

The Multi - Minifermenter



Infors is an international team with branches in Europe and the USA.

Innovative thinking, quality and an understanding of the needs of our partners has secured Infors an unrivalled place amongst manufacturers of fermenter and shaker equipment. An enthusiasm for experiment and a creative mind has guided the company from its establishment in 1965 through its development into a medium-sized enterprise. Independence, a distinctive character and a strong team spirit will continue to serve us well in the future.

The head office on Infors AG is in Bottmingen



Quality Standards



- ISO 9001
- CE
- EMV

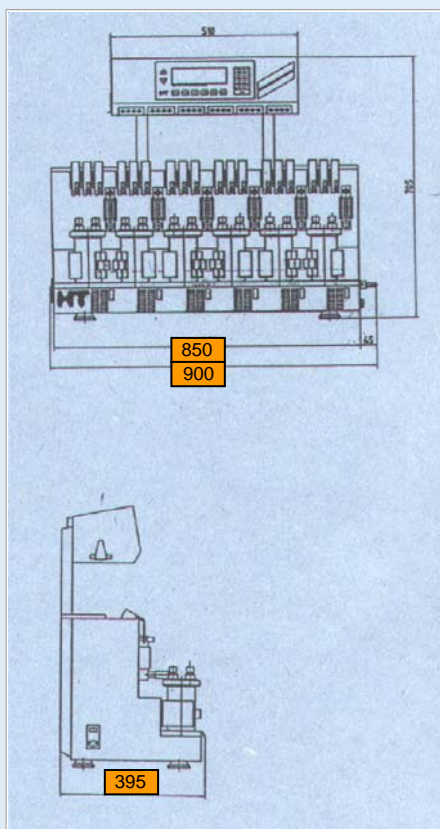
For Process Documentation to GMP

- Documentation
- IQ
- OQ



Fermenter system for „Screening“ and „ Scale up“

The SIXFORS is a Multi-Fermenter system for small culture volumes (approx. 200-500ml WV) in batch, fed-batch and continuous operation. It bridges the gap between shake flasks and laboratory-scale fermenters and offers new possibilities for screening and scale-up studies.



Small footprint

Six individually controllable Mini-Fermenters in 0,36 m²

- Individual temperature equilibration and alteration of gassing rate using parallel manifolds
- Continuous registration and control of pH and pO² values.
- Timed and program-controlled substrate dosing
- Complete data-logging and archiving.

The Sixfors, operates under the digital U-DDC system (*Usual* Direct Digital Control = control via a central microprocessor). This simple, modern technology enables independent and simultaneous parallel control of all important process parameters for one to six fermenters..

The six fermenter positions offer the opportunity for serial experimental sequences by providing the necessary control system.

The U-DDC control system is always configured – except for an optional system with just 4 fermenters- for the control of six fermenters. This allows for future expansion as the additional capacity can be utilised after a simple upgrade to add additional pumps and operational amplifiers.

A particular point to consider is the scarcity of space in the average laboratory. With a footprint of only 900 x 395mm, any laboratory can find space for the Sixfors.

Bacterial or Cell culture

The Sixfors is available in two configurations:

Sixfors with flat bottom vessels for bacteria, yeast and fungi

Sixfors Cells with round bottom vessels and integral gas mixing.

U-DDC Control Unit

The control unit saves space by being mounted above the services base unit. Programming of parameters is via a splash-proof membrane keypad and an LCD display. Part of the control unit are operational amplifiers modules for temperature, pH, PO₂ and antifoam/level.

At the heart of the U.DDC is an extremely efficient micro-processor. This allows parallel operation of up to six fermenters, each having individual control.



Measured and controlled parameters

- Stirrer speed
- Temperature
- pH
- pO₂
- Antifoam/Level
- MassFlow, or
- GasMix; whereby the actual percentage proportion of O₂ & N₂ is adjusted via the optional INFORS Gas Mix Station.

pO₂-Control

pO₂ control can be achieved by one of several options

- Stirrer speed
 - Mass Flow*
 - GasMix *
 - O₂ Supplementation*
- *Options.

System Expansion (Optional)

- Output for external analogue pumps
- Connection for balances for weight-controlled feeding strategies via IRIS Multi-fermenter software.

Memory-Card

All programmed vales are automatically stored on an interchangeable **Memory-Card** and used at the start of a fermentation. Complete recipes can be stored for different types of fermentation and simply loaded from the card when required.



Profile/Ramps

Every parameter, including substrate dosing, can be controlled from the PROFILE menu where 10 time-based stages (ramps) per fermenter can be programmed using a simple listing.



Base Unit

The base unit comprises

- Corrective reagent pumps
- Motor controllers and stirrer motors with magnetic coupling
- Temperature control modules
- Gas supply
- Cooling water supply

Pressure regulators are installed for the water and air/gas supplies so that the fermenter can be directly connected to the house services.

Corrective reagent pumps

The addition of corrective reagents and substrate feeds is achieved using 6 sets of pump stations, each with up to three peristaltic pumps especially developed for use with small fermenters. All 18 pumps are freely configurable. You can set automatic control for eg. pH or use time-based control cycles for dosing. The ON/OFF phase of each pump is switched magnetically and so is completely lag-free for more accurate dosing control. All pumps can be manually primed using simple manual pressure eg. to fill the reagent lines before use. If required, external analogue pumps can be connected to the system.



Temperature Control

Temperature control is achieved using an aluminium heating block which also forms part of the holding mechanism for the vessel. The vessel is held firmly against the heating block and is easily located in a similar way to putting a shake flask in a clamp. The cooling system is also integrated into the aluminium block. Coolant is supplied on demand to each position individually via a magnetic valve.

The heating block facilitates a rapid heat exchange with no problems. Any temperature variations up or down are usually insignificant.

Benefits of the Electrical Heating System:

- Lower cost replacement of glass vessel parts as a double jacket is unnecessary
- Easier to autoclave
- No coupling or uncoupling of pipework connections for a thermocirculator
- No "furring" of the heater due to hard water

The advantages over the double-jacketed glass vessel for the heating block are that connection to a chiller system is simpler (with no chance of damage to the glass jacket due to high pressure). Also, there is no need to ensure the jacket is at least partly filled with water for autoclaving.

Temperature range: 5 ° C above room or coolant temperature ,up to 60 ° C.

Stirring and Gassing

The stirrer system consists of a regulated magnetic drive. Regulation of the stepper motor power guarantees the set stirrer speed will be maintained.

The choices of stirrer system are:

- Standard stirrer bar (magnetic "flea")
- Stirrer shaft with interchangeable flat blade or marine impellers

Magnetic stirrer bar :

This provides a relatively cost-effective system. In normal operation, it offers performance some way towards that of a standard laboratory fermenter. Moreover, any possible cell damage due to a "grinding effect" is minimised.

Stirrer shaft & Impellers

The option of the stirrer shaft in combination with a ring-sparger provides mixing and gas dispersal closer to the laboratory fermenter.

The air going through the ring sparger is finely dispersed and, as is customary in fermenters, enters from beneath the stirrer blades. This allows for better gas entrainment compared with entry above the lowest impellor. The use of a sinter sparger is recommended for applications where the greater energy released from larger bubbles is undesirable (eg. culture of shear-sensitive cells).



Speed range:

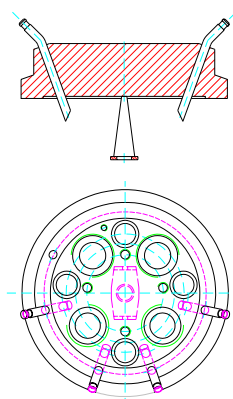
- 50- approx. 700 rpm with a stirrer bar
(Higher stirrer speeds can be reached, necessitating a larger contact surface and, consequently, can result in a more pronounced grinding effect).
- 50 - approx. 1200 rpm with impellers

Clearly, the gassing rate can be set individually for each of the six vessel positions using.

- A manual rotameter
- A thermal mass flow control valve*
- Digitally using the INFORS-GasMix*
* (Options).

Culture Vessels

The vessels are constructed from boro-silicate glass with a stainless steel top plate with an optimal arrangement of port fittings and inlets.



2 x Ø 12mm	PG 13.5 for INGOLD electrodes
2 x Ø 12mm	Rounded thread for inoculation & exit cooler
4 x Ø 10mm	For Pt-100, sparger, adjustable probe inlets, harvest pipe and antifoam/level control probe
4 x Ø 4mm	Fixed, for corrective reagents etc.

Exit gas cooler

A danger with small working volumes is loss of culture fluid over time leading to inaccurate results and/or poor growth. Efficient separation of water vapour from the exit gas is required.

The thermodynamic exit gas cooler from INFORS consists of an inner cartridge and an external jacket with connections for coolant. The jacket is a closed, hollow cylinder with spiral channels for efficient coolant circulation. The inner section has a number of perforated baffle plates for optimal condensation and return of vapourised culture fluids.



Example

300ml working volume, gassed at 1 V.V.M. over 7 days	
Fluid loss without an exit gas cooler	approx. 50%
Cooler with double jacket only, no baffles	approx. 43%
INFORS exit gas cooler with baffles	approx. 17%

Options

GasMix for pO₂ Control

Especially for cell culture, a wide range of various options can be supplied to meet individual requirements.

The Gas Mix unit has been specially developed for cell culture using small working volumes (250-500ml). Regulation of pO₂ is guaranteed even with gassing rates as low as 1NL/hr. It enables an "artificial" mix of gases to be created which can quickly alter according to culture conditions. A thermal mass flow control valve always holds the inlet gas flow rate constant independently of oxygen requirements.

The mechanical part of the Gas Mix unit including the pressure reduction system, rotameters and valves are integrated beneath the SIXFORS as an additional base unit. Set point entry and control output comes from the U.DDC system of the main SIXFORS. The gas flow rates and proportions of oxygen/nitrogen are controlled.

Gases required:

- Compressed air as a "carrier"
 - O₂ as a corrective agent
 - N₂ as a corrective agent
- Possibly CO₂ for pH control, if required

pH-Control by CO₂

Special for cell culture. The GasMix can be extended to CO₂ dosing.

If pO₂ control by gasmix is not required, this control can be offered using a separate supply line and valves

Supplementary O₂ dosing

For fermentations with a very high oxygen demand eg. Pichia, pure oxygen can be additionally dosed via a magnetic valve. Conversely, too high an oxygen level could be adjusted by dosing with nitrogen



Stirring Auto-Restart

It can happen that the stepper motor and the stirrer shaft can become de-coupled.

To prevent this happening, the maximum allowable speed range before de-coupling is ascertained experimentally and used as a starting point. If coupling is lost, this is detected and the speed is temporarily reduced to zero. A re-start automatically occurs. If de-coupling happens three times at a given speed, the set speed is reduced in increments until a stable setting is found.

Process Control and Analysis

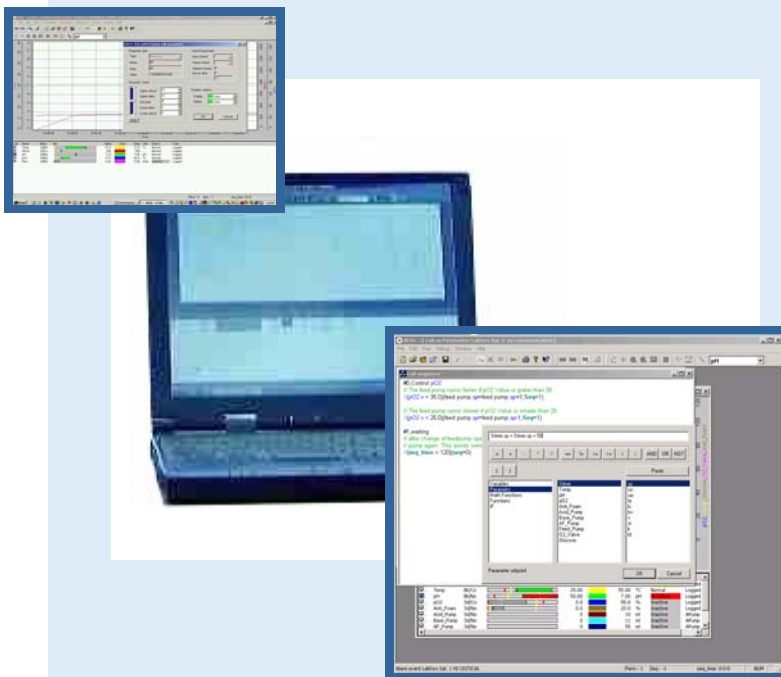


IRIS V 5.0

IRIS V 5.0 is 32-bit software for data-logging, analysis archiving and control of fermenters.

IRIS can operate on a single PC, network, remote control and network/modem. Peripherals such as balances, external pumps, or analysers for exit gas measurement, biosensors, mass spectrometers etc. can be connected online to the system. Through integration of this type of data and off-line analysis information, IRIS is the centre for a true

„ BIOLOGICAL PROCESS CONTROL “.



Also, without specialist knowledge of programming, the user can develop simple yet efficient control scripts to meet their needs for specific parameter control.

Data Logging

- 1 – 8 Fermenter
- Online-Data from sensors
- Offline-analysis data
- Data from external peripherals
- Online display of all Data as text, line or bar graphs.
- Two-stage asymmetrical alarms
- Storage and display of all alarm reports
- No data loss for the sake of smaller file sizes with data logging by time and by difference.

Control

- „Supervisory Setpoint Remote Control“
- Time-based Profiling
- Event-based Profiling
- Calculated Parameters (eg. RQ)
- Control of fermenters over a network
- „Follow File“ > „Cloning“ of fermentations
- Data exchange between fermenters possible

Analysis

All archived data within IRIS can be evaluated using graphical comparison and correlation. Data can be exported in ASCII format to other application (eg. Excel, Origin etc) for further analysis.

Graphical display

- Online Graph
- History Graph
- Bar Graph
- Comparison and Correlation Graphs
- Time-Line Function
- Options for time, value and text message marking

Reports

- Parameter data can be exported
- If required, only part of the data can be included
- If required, details of the fermenter protocol can be included

If required, alarm reports can be included.

INFORS

... Your partner for Research and Production



Minitron



Minifors



Labfors 3



Techfors S



Techfors



TF 600 Production plant

It's all very well to decide you need a better way of doing things but there's no advantage if the equipment is too complex for your needs and not specifically designed with inexperienced or occasional users in mind. Also, the information and support you get must be appropriate to your application and requirements. Finally, when you outgrow this next step you must have a clear pathway to even better things.

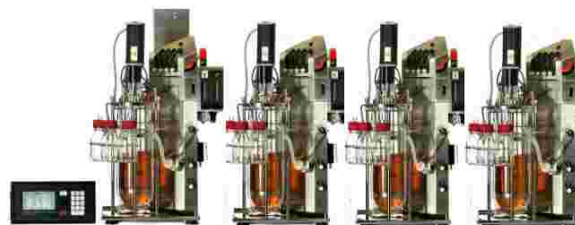
You are not alone.



Training and support are vital for users of new equipment. Help and advice about making a step change in production. It will shorten the time for optimisation and prevent costly, time-consuming mistakes which could easily be avoided.

A long-term partnership with users results in benefits for everybody with a deeper understanding of ever-changing needs. In education, the ability to communicate ideas and methodologies to tomorrow's researchers can be enhanced by being in touch with experts

You expect to be able to progress with changing circumstances and it's likely you will eventually hit the limits of simple bench-scale technology. Either a more sophisticated technology is needed, additional capacity or a complete change in methodology to accommodate a move to a production phase. Knowing that this is not an issue gives you peace of mind today with a promise for the future.



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