the corresponding necessity of additional tubing connections which in turn increase the complexity around the culture vessel; the necessity of expensive circulating pumps etc.

The main reason for using thermal circulating baths lies in the elimination of hot spots on the vessel walls.

All other cheaper heating systems do not eliminate them well or only partially. This is the case of heating blankets, heating clamps etc. The worst of all are heating fingers or rods which even create very dangerous hot spots directly in medium!! They are put into bioreactors by unscrupulous producers only because of their minimal costs. Their inexperienced clients who buy such a "bioreactor" will have to pay for their experience by time and money loss until they decide to throw it away and buy a better bioreactor.

We cannot understand that nobody has thought about using radiation heating before LAMBDA! It solves the problem perfectly and brings so many advantages:

- generation of infrared radiation is so easy and cheap! Just let current flow through a metal wire.
- heat rays are similar to visible light and can be easily reflected by metallic mirrors (gold being the most efficient). A parabolic reflector spreads the radiation evenly to the whole bottom surface. The vessel bottom does not need be perfectly flat.
- heat of certain wavelength is absorbed by glass other wavelengths pass through it and are absorbed directly by the water molecules in the medium in a similar way as sun heats water. Both lead to an extremely soft heating. No hot spots can ever form if the IR radiation is directed on the bottom of the vessel.
- given that no losses occur, the power (wattage) of the IR heater can be much smaller. (Heating blankets and jacketed vessels have higher heat losses than the amount of heat transmitted into medium. They also prevent natural cooling and therefore higher cooling power is necessary.)

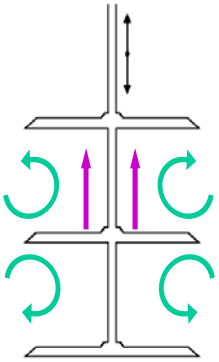
- since only a short piece of wire is required and metals have very low heat capacity, the IR heating is rapidly switched on and off. It heats up and cools down extremely fast. This leads to a much more precise temperature control in the vessel. Think just about the liters of water (having an enormous heat capacity) in the jacket and the bath. This water volume has to be warmed many degrees of centigrade above the desired medium temperature to get any significant heat transfer. When the temperature is attained, this volume of water must be cooled down to prevent temperature overshooting. It is obvious that the temperature control is much more difficult than with radiation heating.

- even a very slight increase in temperature leads to natural thermal convection. Since the radiation is directed to the bottom of the vessel, the convection equalizes the temperature in the medium even without any agitation at all. For example, the variation of the temperature set to 30°C gives deviations of only +/- 0.1°C in a one liter vessel!

4. NOVEL NON ROTATIONAL MIXING

- We have rejected the commonly used stirring of medium by rotation (which is almost a dogma in the field). We were amazed to see how many advantages (at least in the laboratory scale) are obtained by a simple reciprocating up and down movement of stirring discs.

- It is possible to get an easy and complete separation of the inner and outer environment of the bioreactor just by using a simple inexpensive elastic membrane. The results are comparable (if not even better) to the much more expensive magnetic coupling.



more about... Novel non-rotational culture mixing

Almost all laboratory fermenters-bioreactors use circular rotation to agitate the culture medium.

The major technical problem is that the axis of the stirrer (and the motors axis) rotates while the vessel is fixed. Thus, it is a physical necessity that a free space must exist between both, the moving axis and the immobile vessel, otherwise the rotation of the axis would not be possible. This free space allows viruses and microorganisms to get into the vessel. To limit the probability of contamination three ways are used:

The cheapest and less efficient solution is the use of so called lip-seals, which consist of elastic material with a central opening smaller than the axis diameter. This lip pushes onto the axis surface and should make the system tight. At the beginning, the closure can be satisfactory, but with time and especially at high rotation speed the lip is used up and the seal is no longer tight. Contaminating microorganisms can penetrate into the vessel. Therefore, such a system is not recommended for long time cultures or continuous cultures. By the way, even one major provider gives the following advice: “A magnetic stirrer assembly is available by special order if contamination-free work is critical.”....

The second solution is the so-called mechanical seal or axial face seal. In this mechanically more advanced joint the stirrer axis is connected to the head plate by two discs, which glide on each other under a given pressure. The problem of this solution is that the system is mechanically stable only for certain time and if medium salts dry out between these discs their destruction is fast and contamination inevitable. Hence, they must be changed even though they are quite expensive. Much larger seals of this type are used in large, industrial scale fermentors. However, because of the knowledge of the mentioned problems, they are used in double sets with sterile water in between to protect the culture if the packing breaks during a run.

Today’s best solution with respect to contamination problems connected with the rotational stirring is the magnetic coupling. The stirrer axis is completely separated from the motor axis and from the outside environment of the vessel and the driving force is transmitted by two sets of magnets. Since the magnetic force diminishes strongly with distance between poles, the slot separating the rotating cup and the stationary one is very narrow. Frequently, medium deposits and dries out in this space which leads to problems.

Because of the length of the axis and high transmitted force the magnetic coupling is technically quite complex and very expensive. For this reason, it is never proposed as standard equipment for laboratory fermenters. The client can sometimes buy it as an expensive option. In this way, the initial prices of many laboratory fermenters are kept lower

despite of expensive consequences for the client at a later stage, when he is basically forced to buy the magnetic coupling option from the same producer.

LAMBDA has found a very simple, innovative solution for this mixing problem by selecting a non-rotational vertical up and down mixing solution. A simple elastic membrane allows the movement of the stirring axis and serves at the same time as a quality seal between the vessel and its central threaded cap. The membrane separates completely the interior of the vessel from the outside environment and this at low cost for the user.

This new type of stirring has several additional advantages:

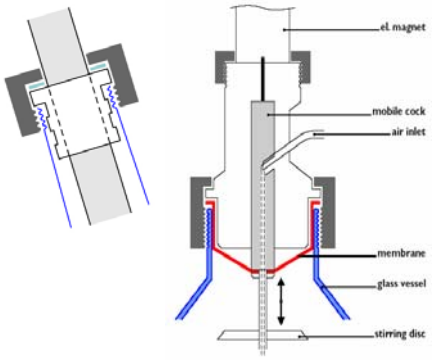
The up and down stirring produces no vortex (eddy) and therefore eliminates the need for baffles. This spares costs, simplifies setting up and cleaning of the vessel and allows the creation new types of vessels (because the large vessel opening otherwise necessary for baffle insertion is no more needed).

The very expensive head plates which are heavy, complicated and long to set up and clean are no longer used. Because no special head plates are required anymore, the cost of passing to vessels of different volumes is much lower. For the same reason, it is no more necessary to buy shorter or longer probes and all other parts*). In the MINIFOR system they are all reused and only few, low cost parts need to be changed (see Optimized vessel design).

*) This important costs lead many users to rather buy fermenters with the largest possible vessel volume and to work under more expensive and high volume conditions, even though this was not required by their experiments. With the LAMBDA MINIFOR fermenter-bioreactor system this is now a thing of the past! Clever users always try to work with the lowest possible medium volume as this offers so many benefits.

5. UNIQUE EASY STERILITY CONSTRUCTION

- Elimination of critical points makes the keeping of bioreactor sterility easy. A strong silicone membrane isolates completely the vessel from the outer environment. The sterility is thus equivalent to magnetic coupling, but is considerably less complex and much less expensive.
- All o-rings have been replaced by large silicone stoppers with multipoint seals. They are permanent and need not be replaced frequently as is the case with o-rings, which become flat after sterilisation.



more about... easy sterility bioreactors

Sterility is the most important quality of bioreactors. Sterility must be easy to obtain and also easy to keep for long time. In continuous processes the culture must be sterile for many weeks. Otherwise the resulting loss of time and money may be very high and even higher than the cost of the bioreactor system itself.

Much time was invested to find out the optimal solutions to warranty a perfect and easy sterility from run to run.

The primary goal was to obtain a complete physical closure (sealing) of the vessel. This was achieved with one large central elastic membrane and a new stirring system (see Novel non-rotational mixing).

The vessel was constructed with several side necks. To make sure that no contamination is possible through these, permanent stoppers with multiple seals were introduced. Like this, the well known sterility problems with flattened o-rings have been eliminated and there is no need to replace seals from run to run.

All tubing connections to ports and bottles are made through special LAMBDA double-seal tubing connectors.

The manipulation of the different ports is as simple as the closing of a bottle with a cap! This provides an additional important advantage: No other bioreactor-fermentor vessel can be set up in such a short time as the LAMBDA MINIFOR.

Since the vast majority of contaminations come from mechanical axis seals and o-rings, the elimination of both in the LAMBDA MINIFOR consequently leads to easy sterility and contamination free runs.

6. SELF-CLEANING MICRO-SPARGER

- Common air spargers are frequently clogged especially in mineralized media. Due to the air flow the medium progressively dries out on the edge of the sparger orifices (openings) and eventually blocks them completely. This stops the air inflow and the run has to be aborted.
- LAMBDA introduces a self-cleaning micro-sparger, which due to its elasticity does release any deposits formed on the sparger holes and thus guarantees gas inflow at all times.

more about... self-cleaning aeration

Many fermentation processes had to be terminated because the air sparger loop was blocked by salt deposits! This problem has now been solved with the self-cleaning microsparger.

When an air bubble forms and is released into the medium, a tiny portion of solution flows forth and back in the sparger orifice. This solution is partially dried up by the next bubble. When this happens many times then, especially in strongly mineralized media, a precipitate forms. This precipitate eventually completely closes the sparger openings. The deposit is sometimes so compact that it can be hardly removed. Some producers deliver special sparger end pieces to get rid of difficult cleaning procedures. A similar behavior is also observed with micro-spargers.

LAMBDA's innovative self-cleaning microsparger eliminates this problem. The sparger is made of special silicone with miniature openings. The elasticity of the material closes the openings when no air passes through. Under the air pressure, these pores open and let the air bubbles form. The medium deposits also form here. This is an inevitable physical process. However, when the deposit accumulates and starts obstructing the air flow the resulting higher air pressure forces the elastic pores to open and thereby the deposit is released into medium. The air passage is free again.

The LAMBDA microsparger can never be blocked even during very long continuous runs!

7. PRECISE ELECTRONIC GAS FLOW CONTROL

- A precise electronic mass flow controller automatically adjusts the pH and pO2 by proportional and continuous gas flow control
- The gas flow measurement and proportional needle valve are microprocessor-controlled
- Exact gas volume information

more about... precise mass flow measurement and control

Gas flow control is an important factor in the reproducibility of microbial and cell cultures.

Even well-known producers of laboratory fermenters supply only simple rotameters (floating ball capillaries) with their systems. The reading of rotameters in not precise and varies with pressure and temperature. Pressure variations are frequent during fermentations and cell cultures because the output filter will progressively be blocked by droplets of medium.

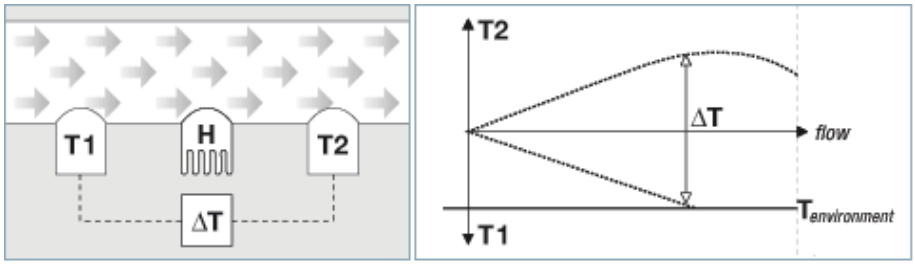
Furthermore, the reading of rotameters can neither be recorded nor can they be electronically controlled. Therefore, the reproducibility of such cultures cannot be assured (which would not be conform to GLP, GMP and other quality systems). Thus, rotameters must be considered rather a toy than a real measuring device in biotechnology.

The only reason for providing rotameters is to lower the initial price of a fermenter or bioreactor system.

LAMBDA does not reduce costs at the expense of quality and therefore does not deliver systems with rotameters at all! All LAMBDA fermentors-bioreactors (even in the lowest cost start-up version) are equipped with high precision thermal mass flow meters electronically coupled with a proprietary proportional needle valve.
The thermal mass flow measurement is based on the electronic measurement of heat transport (see the picture below) which is equivalent to a precise amount of gas molecules transported through the detector. The mass flow signal is independent of variation of temperature, pressure and other factors and delivers a high quality signal which can be recorded. However, such a high quality gas control costs us fifteen times more than a simple rotameter!

The measuring principle of thermal mass flow measurement is particularly well suited for the measurement of gas flows. One of the key advantages is that this measurement method is largely independent of pressure and temperature. Thus, in contrast to volumetric systems (e.g. rotameter), the pressure and temperature do not have to be measured in addition.

The measuring system (mass flow sensor) consists of a heating element (H) and two temperature measurement points (temperature gauges T1 and T2). The gas flowing through the sensor draws off the heat from the heating element.



Schematic illustration of the principle of thermal mass flow measurement

With mass flow measuring and mass flow control instruments, a constant heating capacity ensures a flow-dependent temperature difference. When the gas flow is zero, the heating element (H) distributes the heat evenly so that the temperature difference ΔT=T1-T2 is zero. The presence of a gas flow is accompanied by two effects which generate a temperature difference ΔT: 1) the temperature sensor (T1) located at the entrance of the channel measures a lower temperature. This is due to the cooling of the gas as it enters the chamber. 2) the gas flowing over the heating element transports heat to the temperature sensor (T2) located after the heating element, which results in an increased temperature T2. The hereby generated temperature difference ΔT is a direct measure of the mass flow of the corresponding gas.

The high grade gas flow control allows also a high quality regulation of dissolved oxygen (DO) by air flow rate regulation a not just by variation of stirrer speed as is generally proposed by other providers. We think that DO should be controlled at any stirrer speed. Or should one tolerate bad agitation at low DO values? The bad mixing could lead to accumulation of acid during pH control or generate other problems.

Gas flow modules are proposed in separate instruments MASSFLOW 500 and MASSFLOW 5000, which can be used for the measurement and regulation of other gases (oxygen, nitrogen, carbon dioxide and others). They allow setting up any gas station according to the specific needs of the cultures (see Autonomous precise gas flow control modules).

8. EASY WEIGHT CONTROL FOR CONTINUOUS CULTURES

- The amount of medium in the MINIFOR fermenter-bioreactor can be kept constant by using a special weighing module placed under the front edge of the instrument. The harvesting pump will automatically keep the weight of the culture constant.
- Continuous cultures (chemostat) allow a considerable increase in productivity. In an equilibrated dilution state, culture parameters can be studied more efficiently than in a batch.

more about... easy weight control for continuous cultures

The capability to run weight-controlled continuous processes is an important quality of advanced bioreactor-fermentor systems. Continuous processes allow to optimize experiments faster and at lower cost than batch cultures. Also, the productivity of continuous culture is many times higher. If larger amounts of biomass should be occasionally produced, then for example with a 3 liter vessel, in a continuous run, a productivity of a 30 liter batch system or even more can be attained!

Therefore, all LAMBDA MINIFOR bioreactors and fermenters are electronically prepared for the reception of a low cost scale module, which allows running high quality continuous culture with constant culture weight. This is not achieved by the frequently proposed cheap solutions of using overflow tubes, draft tubes and the like. In not weight controlled vessels the effective amount of culture can vary considerably when agitation or aeration is changed. In such cases, no quantitative conclusions can be made. Reproducibility is thus also not possible and such runs will not be GLP or GMP conform.

9. NEW pH PROBE WITH NANOSUSPENSION

- The new nano-suspension electrolyte provides for long term stability, assures a constant Ag+ concentration at the proximity of reference electrode and zero Ag+ concentration at the porous frit.
- No positive hydraulic flow can be observed during the lifetime of the probe, but the ionic conductivity is good. This ensures good signal stability through the probe lifetime.
- The LAMBDA pH probe is delivered with a new VARIOPIN connector of Swiss production, which has been recognized as industry standard for its quality.
- To decrease the number of available necks and remove one additional cable from the system the temperature sensor Pt 100 has been incorporated into the glass pH electrode. At this place the fastest time response of the temperature measurement is obtained.

more about... nano suspension electrolyte pH electrodes

pH probes are known for so many years, but we are still waiting for a perfect non problematic sterilizable pH probe!

The problem consists of two parts:

1) The glass electrode:

It is almost unbelievable, but only recently the right mechanism of glass pH probe has been discovered by scientists of the German company SCHOTT *).

Many sorts of glasses have been tested but the selection of the right one is always a question of compromises and the glass composition varies according to the intended use.

LAMBDA has selected a glass of optimal compromise for biological processes with increased mechanical stability (which can spare a lot of money to the user!) The glass bulb will not break as easily as in other probes on the market (but one should not insist too much either).

We have placed the Pt100 temperature sensor of highest precision class just into the glass bulb (pH probe tip) to get the fastest possible response to temperature variations. This has an important effect on the quality of temperature control. Additionally, through this combination we spare one port and one cable otherwise required for the temperature probe and the environment around the vessel is less complex.
The lifetime of the pH glass electrode is mainly limited by corrosion of the sensitive glass layer and the speed of response (response time) decreases.

Many factors have effects on the response time and the pH-electrode will age even in pure water. This is due to the underlying physics...

*) F.G.K. Baucke, *„Glass Electrodes: Why and How They Function“*, Ber. Bunsenges. Phys. Chem. **100**, 1466-1474, 1996

2) The reference electrode:

The reference electrode must give a constant and stable reference voltage. To get voltage stability, the environment of the Ag/AgCl layer must be absolutely exempt from any variation. Such conditions are not easy to assure, especially during sterilization and the following long culture runs. KCl leaks out constantly from the reference probe and various substances of the medium diffuse into the reference electrolyte. This also slowly changes the composition of the electrolyte. Ag+ ions diffusing from the electrode may react with components of the medium on the diaphragm and precipitate resulting in the blocking of the electric contact between the glass electrode and the reference electrode. All this can lead to a reference voltage variation and inaccurate pH measurements.

A typical solution of the problem was the continuous washing the diaphragm by large amounts of KCl kept under pressure. Since this was not practical, other solutions such as gel electrolytes have been tested. Because of problems Mettler now goes back to the liquid electrolyte. However, when the outflow of the reference electrolyte is slower than the in-diffusion of substances from the medium, these can get inside and interact with the Ag/AgCl reference electrode.

For these reasons, LAMBDA was looking for new ways of how to achieve stability of the reference signal.

The first step is the blocking of any hydrodynamic flow! We do not want to have any flow neither from inside to outside nor in the opposite direction! (No electrode flushing!)

The second step is the elimination of any movement of electrolyte as well as a maximal slow-down of the diffusion of Ag+ ions towards the medium and of medium components towards the AgCl coated Ag wire.

It is known, that one of the most stable reference electrodes ever was an electrode whose electrolyte was impregnated in pieces of wood. This slowed down the diffusion strongly and therefore, the electrode was insensitive to medium. Unfortunately such a „wood electrode“ cannot be sterilized. If, by analogy, a similar restriction for diffusion could be achieved with a different and compatible material system a comparable signal stability could possibly be obtained.

LAMBDA invested much time in this research and finely found a material system which in terms of diffusion slow down is much superior to natural wood. The micrometric dimensions of the wood structure have been replaced by thousand times smaller nanometric super molecular structures of a nano-porous suspension.

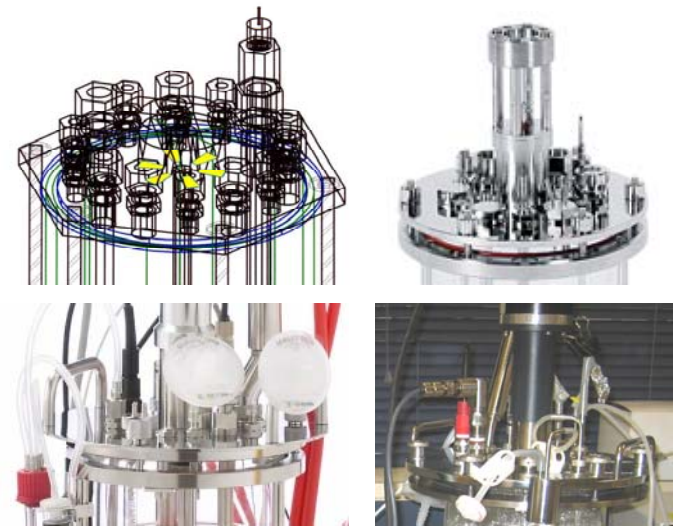
While world leaders in sterilizable pH electrodes worked with gel electrolytes, LAMBDA innovated with a nanosuspension which is perfectly inert and of high stability.
The state of water in a gel is like the state of water in pudding: It cannot flow. The gel “breathes” according to changing conditions, is osmotically active and has also other problems. In a nano suspension water is free to flow like water on a very fine beach sand. However, the dimension of the used „sand“ is in the range of ten to twenty nanometers which results in an extremely long diffusion way. The diffusion gradient is very low and as a consequence the migration speed in both directions is extremely slow.

This is the main reason of the increased time stability of the LAMBDA pH electrodes.

10. ELIMINATION OF EXPENSIVE HEAD PLATES

- Typical fermentation vessels require a rather complex fixing of head plates with many and very closely spaced ports and screws.
- Heavy head plates are expensive and the accessibility of all ports on their top is bad, especially in the case of low volume vessels.
- A new head plate is necessary for each vessel of different volume which leads to high additional costs.
- Threads of ports in head plates are shallow. This, together with the well-known o-ring flattening after sterilization, leads to contaminations.

more about... replacement of head plates



Head plates of traditional fermenter systems

The LAMBDA MINIFOR vessel concept

Head plates on low volume laboratory fermenters/bioreactors have been simply scaled down from larger fermentors. This was not a very good idea. Head plates are the most expensive part of the vessel and also the component which creates most problems:

On small vessels the head plate diameter is so small that it needs a person with really small fingers to be able to fix or loose any part on it. The number of ports is also limited. The plates are heavy and therefore are made quite thin which leads to the difficulty of making the connections tight. The typical technical solution consists in the use of o-rings. O-rings of different sizes are used for the different ports and they must be quite thin. Because of their flattening during sterilization they frequently open a way to contaminations. Thus, they should be replaced before each run. This finally increases the overall fermentation or cell culture running costs in a non negligible way (spare part sets are proposed for many hundreds US$!)

To setup a fermentation vessel with head plates takes much time and each vessel size requires a new head plate but also longer pH and pO2 probes, antifoam and temperature probes and practically everything on the head (O-rings, nuts, lead-throughs,…). This is extremely expensive. Therefore, very often researchers decide to buy the vessel of largest volume to spare investment money. However, working with higher than needed volume is also very expensive and cumbersome. It involves higher medium costs, longer sterilization and cooling times, larger downstream costs and the necessity of disposal of larger amounts of infective material. Large vessels are heavy to put in and take out from the autoclave and their manipulation is definitely problematic for many women, who represent today a large part of laboratory equipment users.

It is the best to use the minimal necessary vessel volume for laboratory scale experiments. It has many advantages and we can only recommend it.

LAMBDA has decided to question the use of head plates and found a very practical, easy-to-use and economical solution instead (see Optimized vessel design, Unique easy sterility construction, Novel non rotational mixing, Exceptional volume range in one single instrument)

11. HIGHEST PUMP QUALITY FOR CONTINUOUS CULTURES

The high quality LAMBDA peristaltic pumps PRECIFLOW, MULTIFLOW, HIFLOW and MAXIFLOW have been **specially developed for long term continuous processes like in fermentations and cell cultures**. LAMBDA's unique tubing compressing mechanics reduces pulsation and is very gentle to the tubing. **No clamps, fixings or stoppers** are required to hold the tubing in place. This leads to a **long tubing life and the long term stability of flow rates even with low cost tubing**.

The tubing economy is such that the LAMBDA PRECIFLOW peristaltic pump is paid back after the use of only 80 m of tubing. Thus, this is **the only pump on the market, which saves more money than it costs!**

Features of the LAMBDA peristaltic pumps:

- **Most compact peristaltic pumps** of this type on the market
- Large range of **flow rates from 0.01 to 10'000 ml/hour**
- Greatly **extended tubing life** with **decreased pulsation** and **very economic in use**
- **Large digital speed setting range** from 0 to 999
- **New motor technology** and **virtually noiseless operation**
- **Flow rate programming** (up to 99 steps) and **automatic switch-on and switch-off** without using any timer
- Extensive **remote controls**
- Access to **reaction kinetics** by using the **Pump-Flow INTEGRATOR** (Flow INTEGRATOR reveals valuable culture information)
- **Low voltage plug-in power supply for maximum safety**
- **RS-485 or RS-232 interface** (optional)
- **PNet control software** (optional)

more about... precise and reliable peristaltic pumps

It is a big temptation for any producer of fermenters and bioreactors to decrease the unit cost by supplying low cost, fixed speed peristaltic pumps using only one size of tubing. Often such pumps are not reliable and the users finally don't use them and buy additional external pumps instead. Recently, even low-cost "nut-shell dimension" peristaltic pump heads have appeared on the market. LAMBDA disagrees with these trends, because the peristaltic pump quality and reliability is a crucial factor, which strongly affects the quality and productivity of the cell culture work.

Both, costs of laboratory infrastructure and personnel costs, are so high today that if a culture has to be repeated after several weeks of experiment just because a peristaltic pump defect the financial and time loss will be so elevated that dozens of high quality pumps could be bought with it. Thus, the economy on low cost peristaltic pumps is a very bad one!

After having made a lot of bad experiences with many commonly available peristaltic pumps, LAMBDA developed new peristaltic pumps with special mechanics, which is gentle to the tubing.

As a consequence the lifetime of the tubing (even lowest cost silicone tubing) is greatly extended and the flow rate is kept constant for many weeks. The risk of tubing rupture or other malfunction has been considerably reduced. The flow rate of LAMBDA peristaltic pumps can be varied in the ratio 1:1000. For example, during the addition of acid the peristaltic pump turns at full speed and reduces the speed as the preset value of pH is being attained. The regulation by such a "soft landing" is much more precise than by merely switching on and off fixed speed pumps.

The worst peristaltic pumps are those which require tubing with stoppers (2-stop or 3-stop tubing) or tubing clamps. This only shows that their mechanics is not good and draws the tubing inside the peristaltic pump head. Moreover, these special tubings are very expensive. LAMBDA peristaltic pumps work well with low cost tubing. The economy obtained by using low cost tubing instead of tubing with stoppers or expensive special tubing material formulations pays the peristaltic pump back after the use of only about 80 m of tubing!

12. AUTONOMOUS PRECISE GAS FLOW CONTROL MODULES

- The LAMBDA MASSFLOW is a **new mass flow controller system** specially developed for the precise flow measurement and control of gases. It uses a **high quality laminar mass flow sensor** that has a very low pressure drop. The gas flow (e.g. air, oxygen, nitrogen, carbon dioxide, …) is continuously measured and controlled.

- The flow rate is regulated by a **special proprietary proportional needle valve** controlled by a microprocessor.

The **flow rate can be programmed** and the **transferred gas volume totalized** with the optional FLOW INTEGRATOR.

- With LAMBDA MASSFLOW the user can **set up high quality gas control facilities** containing **one or more different gas streams** according to his specific needs and is not forced to use common expensive four-gas-stations.

more about… MASSFLOW gas flow control modules

Each LAMBDA MASSFLOW gas flow meter and controller is equipped with a very precise sensor for gas flow measurement based on mass measurement. This sensor measures the heat transported by the stream of gas and expresses the heat capacity of the respective gas. This heat capacity is a function of the number of molecules which passed through the sensor and is therefore independent on many factors such as temperature, pressure and others.

The resulting signal is transformed into an output voltage, which can be recorded. Since the pressure varies during a fermentation or cell culture run, it is important to have pressure independent flow rate measurement. Additionally, the flow rate signal can be recorded and reproduced and the amount of the added gas can be totalized.

The flow rate range is from 0 to 5 l/min in 100 ml/min steps (MASSFLOW 5000) or from 0 to 500 ml/min in 1 ml/min steps (MASSFLOW 500). Additionally, the LAMBDA MASSFLOW can be programmed (up to 50 pairs of flow rates and times).

13. EXCEPTIONAL VOLUME RANGE IN ONE SINGLE INSTRUMENT

- As there has been a lot of progress in analytics and sample preparation methods it is now possible to use, with advantages, much smaller media volumes in smaller vessels than it was before.
- MINIFOR has been conceived so that reliable results can be now obtained in much lower volume than before. No need to use 10, 7, 5, 3 L vessels to study and optimize the living conditions of the cell culture. This can be successfully done in just one liter vessels.
- The MINIFOR fermenter/bioreactor allows you to work with volumes ranging from 35 ml to over 5 liters in one single instrument.

Main advantages for the work with low volumes:

- **Easy and precise control** of the process parameters
- **Shorter sterilization times**
- **Smaller (and cheaper) autoclaves** can be used for sterilization
- **Shorter** medium **heating and cooling times**
- **Cost savings** in culture **media**
- **Cost savings** in the **downstream** processing and equipment
- **Easy elimination** of unused medium and **lower disposal costs**
- **The possibility of continuous culturing increases the productivity by at least one order of magnitude**, thus you can get the same biomass at much lower vessel volumes (see Easy weight control for continuous cultures)

To fully benefit from these advantages we recommend the use of 1L or 3L volume vessels or less.

more about… project stages in biotechnology

Biotechnology praxis shows that there are basically three stages on the way from an idea to an industrially produced biotechnological product: the laboratory scale, the scaling-up or pilot scale and the production or industrial stage:

1. Research on the laboratory scale

The goal is to **select the right organism** for the production, **optimize living conditions** of the strain to obtain the best possible growth and/or productivity. At this stage **all possible growth conditions and factors are studied**.

In short, the objective is to find the optimal living and/or production conditions of the selected organism. At this laboratory stage, one should **work with lowest possible volumes and practical vessels**. This leads to **decreased costs of media and equipment** (e.g. autoclaves, cooling water supplies,…), **shorter set up times, sterilization times, heating and cooling times, minimal requirements for downstream processing, easier handling, more precise control of the process parameters**, etc.

To **get accurate information about the rather complex metabolic behavior of living systems** it is recommended to **measure all accessible parameters and control them with high precision**. The **sterility is very important** on this laboratory scale and, if it is easy to maintain, this results in a big advantage for the researcher, because it increases the productivity and reliability of the research work.

The **vast majority of biotechnology projects are realized at this first laboratory scale level**. It is worthwhile not to hurry up at this stage because **the laboratory experimental work is much less expensive than the following stages**. As there has been a lot of **progress in analytics and sample preparation methods it is now possible to use, with advantages, much smaller volumes of media in smaller vessels than it was before**. There is no use to bother with 5 or more liters of culture volume just to get the same result. The strain does not see the unnecessary large volume around it and **when the control is well done it is possible to get perfect results in much lower volumes than it was about ten years ago**.

This is the main reason why **LAMBDA proposes high quality laboratory bioreactor systems with vessels around one liter**. The **laboratory fermentor is not a production instrument**. An attempt to do so would generally lead only to inefficient use of time, capacity, infrastructure and personnel.

2. Scale up and pilot scale

Essentially, at this stage and scale the goal is to **find out and assure the ideal technical conditions, reactors, processes, downstream processing which will come as close as possible to the optimal living and production conditions previously found at the laboratory stage**.

In larger volumes, it is not possible to get as good aeration, mixing and, more generally, control of any other parameter as it is on laboratory scale. It is not possible to study technological effects with a vessel of ten liters. At this volume, the technological problems are not visible yet. To see these effects well, much larger volumes are required.

The technical means must be selected in such a way that the culture requirements will be practically realizable on large or very large scale at lowest possible investment and process costs.

The **scale-up and pilot stage experiments are at least ten times more expensive than laboratory scale experiments** and any filling and amending of knowledge will cost much.

3. Production and industrial scale

Production stage requires **very high investment and running costs**. Once the production plant has been constructed, **it is generally not possible to make modifications or they are extremely expensive**. Therefore, it is **essential that both laboratory and scale-up stages have been done very well**.

Sometimes, researchers at schools and universities have not enough experience in the matter and do not properly distinguish between this goal splitting in the different stages of a biotechnology projects. This can lead to a mix up the respective goals, which then results in higher costs and longer project times. One should always keep this in mind and present it correctly to the researchers, academic staff and also students.

14. FLOW INTEGRATOR REVEALS VALUABLE CULTURE INFORMATION

- The LAMBDA INTEGRATOR allows to record how much liquid or gas has been pumped as a function of time. This information was not available until now. Examples are:
  - information for the regulation of reaction conditions such as pH, temperature or other parameters
  - information about the kinetics of the respective process
  - completion or disturbances that have occurred during the process

- The LAMBDA INTEGRATOR allows a simple and precise integration of the amount of liquid delivered by the pumps or gas delivered by the MASSFLOW gas flow controller. The electric impulses moving the stepping motor are registered and transformed into a direct current. The resulting voltage can then be measured and recorded. This data yields important information about the culture growth, its kinetics and time of completion.

- The INTEGRATOR can also be used for measuring of enzyme activity (e.g. esterases, amidases, lactamases and other enzymes). It can be placed below the peristaltic pump and does not require additional bench space

more about... flow integration

Frequently scientists want to know how their culture grows and what is its metabolic activity during biotransformation. For that reason, they are looking for instruments which can measure the optical density (OD) of the culture.

Optical density is a logarithmic function and increasing the number of light absorption unit by one means that the intensity of light passing through the sample has diminished 10 times! No need to say that at an optical density of merely 4 the light intensity has decreased by a factor of 10‘000. It is a demanding task for electronics to measure such a low signal with precision. And what about OD 20 or 100? Even though many devices for the measurement of optical density of culture broths have been presented, none is really satisfactory.

There is much interference during such a measurement. The first and most problematic is that OD measurement also measures dead cells. If many dead cells are present in the culture the resulting metabolic activity will be wrong. Also small air bubbles are measured and counted as living cells! The number of microscopic air bubbles, especially in dense cultures, may be quite high.
No need to say that any precipitate or coloration formed during the culture will distort the estimation of metabolic activity of the measured culture.

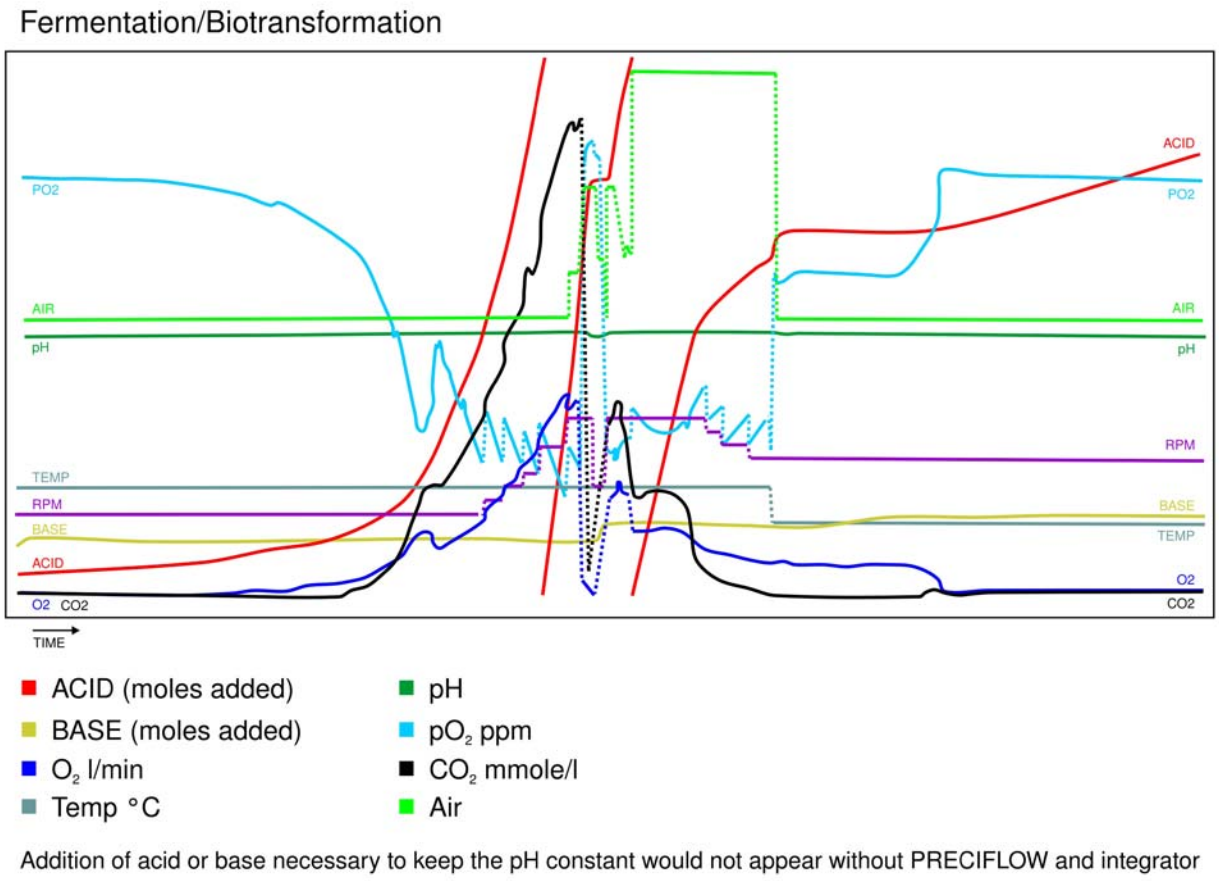
What is really needed is a parameter which could easily be measured and would allow the estimation of the metabolic activity of living cells. With the pump flow INTEGRATOR LAMBDA proposes such a possibility:

The metabolism of all living organisms is somehow connected with the production or consumption of acids or bases. This can be measured and put in relation with cell growth or other metabolic activity. The metabolic activity results then in the change of pH value, which is automatically corrected by the addition of acid or base to remain on the preset pH value. Normally, the amount of required correction solution is not known beforehand.

The LAMBDA INTEGRATOR allows visualizing the amounts of acid or basis added as a function of time. The concentration of acid or base is known and from the data obtained by the INTEGRATOR the added amount of acid or base can be calculated with analytical precision. Thus, the metabolic activity can be calculated with much better precision than from difficult OD measurement. Since the cost of the INTEGRATOR is at least twenty times lower, the economy for the laboratory is considerable.

Enclosed is one example of the trace of an acid pump activity transformed by the INTEGRATOR during one biotransformation culture (red trace with two resets). The red trace is the only one which is clearly exponential, as it should be. By totalizing the consumption of acid, the extent of transformation and the immediate state of the culture

can be derived. No need to say how important such information can be for the control and reproducibility of different cultures.



Addition of acid or base necessary to keep the pH constant would not appear without PRECIFLOW and integrator

Clients of LAMBDA are so convinced about the usefulness of the INTEGRATOR, that they put INTEGRATORs on almost any controlled parameter. No wonder, cells are so complicated that any additional information can only be beneficial.

15. WORLD SMALLEST ANTIFOAM CONTROL SYSTEM

To spare space around bioreactor vessels LAMBDA has developed the smallest anti-foam control system consisting of miniature foam detector ANTIFO and a subminiature syringe pump DOZITO.

more about... miniature antifoam controller and syringe pump

The LAMBDA MINIFOR laboratory bioreactor-fermenter can be equipped with a novel foam detector and control system. The presence of foam in the reactor vessel is detected by measurement of the electrical conductivity. Foaming causes an increase of electrical conductivity. The electrical conductivity can be measured without any expensive anti-foam probe. Instead of such an antifoam probe two needles of the quadruple port of the LAMBDA MINIFOR fermenter vessel are used as electrodes. As a consequence, no additional port has to be used for anti-foam detection.

The antifoam detector/controller ANTIFO is placed just under the peristaltic pump so that it uses only minimal space behind the fermentation vessel. It sends the impulsion to the new subminiature syringe pump DOZITO, which adds a small amount of antifoam liquid into the vessel. If the foam signal persists, a new portion of antifoam is added after twenty seconds. Particular care is taken to prevent an overdosing of the antifoam agent. ANTIFO works either with the DOZITO miniature syringe pump or the LAMBDA peristaltic pumps.

The DOZITO syringe pump is many times smaller than any other laboratory pump on the market. It is hardly larger than the syringe itself. A completely new motion principle is used in the DOZITO syringe pump (no motors, no electromagnets, no compressed gas and the like). The setup and use of the DOZITO syringe pump is very easy.

LAMBDA supplies this mini-pump for controlled addition of antifoam during fermentation in the MINIFOR laboratory fermentor/bioreactor system. The dispensing of the antifoam liquid can be set up from one drop to 15 drops in one step. The pump is vertically fixed using a magnetic support so that it takes only about 10 cm^2 foot print. It is very important to spare space around the fermentor vessel.

The DOZITO can also be used for the dosing of small repetitive amounts of other liquids (e.g. oils, adhesives, cements, glues etc.) in laboratory or industry applications. Since no compressed air is used, the volumetric control is much easier.

16. FULLY INDEPENDENT CONTROL

- The LAMBDA MINIFOR bioreactor can be fully controlled and operated from the front panel. Together with the probes, controllers and pumps it forms an autonomous unit. All parameters can be immediately seen without any scrolling and can be adjusted from the front panel situated on a well visible place just in front of the culture vessel.

- Each MINIFOR has its own two microprocessors and complete regulation electronics. This ensures a continuous measurement, immediate response and the control of all parameters. Such a system is much superior to a partial, sequentially controlled system, where two or more vessels are put on one common control unit, sometimes also called tower. This makes each MINIFOR unit a completely independent bioreactor!

more about... stand-alone bioreactor system

Some bioreactor producers claim that their control unit (or tower) can be used simultaneously with 2 to 6 or more vessels. And this should be advantageous for the client. However, they do not explain that such a control is in principle sequential. The main control unit has to communicate sequentially with one vessel after the other, read the parameter values and react to the data received and regulate the given parameters. During this time (cycle) other vessels stay unattended. The quality of regulation necessarily suffers from such a procedure. The proposed economy is negative for the user and serves only as a not very fair sales promotion argument.

Additionally, in parallel runs, if a centralized control tower breaks down all connected vessels are concerned. With the MINIFOR bioreactor system, if one MINIFOR unit has a failure, only one fermentation run is concerned and thereby, the financial losses as well as time losses are several times lower.

This problem is well-known by certain producers and they now propose a special control unit for each vessel.

Pushed by economy several producers use displays where the user has to scroll to see the different parameter values on the panel. LAMBDA thinks that the user must have the complete and immediate information about the state of his bioreactor. The need to scroll hides relevant information and is therefore very impractical.

On the other hand, to decrease the price of the fermenter-bioreactor system LAMBDA does not use expensive, color displays or fancy touch screens, but shows all data on a LCD display for each bioreactor vessel. Thereby the same function is fulfilled efficiently at much lower cost.

LAMBDA honestly delivers high quality bioreactors/fermentors, where each vessel has a complete and totally independent measurement and digital control system with all data on a large display. It costs us more but the users will surely appreciate it.

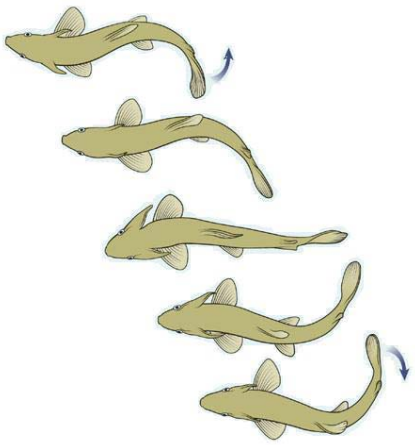
17. TWO PC FERMENTATION SOFTWARE PACKAGES AT THE COST OF ONE

Apart from the direct control of the parameter on the display, a process control system (PCS) for fully automatic control of the batch and data storage is available:

FNet, an easy to use fermentation software for common cultures and up to 6 MINIFOR bioreactors is supplied in one package together with SIAM, a top notch industrial instrument control software which can make almost everything and is unlimited in the number of instruments being controlled. It is upon to user which one he prefers to use. No additional licenses for additional bioreactors are required!

18. NEW SOFTEST AGITATION – THE "FISH-TAIL"

- A special "fish-tail" stirring disc based on the principle of the tail of a fish has been developed. The up and down movement of one or more „fish-tail" stirring discs provides gentle mixing both in horizontal and vertical direction. At the same time this type of stirring is more efficient and it eliminates cutting edges and micro-eddies formed on all common impellers used in bioreactors. As a consequence, the cell viability is increased.



- In analogy to a fish tail, this shape of the stirring disc produces a long range movement of the liquid (culture medium). No other stirrer type provides a similar positive combination of advantages for the agitation in cell cultures.

more about... gentle but efficient cell culture mixing

The agitation of cell cultures is problematic because the large mechanically sensitive eukaryotic cells can be destroyed by the cutting edges of any stirrer. And even completely round stirrers create eddies on their back side! Thus, the question arises: What is better?

1) either increase stirring speed and get good medium oxygenation and gas exchange and partially destroy cells or

2) to protect cells and work under suboptimal gas exchange in medium?

Nature has invented the right solution long before mankind appeared on earth! It is the shape of the fish tail, which has a perfect design which completely eliminates eddies (turbulences) in order to maximize the propulsion of the fish in water. When, in contrary, the fish tail is fixed then water will stream away with maximal efficiency.

It is clear that the very thin and soft rim of a fish tail has no cutting edge which would break cells. By mimicking the fish tail, LAMBDA created a new mixing disc, where high efficiency of stirring is provided without the destructive mechanical damaging and cutting of living cells. Thus, with the "Fish-Tail" stirring disks cell cultures with sensitive cells can be well aerated without destroying the cells.

19. AUTOMATIC RECOGNITION OF THE CULTURE VOLUME

- A very compact control system, which will allow good measurement and control of all important parameters by the same unit, is preferable for the user. Living organisms are extremely complex and it is desirable to measure and control as many parameters as possible. This will help to identify problems when they possibly arise.

- Therefore, we decided to measure and control the five most important parameters: temperature, pH, pO2, air flow rate and stirring. In addition, we wanted to provide the option of controlling one supplementary parameter such as weight, glucose concentration, conductivity, redox potential, optical density (OD) and the like. For this reason, one selectable and controllable parameter “X” has been included. All readings can be seen at a glance without the necessity of scrolling or selecting menus.

- The quality of regulation especially in PID controllers depends on the right setting of constants. From experience we know, that only few users know how to set these parameters properly. LAMBDA therefore leaves this task to the microprocessor which monitors what is going on in the current process and sets the right constants continuously. The working volume is recognized from the heating response on medium temperature and the most appropriate parameter setting is made automatically.

more about... automatic culture volume recognition

It is impossible to set the right regulation (PID) constants for all medium volumes. The LAMBDA MINIFOR bioreactor-fermentor system has the broadest volume range of any laboratory bioreactor - starting from as little as 35 ml to over 5 liters of working volume. For this reason, LAMBDA has greatly simplified the setting of the controller parameters by automatic volume recognition. Thanks to our new and very efficient radiation heating, where heat losses are in the range of only few percents, it is possible to calculate the medium volume from the temperature increase corresponding to the amount of heat supplied.

The microprocessor then makes the optimal controller settings automatically. Therefore, a high precision of control can be achieved in culture volumes varying by more than 100 times! Nevertheless, the user has also the possibility to make the volume setting manually.

20. MAXIMAL ACCESSIBILITY AND VISIBILITY

- A cascade casing guarantees overall easy visibility, accessibility and handling.
- The display showing all parameters and control buttons is located in the front.
- Very good visibility into the vessel which is fixed on the first platform above the infrared radiator.
- Easily accessible probes, ports, tubing and stirring connections.
- Storage of bottles next to reactor quickly fixed and changed in position by magnetic holders.

- Good accessibility of the pumps which are positioned on freely adjustable support plates above reactor vessel and provide shortest possible tubing connections to the reactor vessel.

more about... perfect bioreactor accessibility and visibility

There has always been a big accessibility problem in small volume laboratory bioreactors.

The LAMBDA bioreactor was constructed like a stairway. This allows the best visibility, optimal access to all parts, requires minimal connection distances and all components are located on their logical place.

The display with pressure keys was placed in front of the vessel on the place where it is best seen. The user will see the state of the culture by just one glance. All measured values, all preset values, all alarms, the measured values and pump activity are displayed. It is important that the user does not need to scroll to be able to see the whole information.

The vessel is located on the “first step” behind the display. Here maximal visibility from all sides is provided. The access to the probes, ports and connections have been solved by a new vessel design. Side necks distributed around the vessel give an easy accessibility to all parts of the vessel.

The connections for probes and the stirring are placed between the first and second step, just behind the vessel. Like this, the cable distance is shorter and the cable order logical and is not mixed with tubing coming from the reagent bottles.

The reagent bottles with their magnetic holders are secured in place on the “second step” behind the fermentation vessel. The magnetic holders give the maximal freedom for the placement of bottles of different sizes and number on the smallest possible surface.

The “third step” are adjustable supports for the peristaltic pumps placed above the reagent bottles. This gives the shortest possible distance for the tubing between the bottle, the peristaltic pump and the culture vessel. Additionally, the activity of the pumps (speed and state) can be seen immediately.

The arrangement and distribution of all bioreactor elements and functions (which in all competing bioreactors are placed in big towers aside the vessel) to a minimal space under and around the vessel brings an extreme economy of the very expensive laboratory bench surface. We are convinced that it is not possible to construct a more compact bioreactor for this large vessel volume range, starting from few tens of milliliters to over 5 liters of working volume, with such a good accessibility from all sides!

21. NEW LOW DEAD VOLUME CELL RETENTION DISC

Coming soon:

LAMBDA is testing a new modular cell retention system, where the total filter surface can be selected by the user. This cell retention system will have efficient automatic back washing and an extremely small dead volume. In comparison to so-called spin filters this innovation will considerably increase the efficient volume of the bioreactor and fouling will also be reduced.

You can find the answers about our solutions also on our website: www.bioreactors.eu