# BIOREACTORS

# NEW SOLUTIONS FOR OLD PROBLEMS

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LAMBDA – Laboratory Instruments

www.rhone.ch/lambda

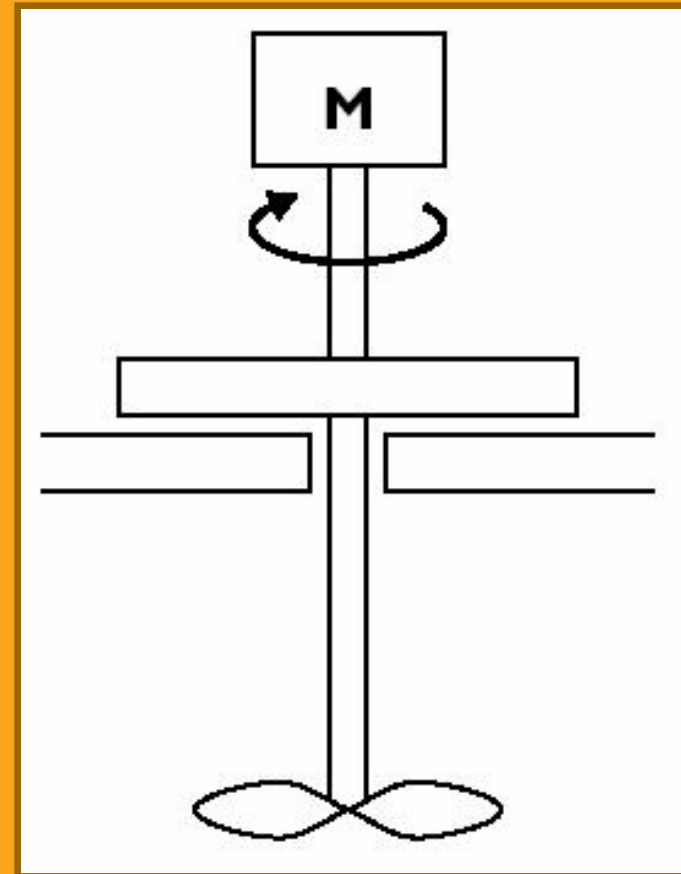# OUTLINE

- Stirring mechanism

- IR-heating system

- Approach used in the MINIFOR

- Probes

- Fermentation accessories (Pumps and gas flow controller)

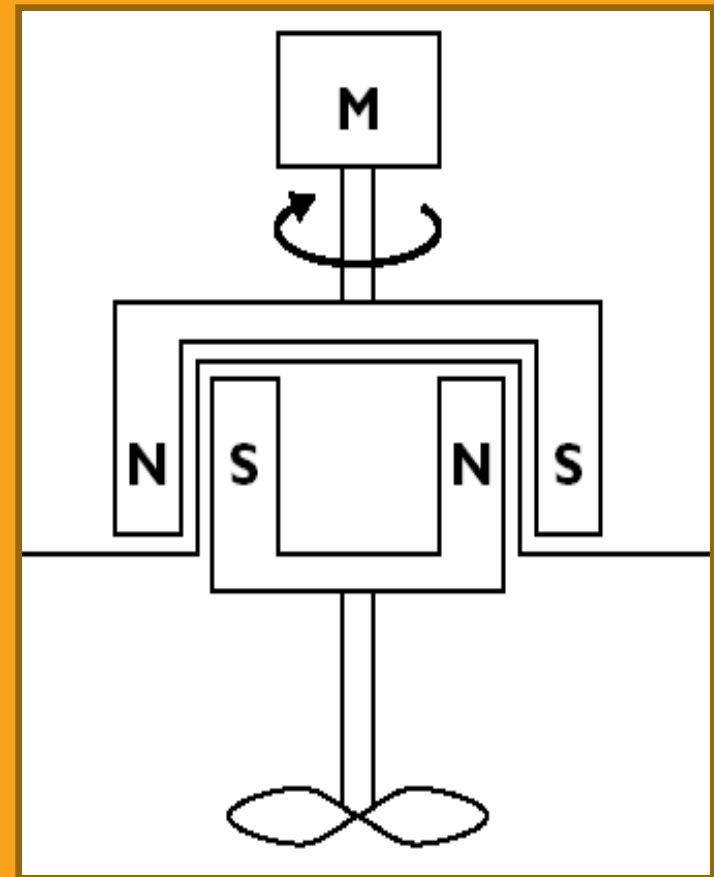- Conclusions

# TRADITIONAL STIRRING

## a) Mechanical seals

- No physical separation

- Contaminations

- Service "sensitive"
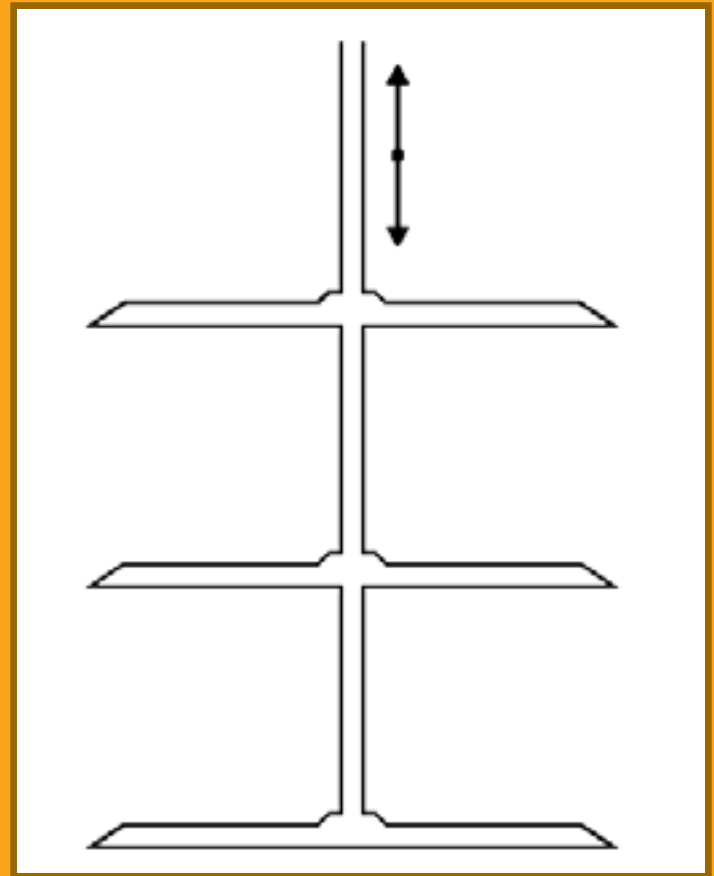
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# TRADITIONAL STIRRING

## b) Magnetic coupling

- Separation ⇨ Sterility

- Dead spaces

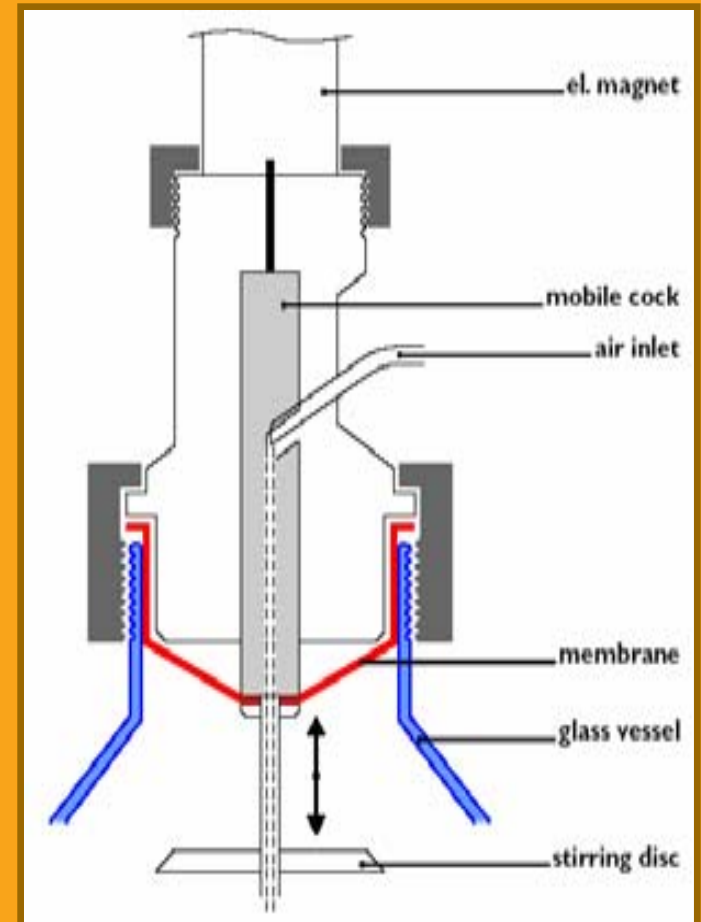- High cost

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# NEW STIRRING SCHEME

**Up and down movement**

# NEW STIRRING SCHEME

## Fermentor head

- Separation ⇨ Sterility

- Electromagnet ⇔ Motor

- Easy to mount (one hand)

- Threaded necks

- Low cost



el. magnet

mobile cock

air inlet

membrane

glass vessel

stirring disc

# NEW STIRRING SCHEME

## Stirring discs

- Counter rotating flow paths

- Vertical stream (through the holes)
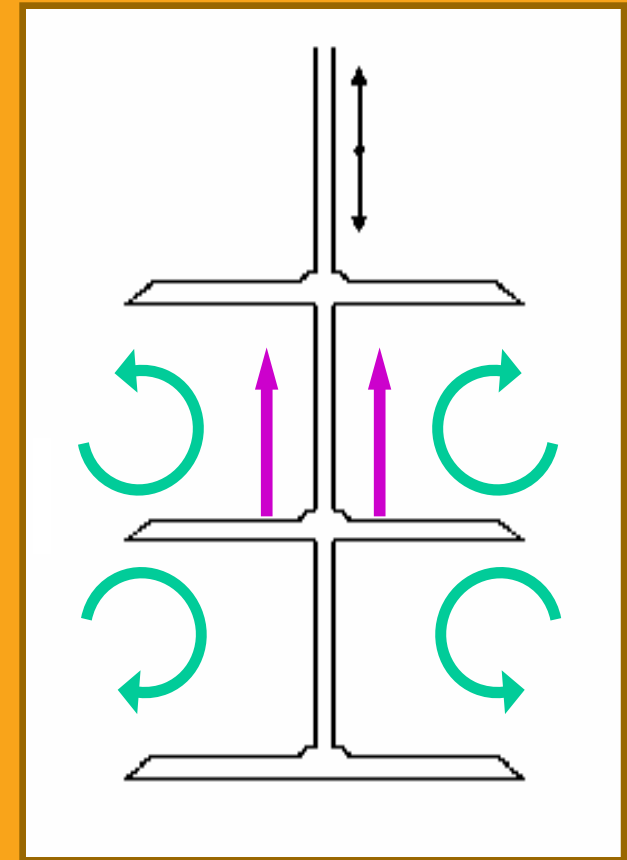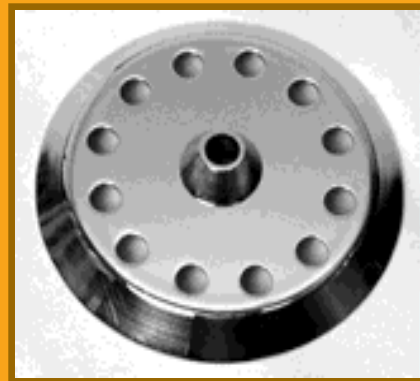
# NEW STIRRING SCHEME

## Stirring properties

- Whole volume stirring

- Good gas distribution

- No vortex formed

- No baffles needed

- Reduced foaming
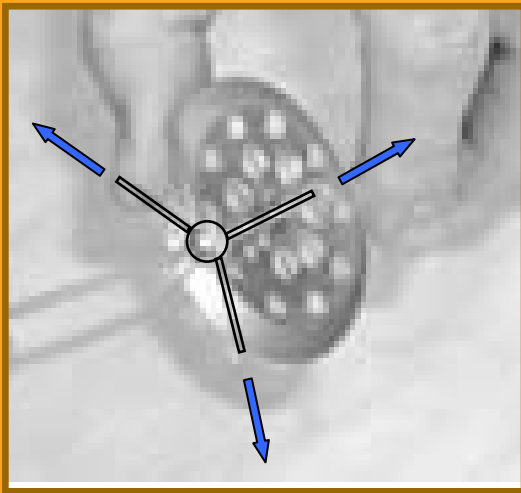
- Gentle to cells

# NEW STIRRING SCHEME

In action...

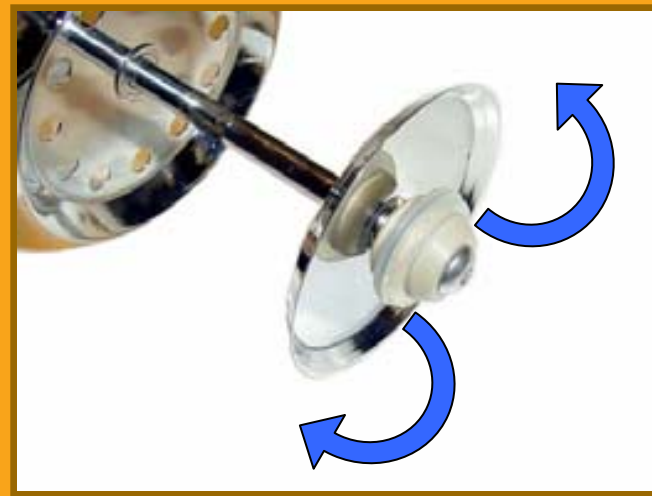# AIR SPARGERS

## a) Capillary



Possible blocking by salts

## b) Silicone



- No blocking by salts
- Good bottom circulation and bubble breaking

# FERMENTATION VESSELS

- Adopted from cell culture

- Up to 8 threaded side necks

- Good accessibility

- Variability

- Low cost

- "jacketable"



3 litre     I litre     0.3 litre
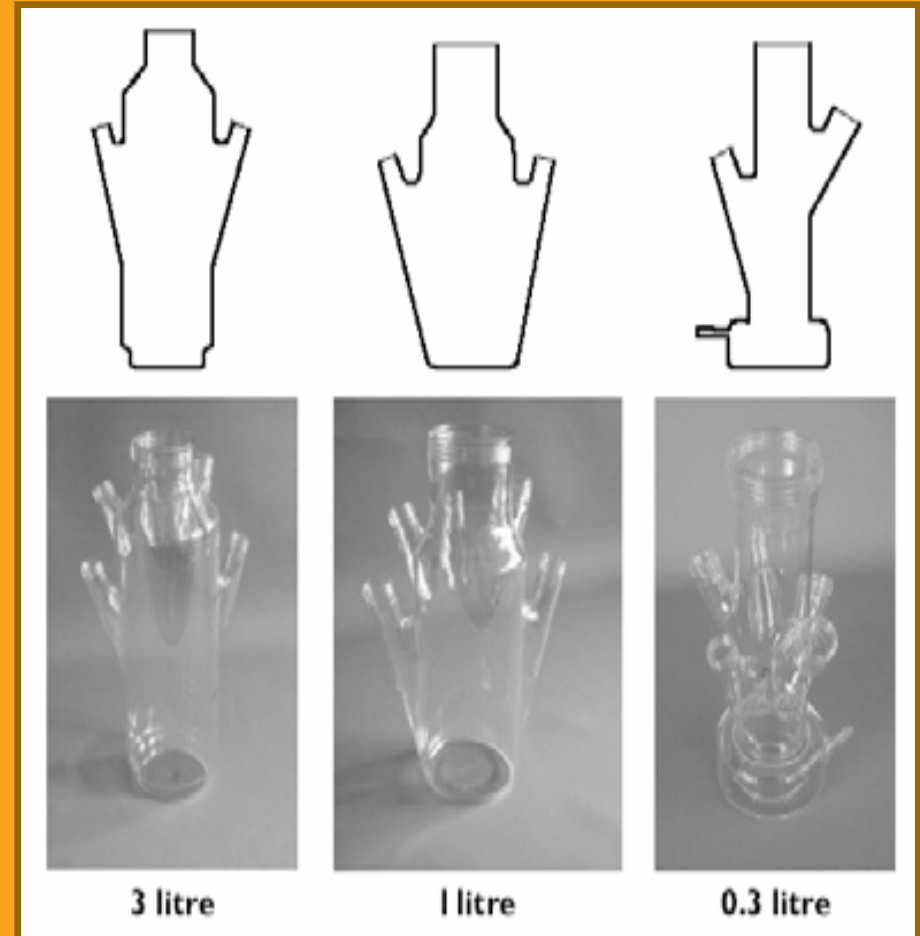
# STOPPER

- Efficient sealing

- Reusable many times

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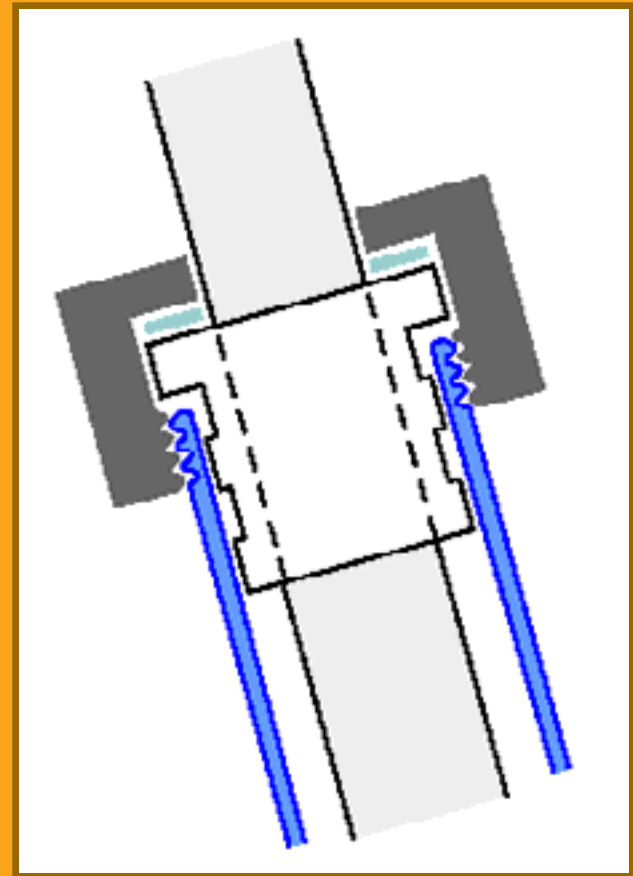
# "COFFEE CUP" RADIATOR



- IR-heating ⇨ gentle sun-like heating

- Natural convection

- No contact with vessel

- No overheating at any volume

- Up to 60°C in 3l vessel

- 98% energy yield

- Negligible heat capacity

- Low voltage

# THE MINIFOR APPROACH

## Fermentor case

- Integrated ⇔ free-standing vessel

- Cascaded design

- Ergonomic arrangement

- Excellent accessibility

- Extremely compact

# THE MINIFOR APPROACH

## Control panel

- Closest to operator

- All information at a glance (no scrolling or menu selection)

- Easy operation

# THE MINIFOR APPROACH

## Radiator

- Sealing vessel holder ⇨ spill protection

- Vessels above heat source

- Shielding of the hot coil ⇨ protection against burning

# THE MINIFOR APPROACH

## Front connectors

- Shortest connection between probes and vessel

- Sealed cables

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# THE MINIFOR APPROACH

## Fermentor platform

- Air output and storage bottles behind the vessel

- Shortest connection between pumps and vessel

- Magnetic holders

# THE MINIFOR APPROACH

**Rear side**

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# THE MINIFOR APPROACH

## General view

- Up to 4 pumps on supports

- Pump protection in case of tubing rupture

- Good visibility of pump status

- Easy accessibility from all sides

# THE MINIFOR APPROACH

## Serial fermentation



- Optimisation in series

- Can be used separately (completely independent)

# PROBES

## pH and temperature probe



- Variopin connector (freely sterilisable)
- Pt 100 integrated in the glass electrode

# PROBES

## DO probe



- PEEK body

- Freely sterilisable connector

- Large cathode system

# PROBES

## DO probe membrane module

- Glass supported PTFE membrane

- Fast response

- Membrane protection

# INOCULATION & SAMPLING



- Stainless steel capillaries

- Luer-Lock adapters

# PERISTALTIC PUMPS



PRECIFLOW    HiFLOW    MULTIFLOW

- Constant compression control

- Large rollers

- Asymmetric head

- Compact

- Reliable

- Economy of tubing

- Progressive speed control

# PERISTALTIC PUMPS

In action...

# MASSFLOW

## Gas flow control

- Controlled automatic addition of $CO_2$ or $N_2$ during cell cultures

- No need of expensive gas stations

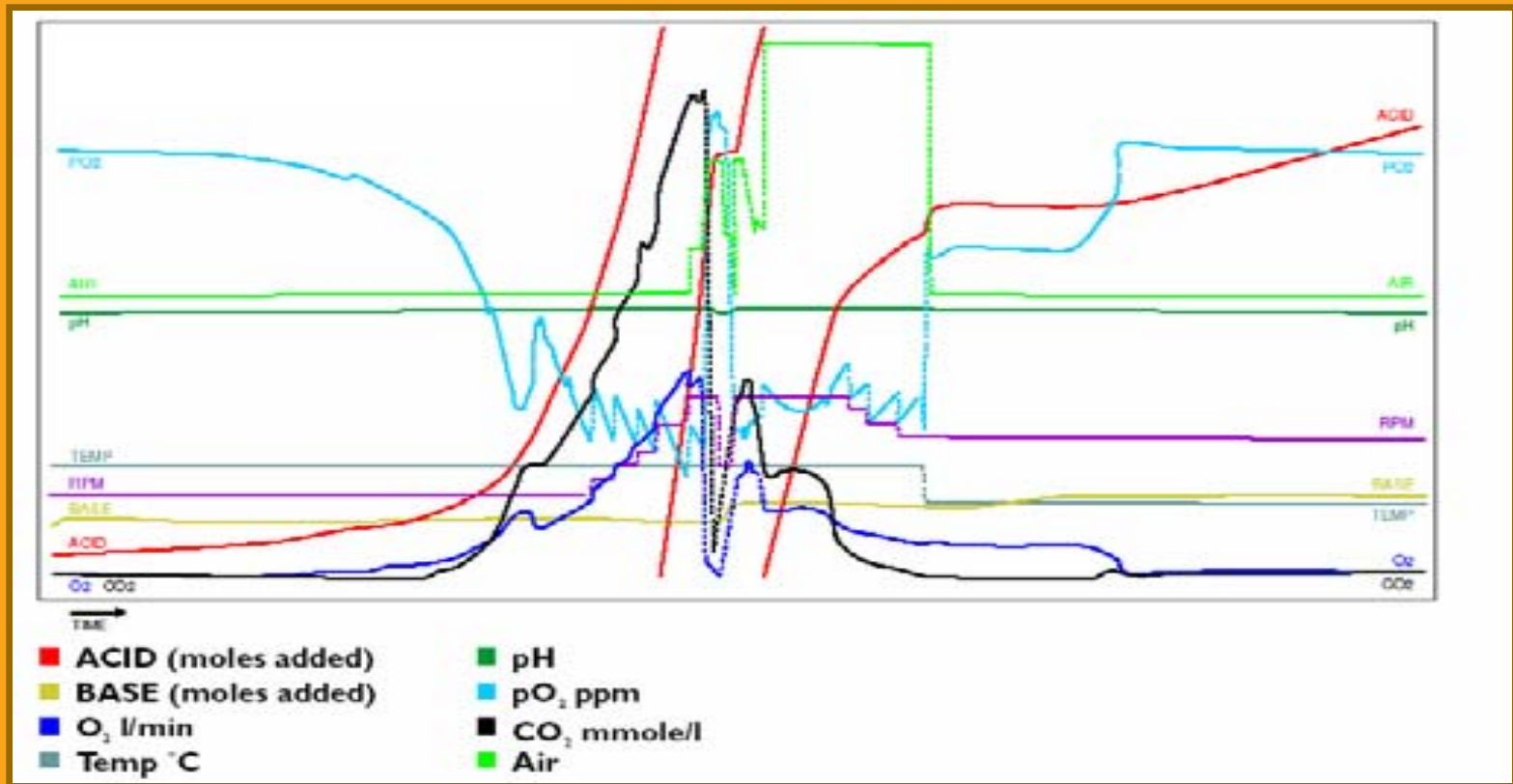- Programmable

- Totaliser

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# CELL CULTURE ADAPTOR



- Very gentle stirring
- Oxygenation through moving coil

# INTEGRATOR

- Totalisation of delivered liquid or gas
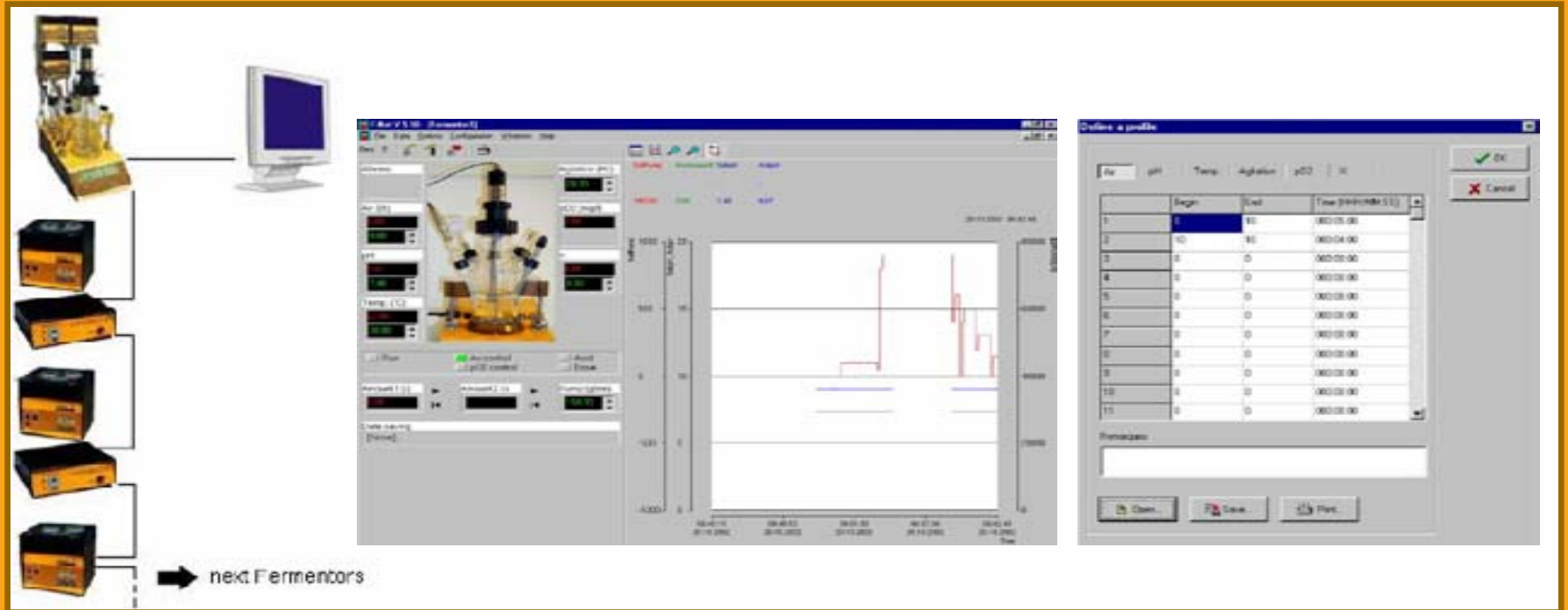
- Access to growth kinetics

- Enzyme activity measurement

# FERMENTATION



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

# FNet – SOFTWARE (Sysmatec)



- Complete easy to use software for laboratory fermentors
- Connection of up to 6 fermentors, 12 integrators and 6 pumps

- Data saving
- Graph scaling
- Profile definition
- Alarms

# CONCLUSIONS

- A major effort was invested to make bioreactors more efficient and simple

- New up and down stirring concept providing easy sterility

- IR-heater for gentle heating

- pH and DO probes

- Pumps and gas flow controller

# This work would not have been possible without:

**Jaroslav Bernášek, Vladimir Čermák, Rainer Glöckler, Vlastimil Hanuš, Hans Kulla, Lida Lehká, Jan Marc Lehky, Petr Lehky, Stanislav Tříska, Daniel Venetz, Patrick Yax, Michal Zemek**

# THANK YOU !!!