

LAMBDA MINIFOR laboratory fermentor

The MINIFOR fermenter/bioreactor was developed as a result of the need to construct a small laboratory fermentor for volumes from **0.035 to over 5 liters**. Based on long personal practical experience of fermentations we wanted to create a fermentor, which was **easy to use** and with the capacity to **measure and control all the important parameters** of the biological culture.

The fermentor had to take up **minimum space** on the bench but with **good access to all parts**. Several fermentors should when placed side by side be suitable for the optimization of the parameters of growth of culture or optimization of bio-transformations etc.

Each fermentor should be able to **work independently or be connected to a PC** for **advanced regulation and extensive data treatment**.

To keep the cost of the MINIFOR fermentor low without compromising quality several new ideas and innovations have been introduced:

- Instead of a fermentor flask with a stainless steel cover, which is expensive, we use **whole glass vessels with threaded fittings**. They have been used for many years in cell culture and are proved to maintain perfect sterility.
- Instead of a traditional propeller agitator, which requires an expensive motor and magnetic coupling, we have introduced a **new vibration agitation**. An electromagnet and an inexpensive membrane which can **perfectly assure sterility** and produce an **efficient mixing** without formation of a vortex (**no baffles** needed). At the same time this type of **mixing is gentler on cells** and **produces less foam**.
- The culture is heated by **heat radiation** produced in a parabolic radiator with a gold reflector placed under the fermentation vessel. The heat is adsorbed gently in the culture in a similar way to the sun heating water. There is **no overheating** of the culture, as is usually the case when a heater is placed in the medium and expensive double wall vessels with thermostatic baths are eliminated. At the same time pipes and cables disappear making the fermentor **less complex**.
- As far as possible expensive pieces of equipment have been replaced by **new high performance plastics**.
- By using modern microprocessors it has been possible to position all the electronics in the front part of the instrument this makes the fermentor **unbelievably compact** and eliminates the casing tower usual in other products. Despite its small size **six parameters are measured and controlled** in the basic configuration of the MINIFOR.

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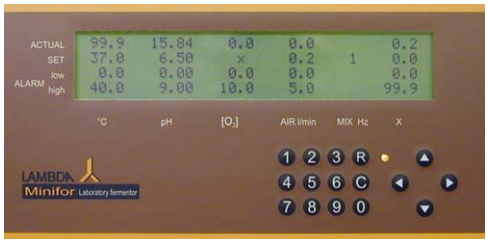
Technical Description

Basic unit

The main feature of the MINIFOR is that all the electronics, power supply, IR heater, air valve, mass flow meter, cables and tubing are positioned in one base unit, which is used as a support for a fermentation vessel and all other necessary equipment. The platform arrangement of the base unit makes **all parts** of the fermentor **clearly visible and easily accessible** from all sides despite base dimensions of only 22 x 40cm (approx. an A4 sheet of paper).

Up to five reagent bottles in **magnetic holders** can be placed behind the fermentor vessel and up to 4 pumps can be placed on **adjustable holders** mounted on bars at the rear part of the base unit. The sockets are located on the rear side of the base unit thus removing cables from the work area.

Measurement and regulation



The control panel consists of an LCD display and control buttons. All parameters (**temperature, pH, pO_2, air flow rate, agitation and one free selectable parameter** (e.g. pCO_2, optical density, antifoam etc.) are visible at a glance on a large LCD back light display (4 x 40 digits). The **controls are simple and logical**.

On most parameters the limits of **low or/and high alarm** can be set. After alarm activation an acoustic signal is heard, the indication appears on the display and an electric signal is generated on the rear side connector of the fermentor. Each fermentor can be operated in an **autonomous** way or can be coupled to a PC (over RS 485) using a **special fermentation program** FNet (for **up to 6 fermentors** in parallel) or larger SIAM software. The later allows almost unlimited possibilities for control and data treatment

Fermentation vessel

The standard fermentation vessel has a total volume of 1 liter (other volumes can be delivered on request). The vessels are made of **high quality Pyrex glass** with one large threaded central opening for the fixation of the membrane and Vibromixer and **6 to 8 threaded necks** for the fixation of different sensors, air outlet, sample withdrawal, inoculation etc. Two adjustable holders maintain the vessel in position.

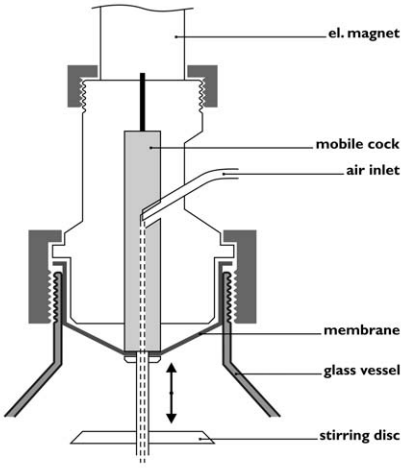
Sterilization

The fermentation vessel is sterilized **in an autoclave** after disconnection of the cables from the electrodes and electromagnet.

Dimensions

A lot of effort was made to make the MINIFOR **as small and as compact as possible**. The platform arrangement of the fermentor makes an **easy control and access to all parts from all sides**. The distance between the reagent bottles, pumps placed above them and the fermentor vessel is the shortest possible.

Agitation



Instead of a traditional propeller agitator a **new vibromixer** is used in the MINIFOR. A strong electromagnet moves one or more perforated discs up and down. The major advantage is an **efficient mixing** and aeration of the culture medium together with very **complete separation** of the inside of the vessel from the outside by a low cost silicone membrane. **No vortex** is built up and **baffles are eliminated**. This type of **agitation is also gentler on the cells** and **foaming is reduced**. The frequency of vibration is controlled by a microprocessor and can be varied through a broad range. The input of air is made through elastic **self-cleaning micro-sparger** fixed under the lowest disc.

Temperature control

A **new infrared (IR) radiator** with a gilded parabolic reflector is used to warm the culture broth. The heat radiation (150W) is concentrated on the **bottom of the vessel** where it is absorbed by the medium in a similar way to the sun heating water. There is **no overheating at any volume** of the culture (common with heaters placed directly in the medium). Thanks to the low heat capacity of the IR source, overshooting of the temperature is reduced and the **temperature can be controlled more precisely**. The temperature **sensor is placed directly in the pH sensor** and is used at the same time for an **automatic correction of pH and pO_2 electrodes**.

pH measurement and control

pH is measured by a combined, sterilizable pH electrode with **incorporated temperature sensor**. Thanks to a new multiple plug Variopin it can be sterilized without any protection. A novelty is the fixing of the reference electrolyte in a nano-suspension. This increases the signal stability and eliminates the problems of gels. The two-point **calibration** of the electrode is **semiautomatic**. The pH value has an **automatic temperature correction**. The addition of acid or base is controlled by a microprocessor. The **flow rate of the peristaltic pumps PRECIFLOW, MULTIFLOW, HIFLOW or MAXIFLOW is varied between 0 to 100%**, which makes the **pH control smoother** than with the common ON/OFF switching of fixed speed pumps. The **unique PUMP FLOW INTEGRATOR** (option) when coupled to the pump enables monitoring of the pump's activity during the process. This yields precise kinetic data concerning the culture state and activity.

pO_2 measurement and regulation

A sterilizable Clark-type electrode with **large cathode** measures the concentration of dissolved oxygen with a special **glass reinforced TEFLON membrane** giving fast response times and short polarization. The major part of the membrane is protected against mechanical injury by a thin wall of PEEK. The microprocessor performs a semiautomatic two-point calibration with **automatic temperature compensation**. The regulation of dissolved oxygen is obtained by a **variation of the flow rate of air**.

Air input

The flow rate can be set from 0 to 5 l/min. in 0.1 steps. A **precise mass-flow meter** is used. This measurement is independent of the pressure and temperature variation of the air. Commonly used floating ball capillaries (rotameters) give inaccurate readings in this case. A proprietary **proportional air valve adjusts the flow rate continuously**.

A new **self-cleaning elastic air micro-sparger** has been developed. Its special construction allows an automatic elimination of salt deposits, which would block the airflow in normal spargers. This is important particularly for micro-spargers having very narrow channels.

Air output

Used air is cooled on a glass condenser and filtered by a PTFE (Teflon) filter. An **optional Peltier condenser, which does not require cooling water**, can be used to remove water vapor from the air stream.

Inoculation and sampling ports

Inoculation, addition of acid or base and sample removal is made through **four stainless steel capillaries** equipped with Luer-Lock adapters or **double seal** PEEK fittings.

Pumps

Up to four peristaltic pumps PRECIFLOW, MULTIFLOW, HIFLOW or MAXIFLOW can be placed on holders fixed on two bars at the rear of the fermentor. They are connected by a single cable to the sockets on the rear side of the fermentor. Since the **pumps are not integrated into the fermentor** they can be used for other applications elsewhere in the laboratory (e.g. for chromatography etc.). This represents **considerable savings** for the user.
A new connection system provides **double sealing of the tubing** and therefore reduces strongly the contamination probability during the transfer of solutions into the vessel.

Gas flow controller

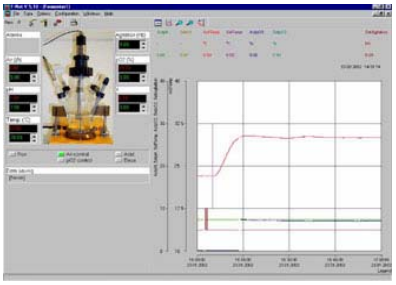
LAMBDA MASSFLOW is a **new mass flow controller system** specially designed for the use together with LAMBDA laboratory bioreactors and fermentors. It allows the control of pH of cell culture by controlled addition of gaseous CO_2, control of nitrogen or of any other gas with suitable controller. However, it can be also used quite independently, since all functions can be accessed from the front panel of the MASSFLOW.

A **high quality laminar mass flow sensor** measures the flow rate. The result appears on the digital display. The mass flow cell has a very low pressure drop and a linearity error less than ±3% reading. The repeatability is better than ±0.5% reading. The flow rate is regulated by a **special proprietary proportional needle valve** controlled by a microprocessor. The **flow rate can be programmed and volume totalized**. MASSFLOW allows a **precise, automatic control of pH in cell cultures without need of any other gas station**.

Continuous fermentation

A new **scale adaptor** (optional) allows weighing of the fermentor. It is simply placed under the front part of the fermentor body and connected to the X-channel input of the fermentor. By means of a pump connected to the ”Pump X”-socket of the fermentor, the weight (volume) of the culture can be kept constant. This function is included in the start-up kit already. This allows the running of **continuous cultures at low cost**.

PC software



FNet was **specially developed for the monitoring and control of fermentation processes and cell cultures** with the LAMBDA MINIFOR fermentor. The software runs under Windows NT, 2000 and XP:

- Easy to install and to use
- No need of programming knowledge
- Recognizes the connected fermenters at start-up
- For up to 6 fermentors, 12 integrators and 6 pumps on one PC
- All the cables use standard connectors

For very high requirements we propose an **industrial fermentation software SIAM**. There are almost no wishes, which could not be satisfied with SIAM. Special functions can be added according to the client’s needs.

Technical parameters

The LAMBDA MINIFOR fermentor/bioreactor is controlled by two microprocessors.

Power:	*Mains 100-245 V AC/50-60Hz, 400W, CE conform*
Dimensions:	*22x40x38cm (WxDxH)*
Display:	*LCD 4 x 40 digits with backlight illumination*
Fermentor vessel:	*Pyrex glass with 5 to 8 side necks 0.2,5, 1, 2, 3 and 5 l (other volumes on request)*
Temperature control:	*IR radiation heat source with gilded reflector 150W*
Regulation:	*from 5°C over RT to 70°C*
Measurement:	*from 0 to 99.9°C in 0.1°C steps*
Precision:	*± 0.2°C (0 to 60°C)*
Sensor:	*Pt 100 incorporated in the pH sensor*
pH control:	*sterilizable pH electrode (pH 0-13), with automatic temperature correction, Variopin connector, two-point semiautomatic calibration*
Resolution:	*0.01 pH unit*
Precision:	*± 0.02 pH unit*
pO_2 control:	*sterilizable Clark type oxygen sensor with fast response, reinforced Teflon membrane and automatic temperature correction, control through regulation of air flow rate,*
Range:	*0 to 25 mg oxygen/l, in 0.1 mg/l steps*
Air flow:	*0 to 5 l/min. in 0.1 l/min. steps, mass flow meter, linearity ± 3%,* *reproducibility ± 0.5%*
Control:	*proportional valve*
Supplied air pressure:	*between 0.05 – 0.2 MPa*
Agitation:	*40 W Vibromixer 0 to 20 Hz with 1 or more stirring discs* *Sterility comparable to magnetic coupling*
Selectable parameter:	*an additional parameter can be controlled by the instrument (foaming control, pCO_2, optical density, conductivity, etc.)*
Sampling ports:	*up to 4 needles with Luer-Lock fittings can be used for sampling and addition of correction solutions*
Pumps:	*up to 4 independent peristaltic pumps (PRECIFLOW, MULTIFLOW, HIFLOW or MAXIFLOW) with speed variation from 0 to 100 % can be used with MINIFOR*
Working temperature:	*0 – 40 °C*
Working relative humidity:	*0 - 90 %*
Weight:	*7.5 kg*
PC control:	*complete PC control and data treatment using FNet or SIAM fermentation software*
Warranty:	*2 years*

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