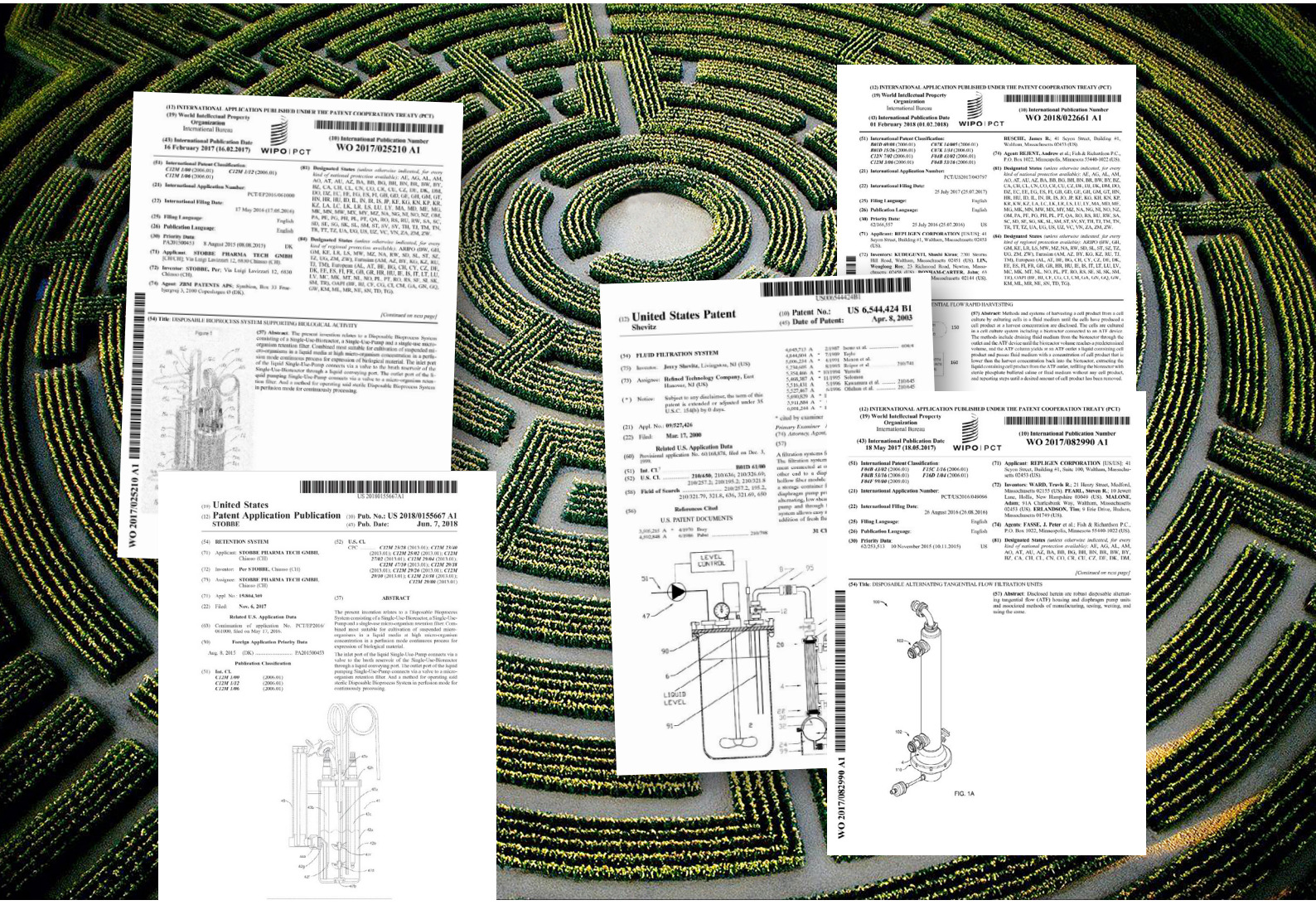
PerfuseCell

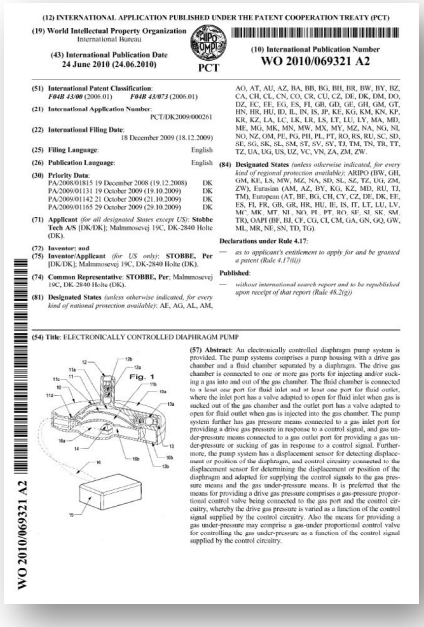
Customized Perfusion

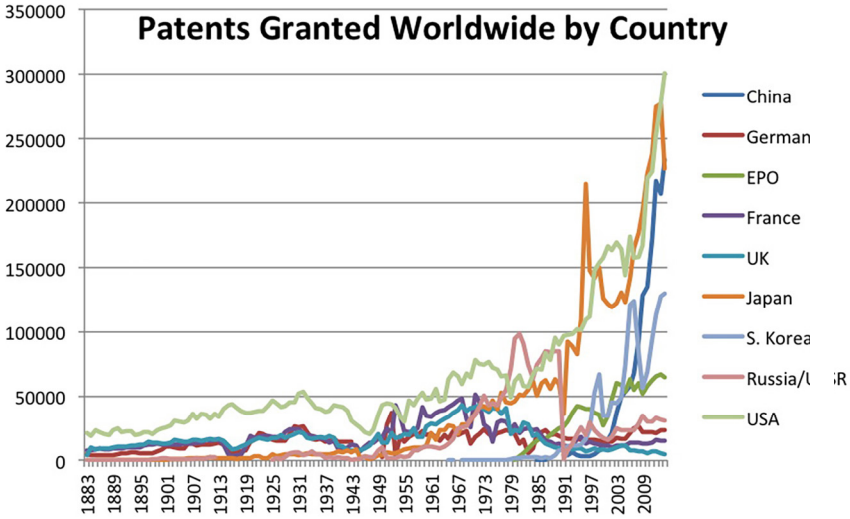
Single-Use-Bioreactor

Semi-Continuous Biomanufacturing

IPR – Intellectual-Property-Right's







PerfuseCell

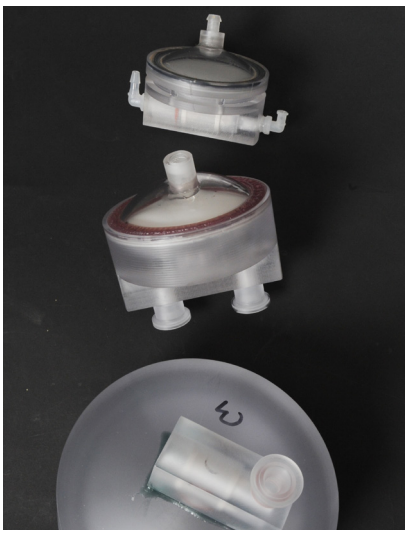
The building block's for Perfusion-SUB's

Ready to use "right out of the box"

1 SUB Single-Use-Bioreactor

A SUB designed for your application.

Scalable Working Volume, selectable impeller and aerator, extra long hoses which fit your existing PCS, etc.



2a Clio Single-Use-Pump

Clio in an One-way-Single-Use-Pump (O-SUP) combining the HFF and SUB into the P-SUB.

Clio is a true Positive Displacement liquid pump fully computer controlled.

2b Thalia Single-Use-Exchanger

Thalia is an Alternating-Single-Use-Exchange (A-SUE) connecting the HFF with the SUB.

Thalia is a true Positive Displacement fully controlled broth exchanger.

3 SUS Single-Use-Sensor's

Single-Use-Sensor's which fit your existing Process-Control-System connections.

Parameters measured with VisiFerm, OneFerm, PICO or BugLab bio-mass, and level.

4 HFF Hollow-Fiber-Filter

Choose your preferred size Hollow-Fiber-Filter combined with the O-SUP or A-SUE and the SUB.

Any type, number and brand of HFF can be added.

5 Clotho Drive Units

Perfusion-SUB's are driven by the Clotho Drive Unit and software for super accurate Single-Use-Pump control and comprehensive data acquisition.

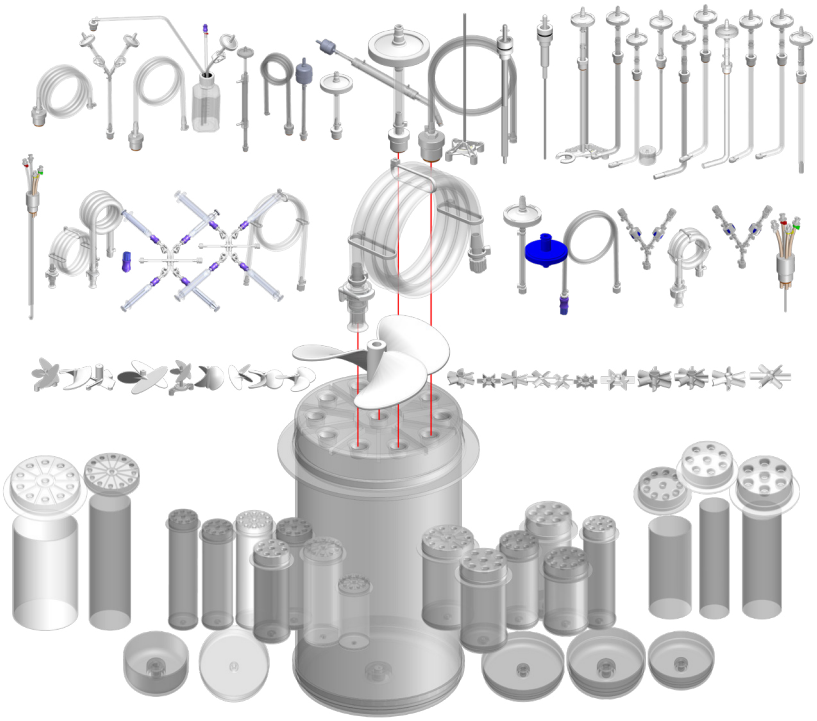
1 What does “scalable and customizable” really mean?

Rigid wall Vessel Volume range from 0,5 to 30 liter.

PerfuseCell offer as standard 10 different and fully configured Perfusion-SUB. Ready to use right out of the bag.

If you have a silicone tube welder no autoclave or hood is needed.

That’s scalable!



Build your next Perfusion-SUB exactly to your needs …

We have more than 5.000 components designed to fit each other. That´s millions of combinations!

That’s customizable!

Clio

2a One-way-Single-Use-Pump

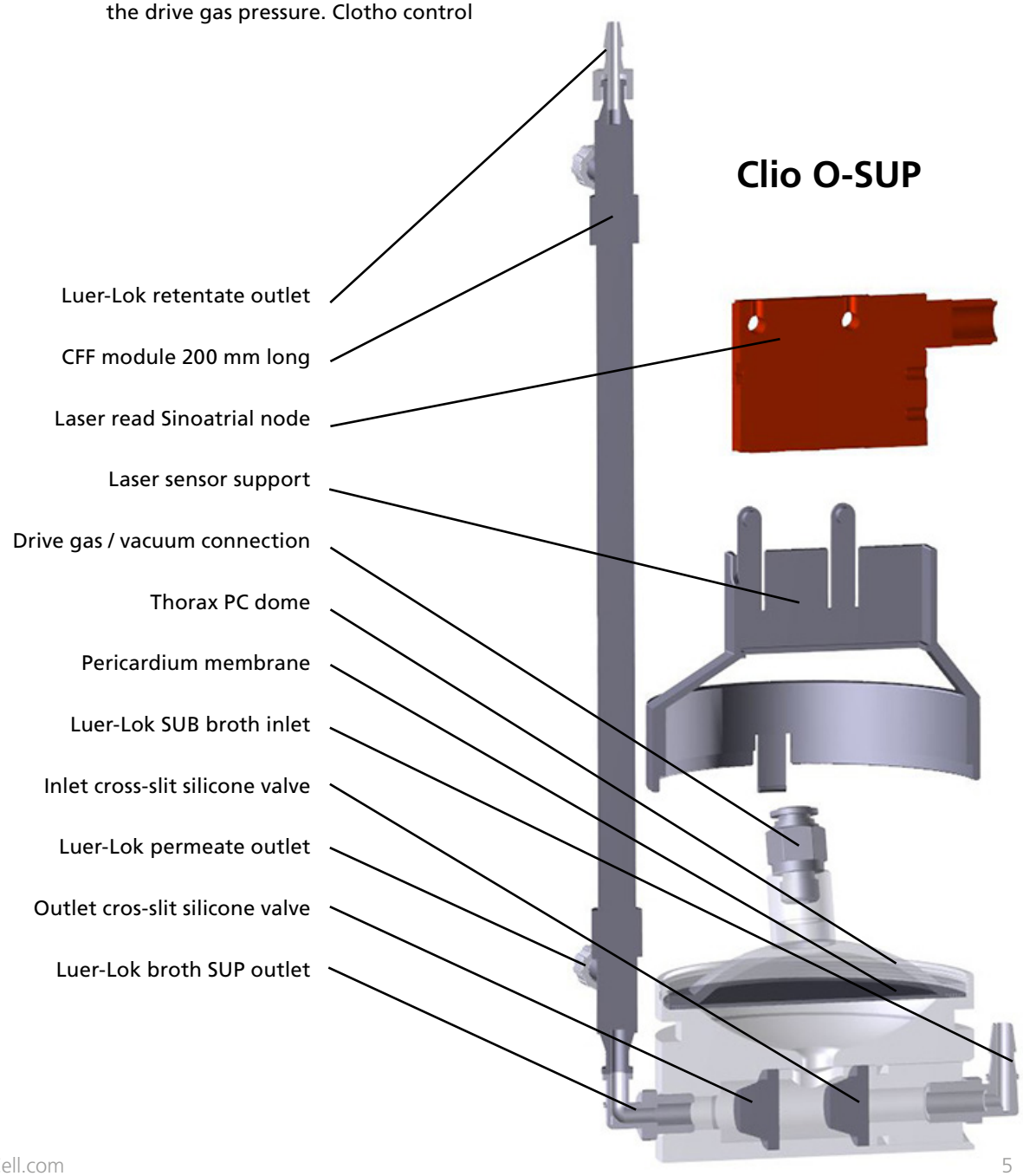
Measures accurate volume and velocity

The O-SUP is a pump arranged inside a Polycarbonate housing with a set of passive liquid conveying valves.

The 1,0 mm thick silicone Pericardium membrane separates the drive gas pressure and / or vacuum from the broth.

The red tri-angular laser sensor read the membrane position with 0,1 mm accuracy at any time. Pressure sensors inside Clotho Drive Unit help calculating online the drive gas pressure. Clotho control via proportional valves and PID loop the wanted membrane position.

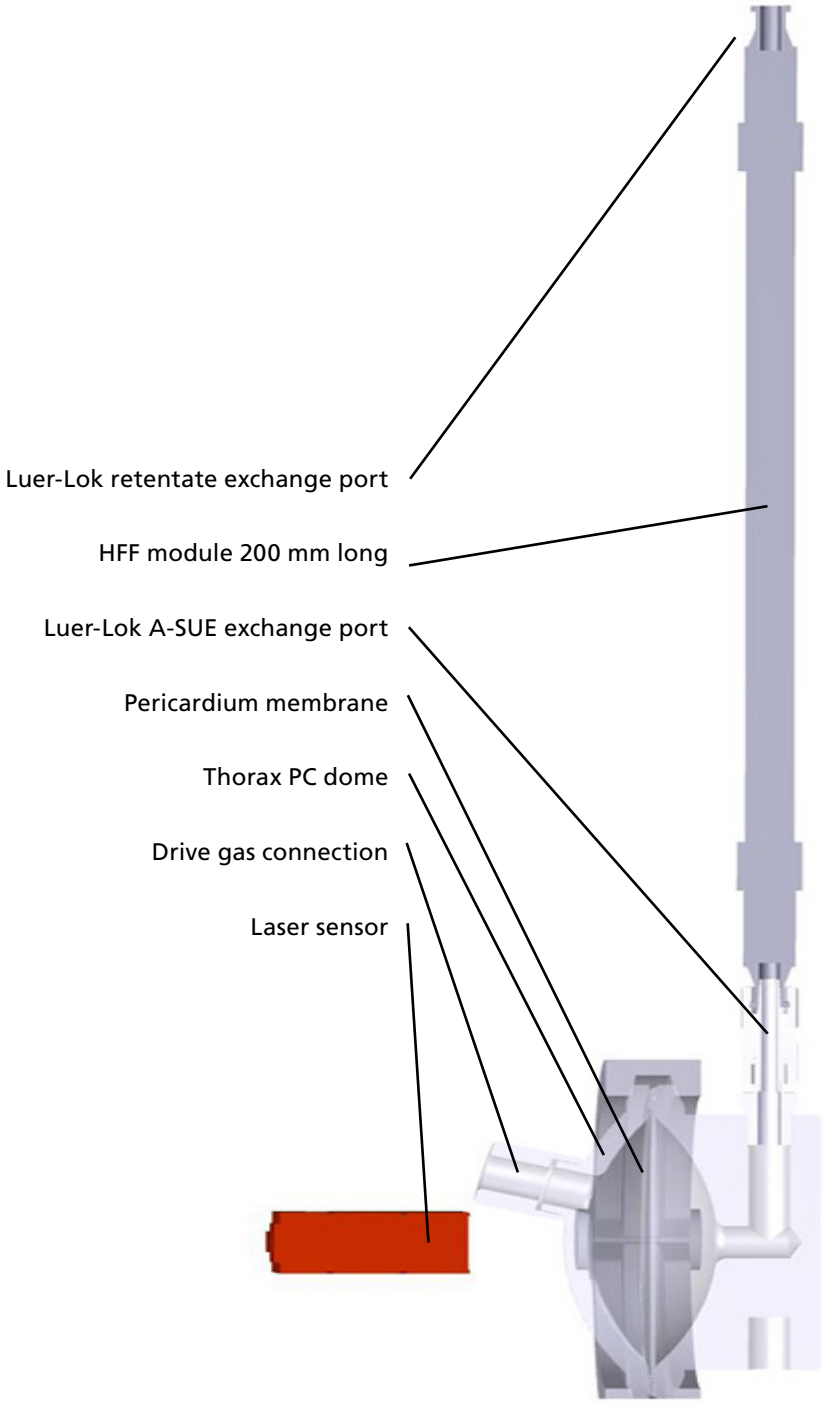
Clio can easily be programmed to pump fluids in 1:1000 range over time or by conveyed amount of fluid. Clio is a true Positive Displacement (PD) pump where every stoke is measured accurately independent of the ever dynamic stroke volume. Each stroke duration can vary between seconds and multiple minutes.



Thalia

2a Alternating-Single-Use-Exchanger

Measures both volume and velocity



The A-SUE is arranged inside a Polycarbonate housing with no liquid valves. The A-SUE exchange liquid forth and back.

The 1,0 mm thick silicone Pericardium membrane separates the drive gas pressure and vacuum from the broth.

The red tri-angular laser sensor read the membrane position with 0,1 mm accuracy at any time. Pressure sensors inside Clotho Drive Unit participate in online calculation of the needed drive gas pressure. Clotho control proportional valves and hereby in PID loop the wanted membrane position.

Thalia can easily be programmed to convey fluid in 1:1000 range over time or by exchanged amount of fluid. Thalia is a true Positive Displacement (PD) exchanger where every stoke is measured accurately independent of the ever dynamic stroke volume. Each stroke duration can vary between seconds and multiple minutes.

Thalia A-SUE

❸ The unique Single-Use-Sensor's

measures DO, pH, bio-mass, level, Glucose

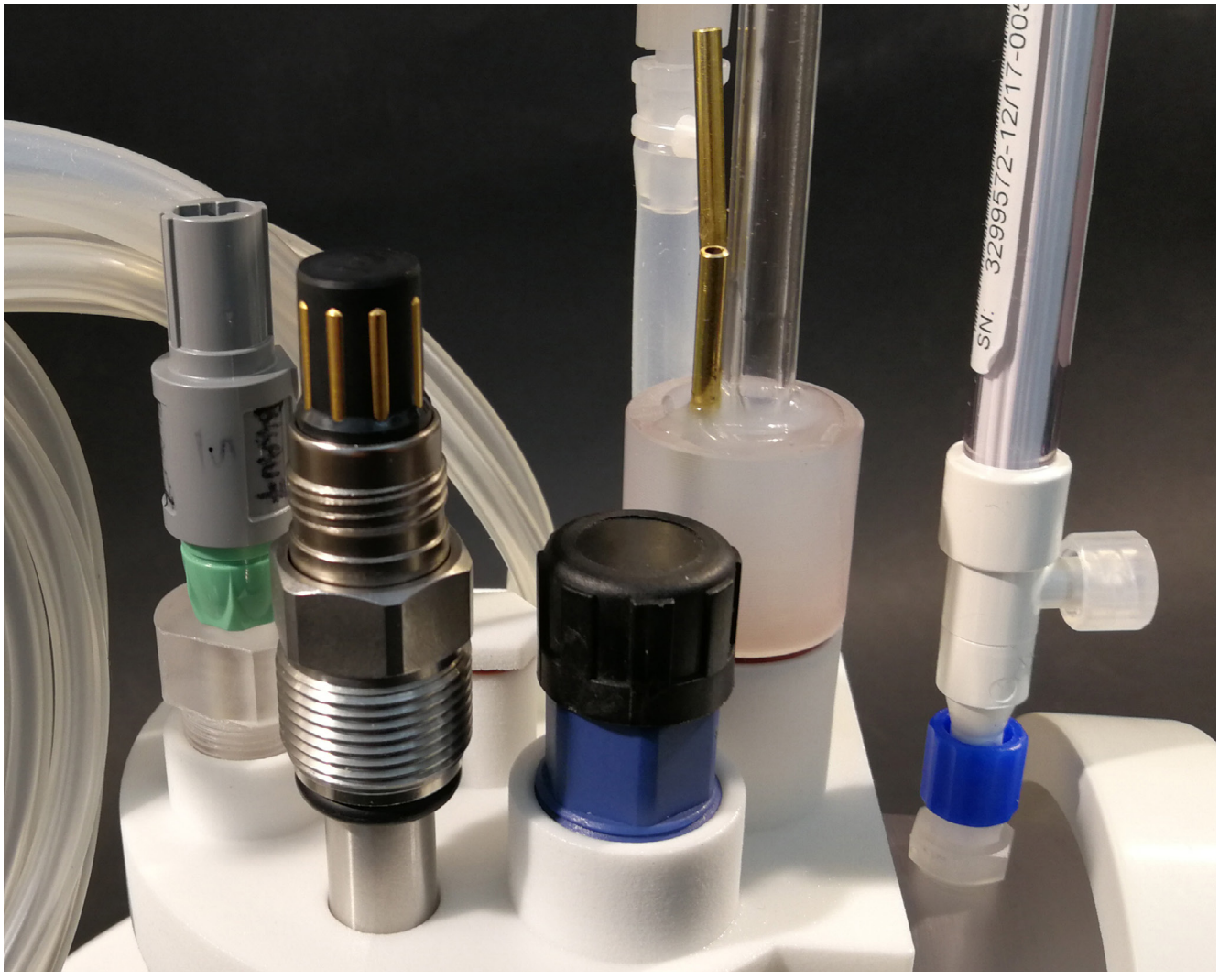
The complete P-SUB family as standard include through the head-plate vertically mounted pre-installed Single-Use-Sensor's (SUS) for DO, pH, and level.

Depending on P-SUB size bio-mass SUS mounted vertical through head plate or scanning horizontal through vessel wall.

For accurate DO measurements we pre-install either VisiWell or PolarWell. Use the optical or polarographic Re-Usable-Sensor supplied with your PCS.

For pH measurements standard PCS cabling with either AK9 or AS8 connector coupled to the pre-installed pH SUS is recommended.

PICO Futura SUS capacitance on the 500 ml and BugLab miniBE OD SUS on the 3.200 ml as standard.



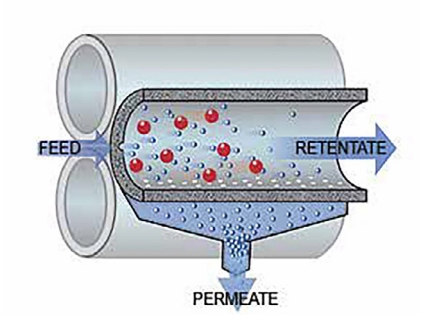
❹ The Hollow-Fiber-Filter

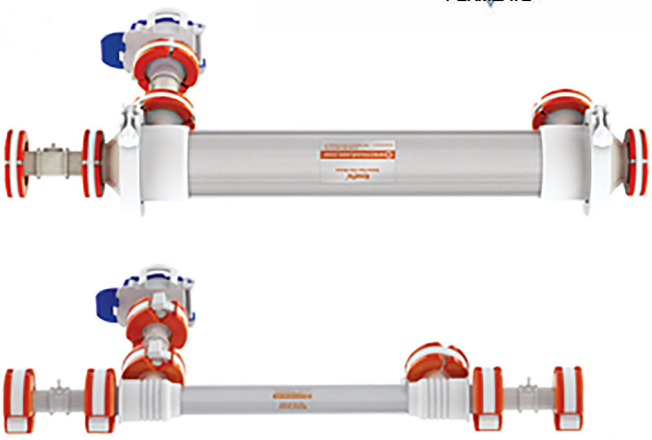
separates at only 200 nm

Cross Flow Filtration is an efficient method for filtration and separation of solutions containing biomolecules, or particles such as viruses, bacteria or cellular material. It is a process whereby product flow (broth feed) is directed inside the multiple straw /tube shaped membranes with most of the solution as retentate circulated back into the SUB. A minimum of the broth feed pass tangentially across the membrane as permeate.

The rapid flow of broth along the membrane acts to 'sweep' the surface, reducing concentration polarization. It also prevents build-up of foulants that can plug the pores at the membrane surface. The rapid cross flow creates a pressure drop, which forces some of the feed solution and dissolved molecules that are smaller than the pores in the membrane, through the membrane filter as permeate.

The solution that passes through the membrane is referred to as filtrate or permeate. Molecules or particles larger than the membrane pores are retained in the feed,





❺ Ultra compact
Clotho-2 Drive Unit

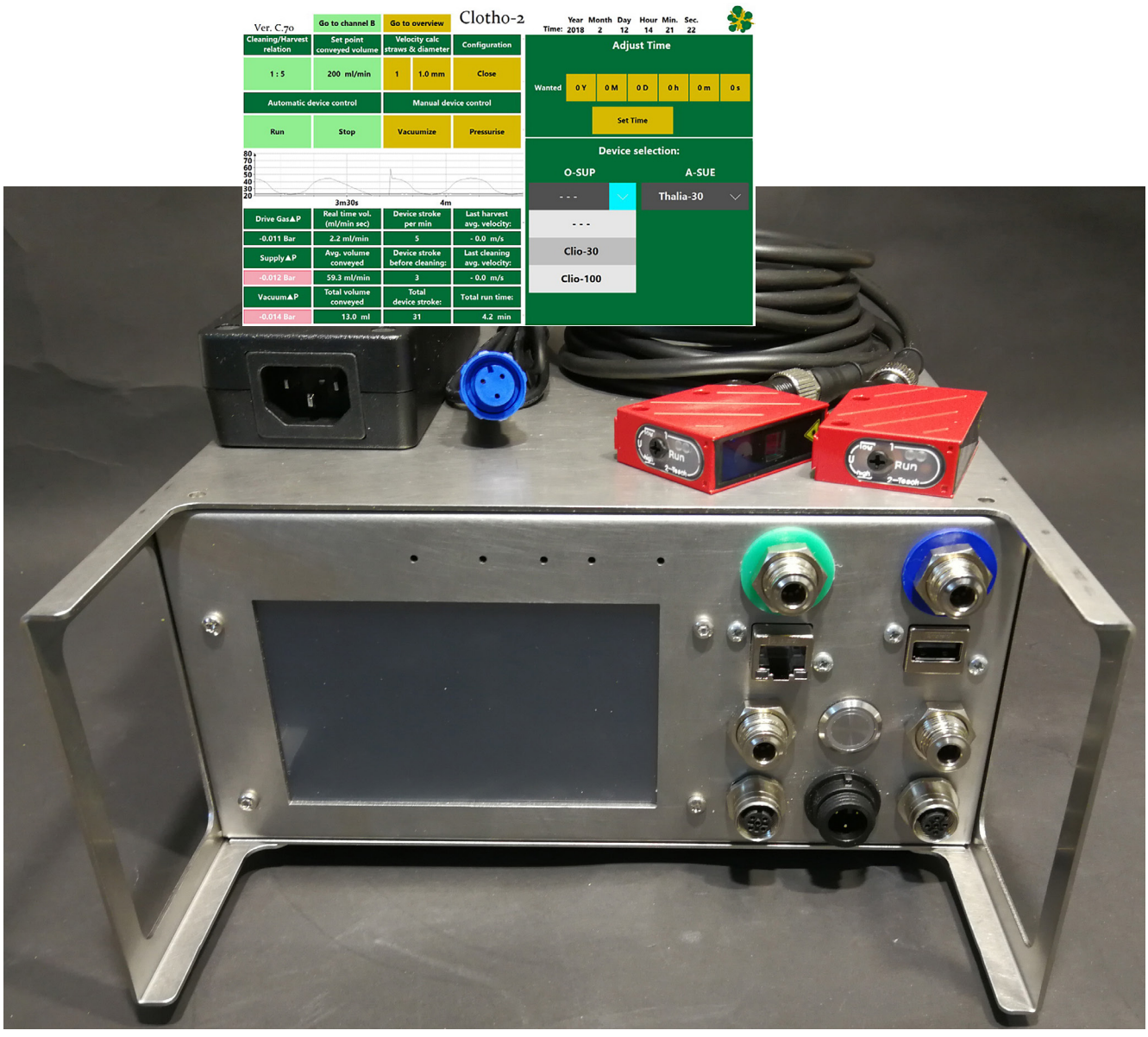
for CellMembra and CellRetention

The portfolio of CellMembra and Cell-Retention Perfusion-SUB's are all driven by the green Clotho software for super accurate control and comprehensive data acquisition.

The ultra compact Clotho-2 Drive Unit is able to control both the Clio One-way-Single-Use-Pump's (O-SUP) and / or the Thalia Alternating-Single-Use-Exchanger (A-SUE) over distances up to 2 meter with 1% accuracy.

The all stainless steel and stackable Hephaestus U2 cabinet measures (in mm):

- W: 230
- D: 230
- TD: 295
- H: 110



PerfuseCell

Mini P-SUB

integrated Single-Use-Pump, Single-Use-Sensor's and Hollow-Fiber-Filter

CellMembra-500

Miniature P-SUB for cell retention in perfusion cultivation setup in a fully single-use setup. CellMembra-500 integrates a customized CellVessel Single-Use-Bioreactor (SUB) and a One-way-Single-Use-Pump (O-SUP) and 4 Single-Use-Sensor's combined with the HFF (Hollow-Fiber-Filter).

Features of CellMembra-500:

- CellVessel SUB designed for your applications and setup.
- Supplied with Single-Use-Sensor's (SUS) being DO, pH, bio-mass, and level.
- Pumped volume and obtained velocity accurately measured – no guessing.
- The complete and pre-assembled unit packed in dual film bags and precision irradiated – forget the autoclave.
- Working Volume (WV) range from 100 ml to 400 ml.

Mini P-SUB

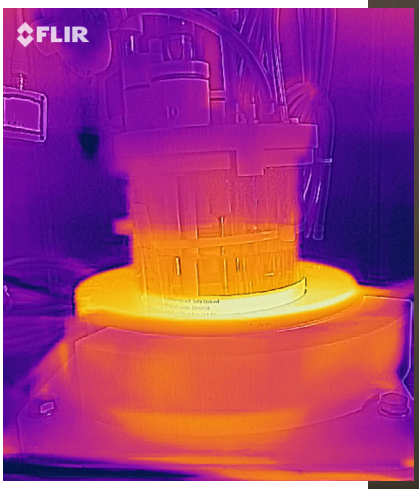
driven by standard PCS

CellMembra-500

Mini CellMembra™ P-SUB's may easily be driven by traditional Process-Control-System`s (PCS) servo motor's. Select either electrical or water thermal control. The high thermal mass Heating-Support-Foot (HSF-E) insure good PCS PID algorithm regulation.

Features of CellMembra-500:

- Select the impeller for operation with your application and PCS setup.
- Single-Use-Sensor`s (SUS) as currently available (DO, pH, bio, level, Glycose).
- 500 ml Vessel Volume (VV) for Working Volume (WV) ranging from 100 ml to 400 ml.
- The complete and pre-assembled unit packed in dual film bags and precision irradiated – forget the autoclave.



PerfuseCell

Mini P-SUB

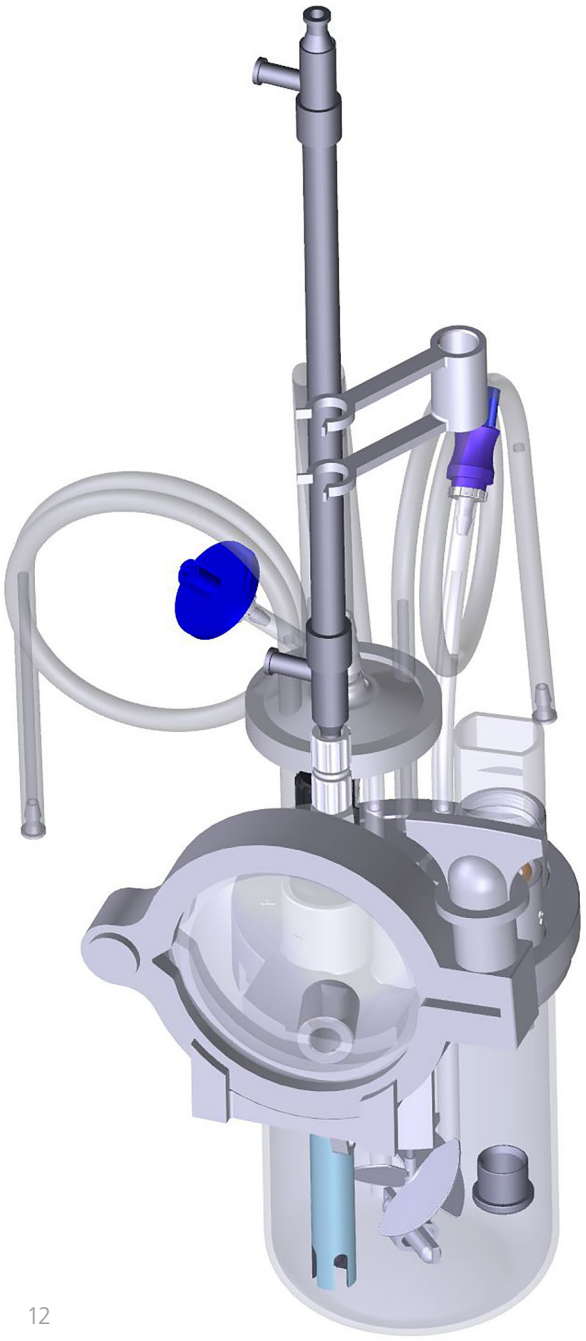
with Single-Use-Exchanger, Single-Use-Sensor's, Hollow-Fiber-Filter

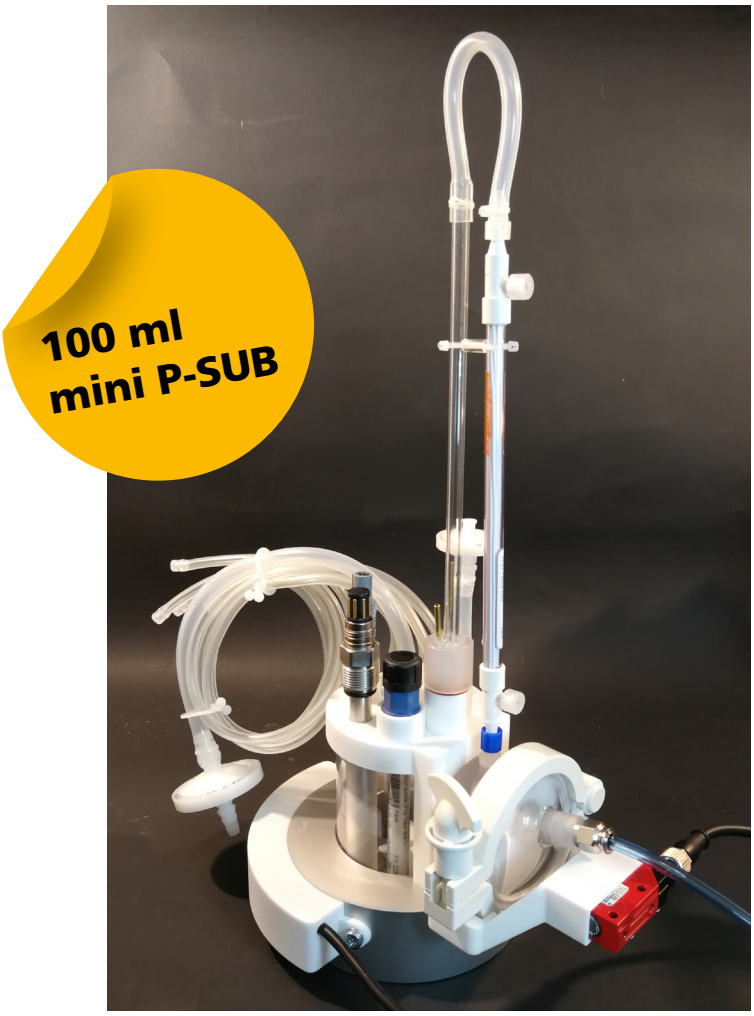
CellRetention-500

Miniature P-SUB for cell retention in perfusion cultivation setup in a fully single-use setup. CellRetention-500 integrates customized CellVessel Single-Use-Bioreactor (SUB), Alternating-Single-Use-Exchanger (A-SUE), and 4 x Single-Use-Sensor's with the HFF (Hollow-Fiber-Filter).

Features of CellRetention-500:

- CellVessel SUB designed for your applications and setup.
- Supplied with 4 x Single-Use-Sensor's (SUS) being DO, pH, bio-mass, and level.
- Exchanged (alternating) volume controlled and obtained velocity accurately measured and displayed – no guessing.
- The complete and pre-assembled unit packed in dual film bags and precision irradiated – forget the autoclave.
- Working Volume (WV) ranging from 100 ml to 400 ml.





Parallel P-SUB's

designed for any Process-Control-System

Perfusion-SUB-500

Do you need like 4 or 8 or 16 P-SUB's operating in parallel? Mix freely between the 500 or the 3.200 size P-SUB's and even CellVessel SUB's? Do you already have 4 or more Process-Control-System's (PCS) available in your lab. Straight forward with all the accessories available from PerfuseCell.

Its all Plug & Play!

Whatever servo motor you may have the MST can adapt – with agitation for both 500 ml and 3.200 ml VV P-SUB's.

The width of 4 x P-SUB's mounted in HSF on MST is less than 0,8 meter space on your lab table.

This setup fits in particular well the DasGip Parallel PCS system with RE30 or RE40 servo motors (PCS pn 76DG04CC or 76DG08CC or 76DG16CC).

Customized to your wish

PerfuseCell

Medium size P-SUB

with Single-Use-Pump, Single-Use-Sensor's, Hollow-Fiber-Filter

CellMembra-3200

- CellVessel SUB with 3,2 liter Vessel Volume (VV)
- CellVessel SUB ranging 0,4 – 2 liter Working Volume (WV)
- Integrated Clio-100 O-SUP with fully controlled and measured 1 – 100 ml volume conveyed per stroke
- Any available HFF can be specified and pre-installed and as many as needed
- SUB with any type of impeller and as many as needed
- Agitation from top (HPD) facilitates RE30, RE40, P100 servo motor with ID25-A adaptor, or Biostat with ID39-B adaptor
- Agitation by Magnetic-Bottom-Drive (MBD) by PerfuseCell Magnetic-Stirrer-Table (MST) by any servo motor. Such as Biostat servo motor with ID39-B adaptor
- Single-Use-Sensor's with connectors which fit your PCS

The 3,2 liter Vessel Volume (VV) P-SUB is a fully customizable CellVessel expanded into the CellMembra concept

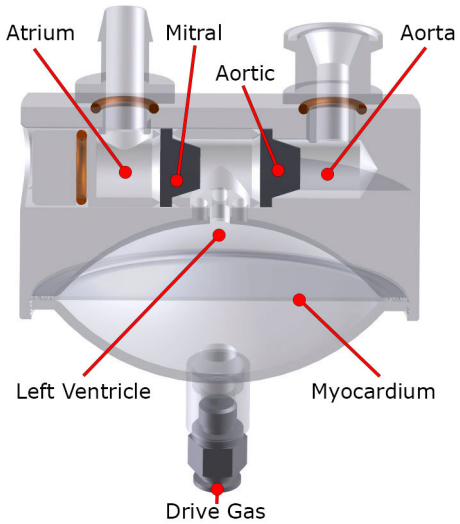
Ready to use "right out of the box"

Medium size P-SUB

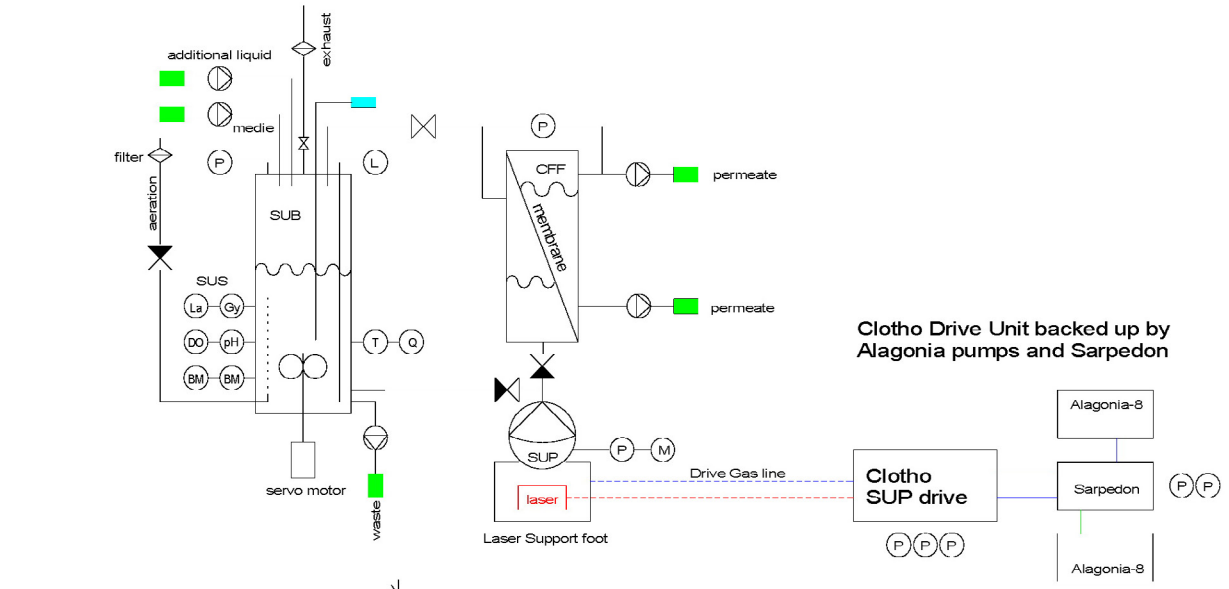
with Single-Use-Pump, Single-Use-Sensor's, Hollow-Fiber-Filter

CellMembra-3200

- CellMembra-3200 is all pre-assembled and ready to use
- O-SUP is Clio-100 with selectable 1-100 ml volume per stroke
- O-SUP fully controlled volume and velocity by Clotho with 1 % accuracy
- Fully customized setup and any HFF mono or dual
- Single-Use-Sensor's (SUS) as required (DO, pH, bio-mass, level)
- Compact Clotho Drive Unit is needed
- Alternatively Alagonia-8 pumps and perhaps Sarpedon
- Drive Unit is available in both a single channel and dual channel version within the same U2 cabinet



CellMembra Perfusion-SUB integrating Clio O-SUP pump, sensors, valves
Perfusion, cell retention, one direction pulsating flow through CFF

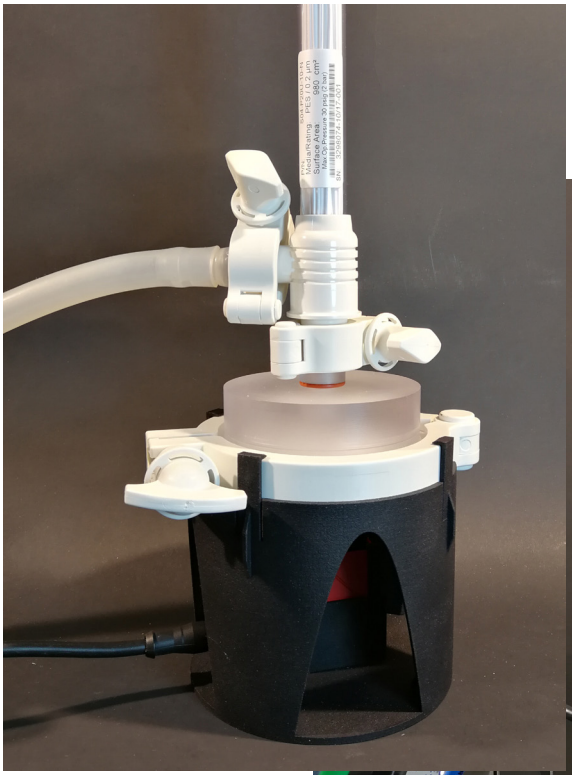


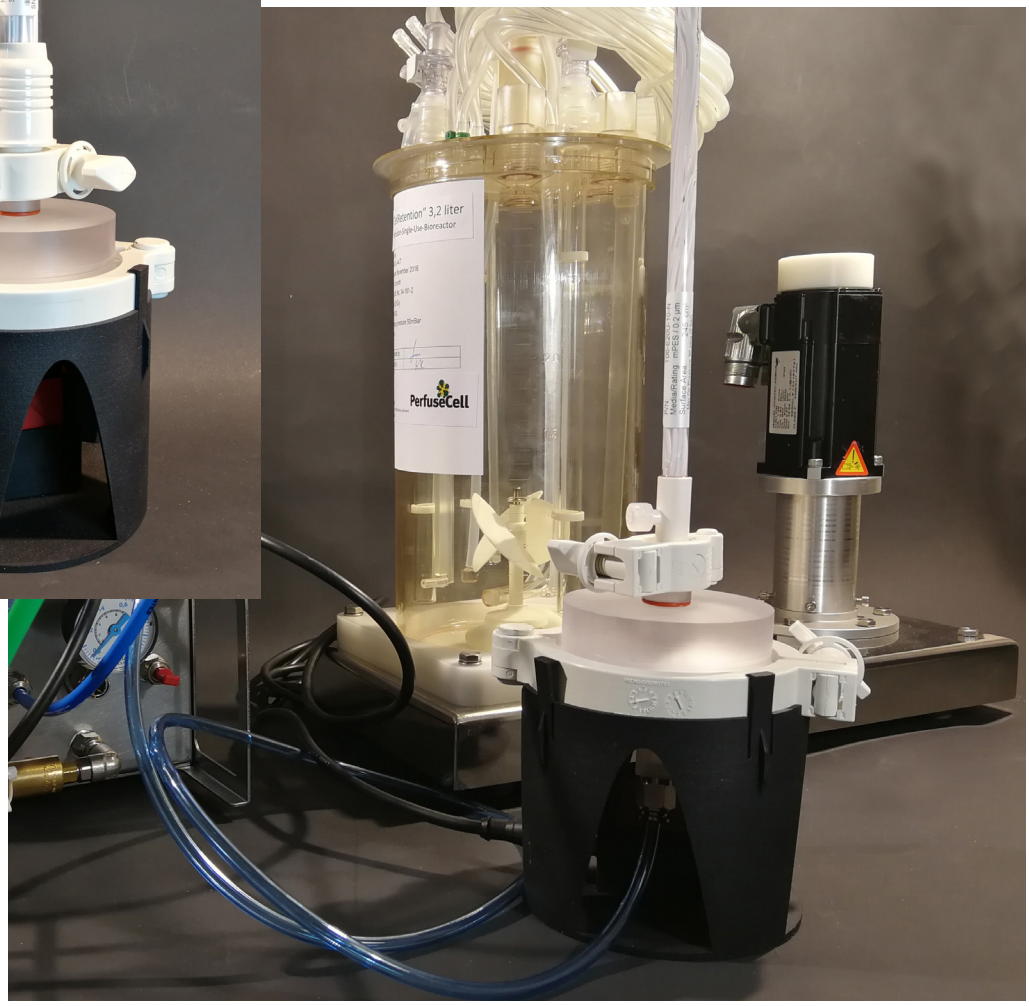
Medium size P-SUB

integrates Single-Use-Exchanger, Single-Use-Sensor's, Hollow-Fiber-Filter

CellRetention-3200

- CellVessel SUB with 3,2 liter Vessel Volume (VV)
- CellVessel ranging 400-2.000 ml Working Volume (WV)
- Integrated Thalia-100 A-SUE fully controlled and measured 0-100 ml volume per stroke
- Any available HFF can be specified and pre-installed and as many as needed
- SUB with any type of impeller single or dual
- Agitation by Magnetic-Bottom-Drive (MBD) by PerfuseCell Magnetic-Stirrer-Table (MST) with any servo motor
- Range of Single-Use-Sensor's with connectors which fit your PCS
- Check out thermal control below



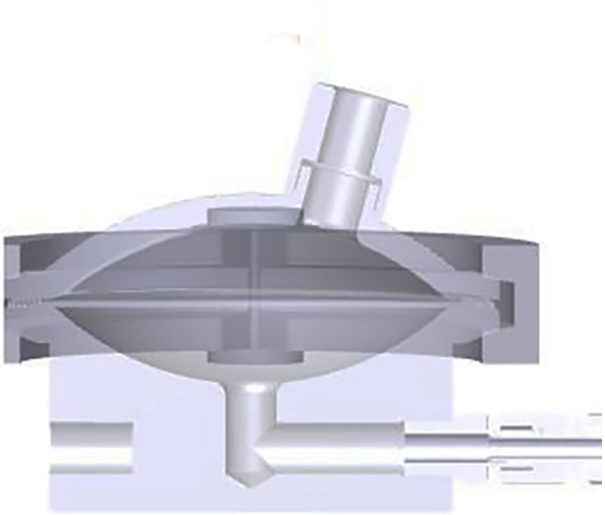


Medium size P-SUB

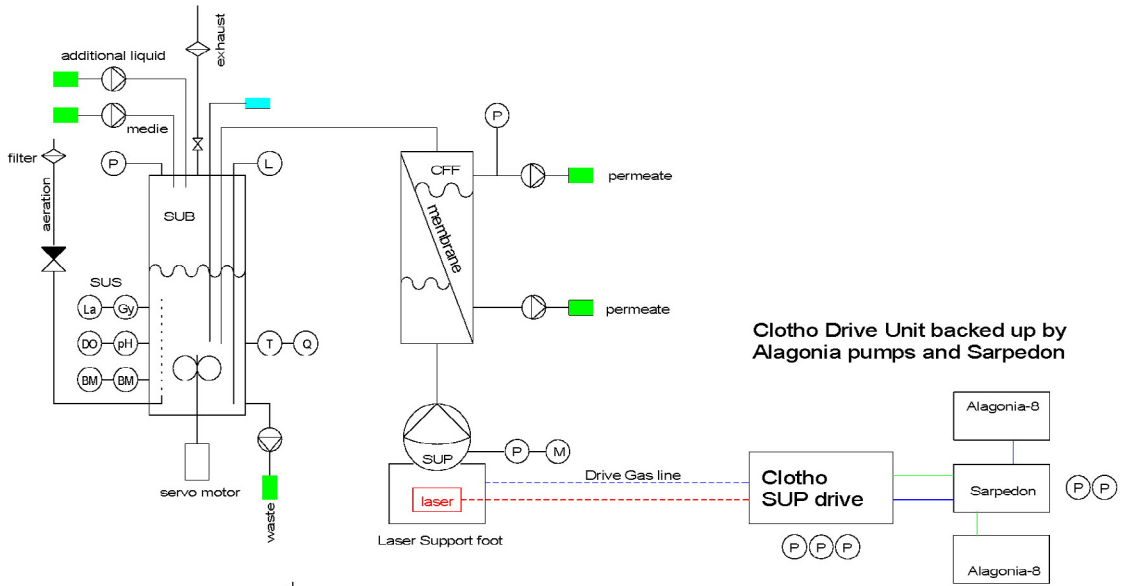
with Single-Use-Exchanger, Single-Use-Sensor's, single-use Hollow-Fiber-Filter

CellRetention-3200

- CellRetention-3200 is all pre-assembled and ready to use right out of the box
- A-SUE is Thalia-100 offering 0-100 ml per stroke accurately programmed
- A-SUE fully controlled volume and velocity with 1 % accuracy
- Fully customized setup and any or multiple HFF
- Single-Use-Sensor's (SUS) as required (and available)
- Clotho Drive Unit is needed
- Alternatively Alagonia-8, Alagonia-12 drive gas pumps and Sarpedon



CellRetention Perfusion-SUB integrating Thalia A-SUE, Single-Use-Sensors, Cross-Flow-Filter for alternating pulsating flow through CFF



SUB = Single-Use-Bioreactor
SUS = Single-Use-Sensor
SUP = Single-Use-Pump
CFF = Cross-Flow-Filter
BM = Bio mass SUS
CN = Conductivity SUS
Gy = Glucose on-line SUS
La = Lactate on-line SUS
L = 0 - 100 % level sensor
SM = Servo Motor
Q = heating input for temperature control
PCS = Process-Control-System

proportional valves
V1-V? pinch valves
C1-? = hose clamps
Sterile coupling
Swabable valve

Per Stobbe 2018-01-15
per.stobbe@perfusecell.com

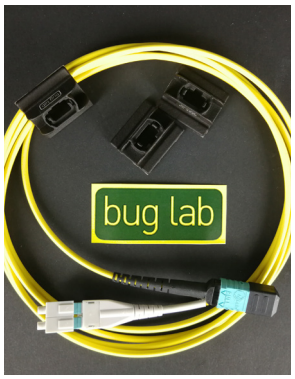
PerfuseCell

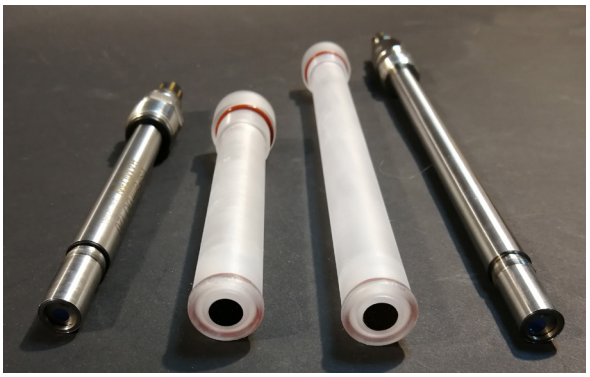
The unique ❸ Single-Use-Sensor's

measures DO, pH, bio-mass, level, Glucose

All pre-installed:

- Capacitance bio-mass or OD bio-masss
- Customized high quality pH and DO
- Customized high quality Glucose
- Customized high quality level





Thermal control

The best thermal control for P-SUB's

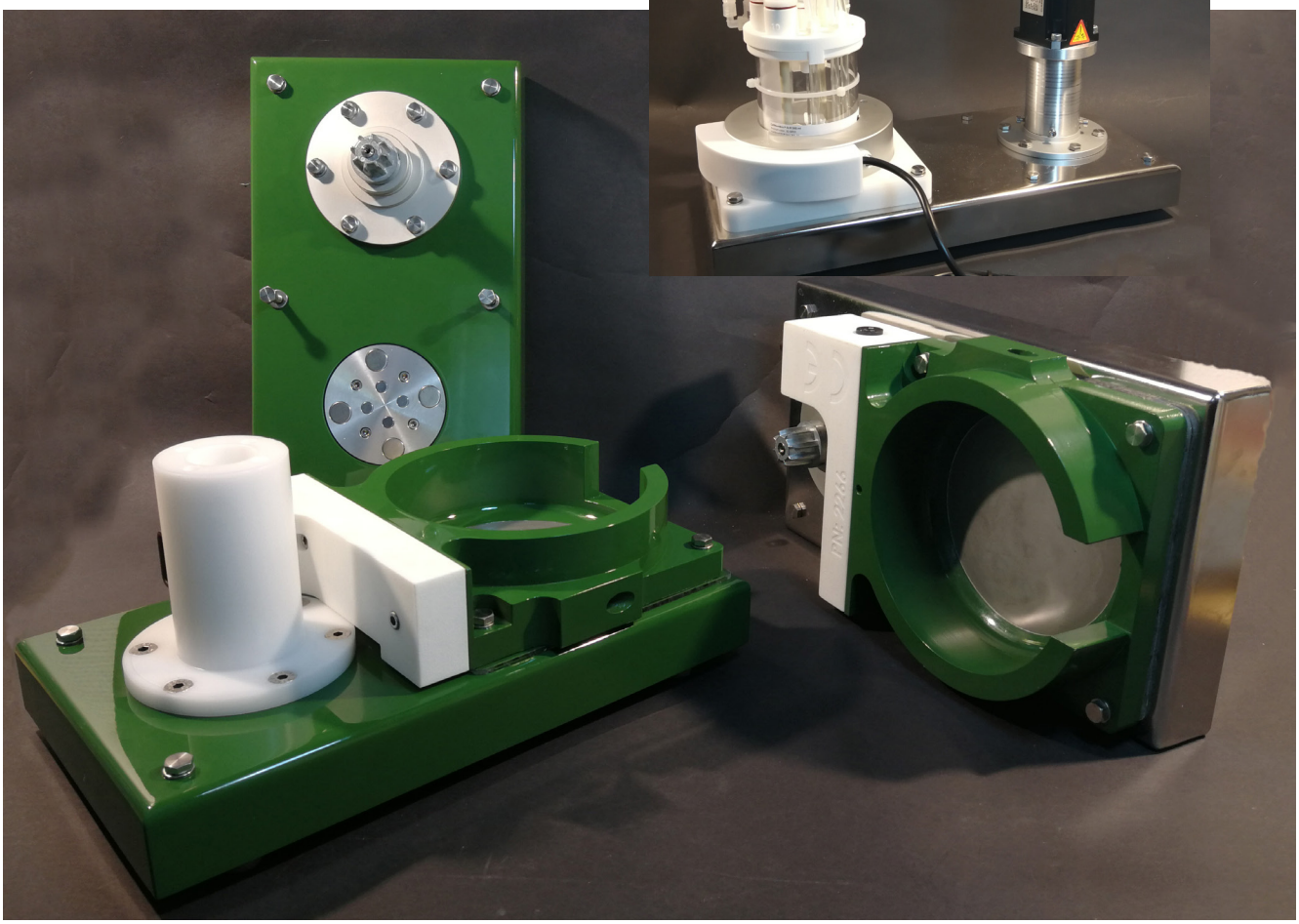
Its all Plug & Play!

Heating-Support-Foot (HSF) that fits any of the 500 ml and 3.200 ml vessel's. Able to operate with small volumes starting from few hundred ml up to 2.000 ml.

Allow installation of CerCell SUB's as well as the CellMembra and CellRetention p-SUB's on the Magnetic-Stirrer-Table (MST).

Medium size and larger sizes P-SUB's allow use of conventional heating blankets.

Whatever happens – you can run the P-SUB dry, forget media, thermo couple fall out, PCS breaks down … this advanced HSF will newer destroy the P-SUB and leak out media or burn your fingers when trying to solve the problem!



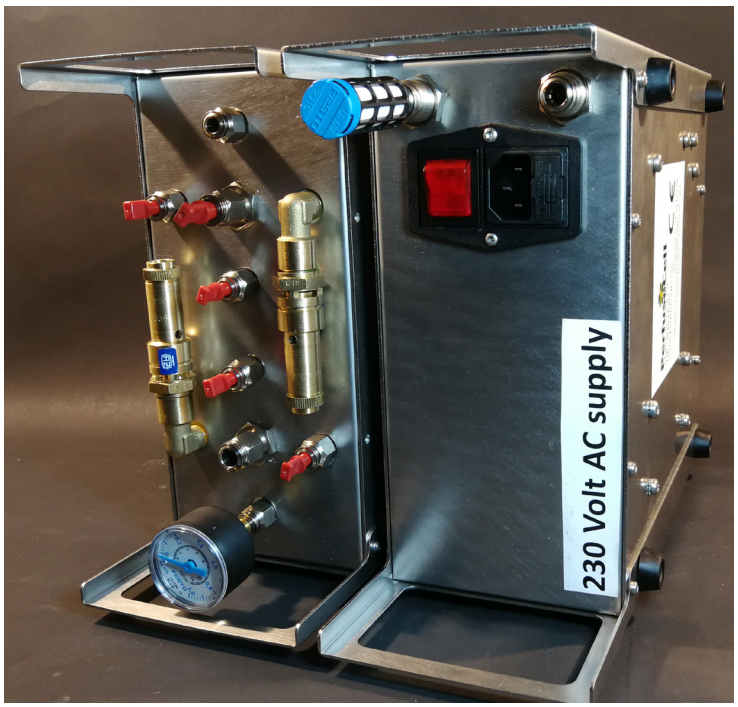
Clotho Drive Unit drive gas accessories

Clotho Drive Unit is housed in ultra compact stainless steel Hephaestus size U2 cabinet.

Clotho-2 facilitate two (red) Laser sensor input and several internal pressure sensors. For independent control of two in parallel and selectable size operating Single-Use-Pump's and / or Single-Use-Exchanger's.

For simple, low noise, ultra compact and fast setup – Alagonia drive gas pump's and Sarpedon manifold / reservior.

Run on either 110 VAC or on 230 VAC.



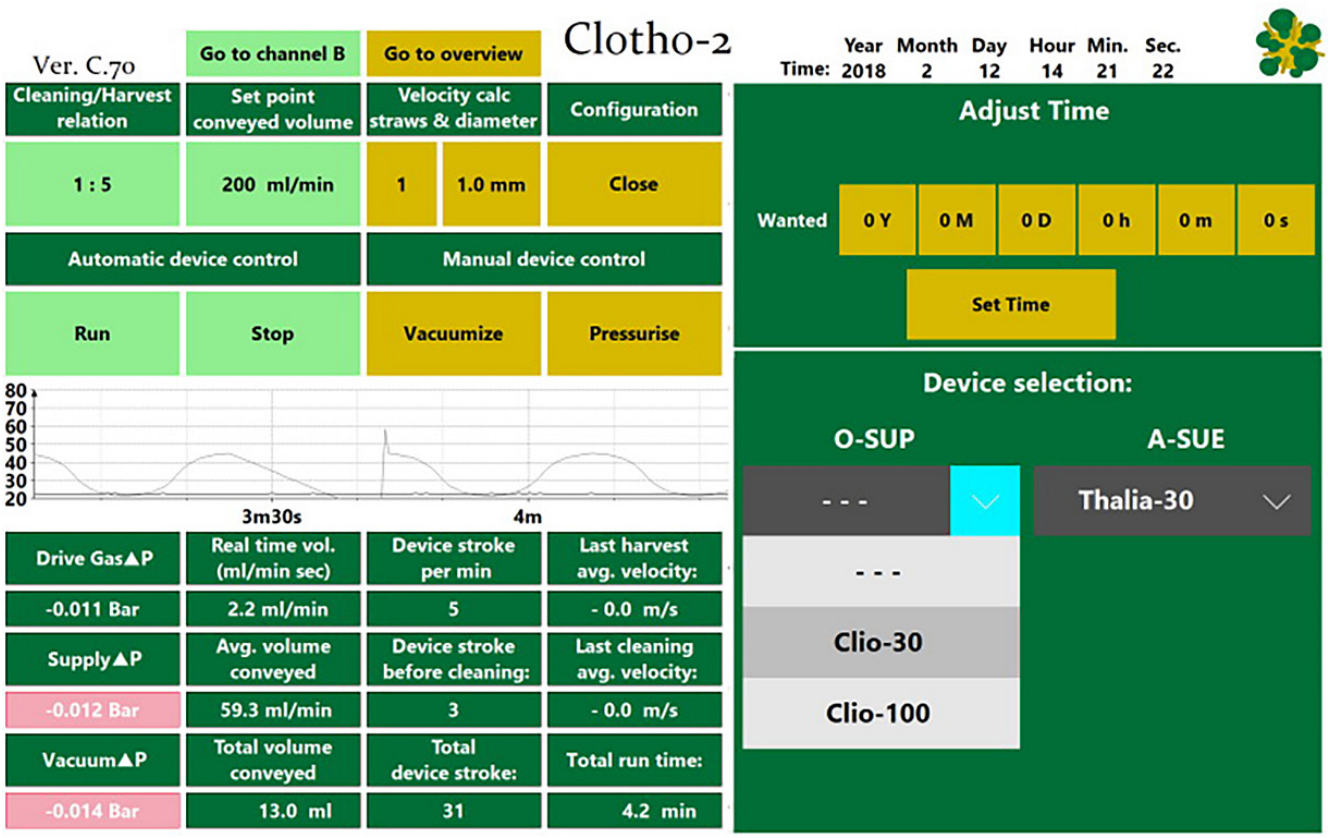
Clotho software

drive both O-SUP and A-SUE diaphragm pumps

Clotho Drive Unit's contains a webserver displaying online information on the build-in display. The webserver also allow the end-user with a smartphone, PAD or PC to connect to the webserver for programming. Linux runs on a 900 MHz quad-core ARM Cortex-A7 CPU. Clotho software is based on CodeSys PLC platform on top of the Linux firmware with OPC capability.

When Clotho is connected to a supply of drive pressure and vacuum source with sufficient capacity, then the spec is:

- Stroke frequency, per minute: 0,5-15
- Stroke duration, seconds: 1-60
- HFF broth velocity, m/s: 0,1-12



PerfuseCell

Clotho-2 Drive Unit setup

for CellMembra & CellRetention

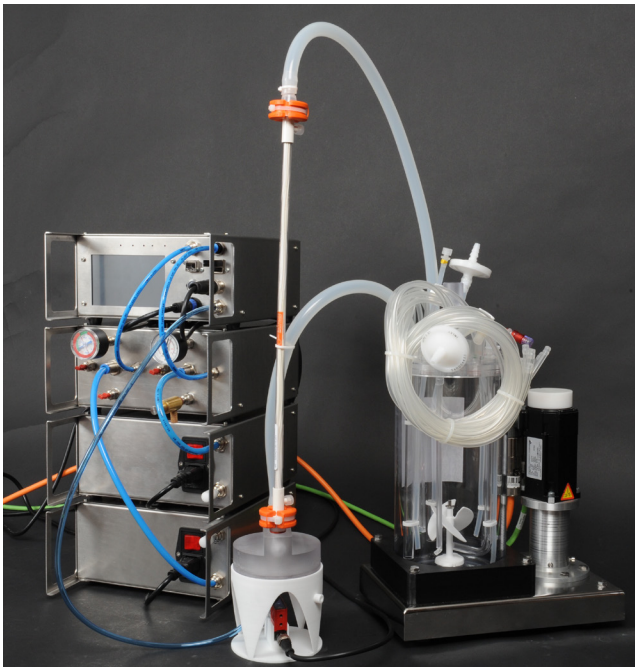
Dual Perfusion-SUB's, different sizes, fully independent operated by the dual channel Clotho-2 Drive Unit.

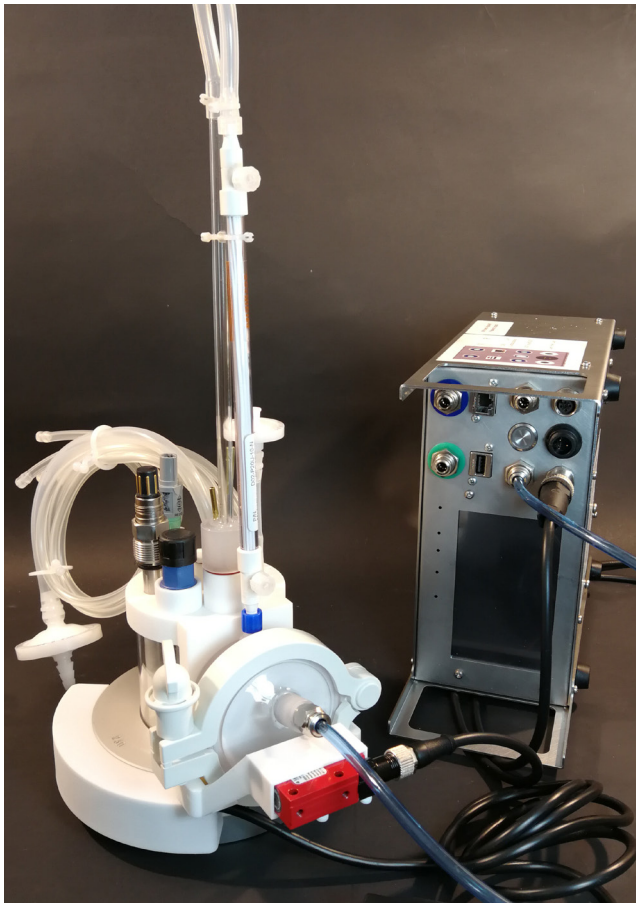
Clotho-2 designed for control of two in parallel operating Single-Use-Pump's and / or Single-Use-Exchanger's.

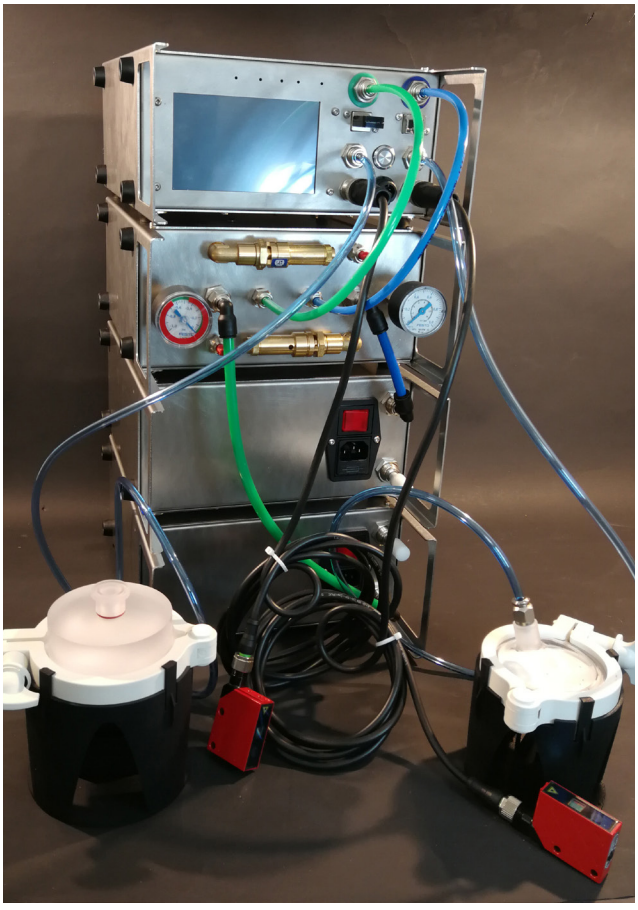
If no drive gas pressure and vacuum is available your lab use PerfuseCell units.

As shown with Alagonia-8 drive gas pump's and Sarpedon manifold / reservior – all in the same ultra compact Hephaestus U2 cabinet's.

If no drive gas pressure and vacuum is available in your lab – then use the PerfuseCell units.





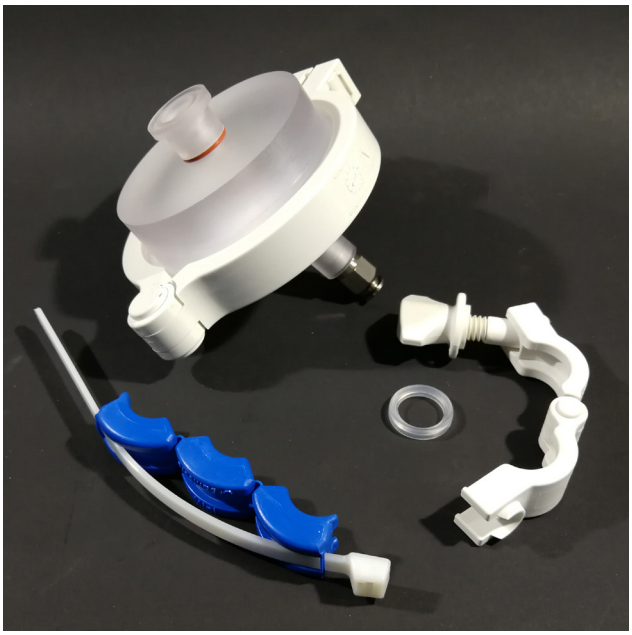


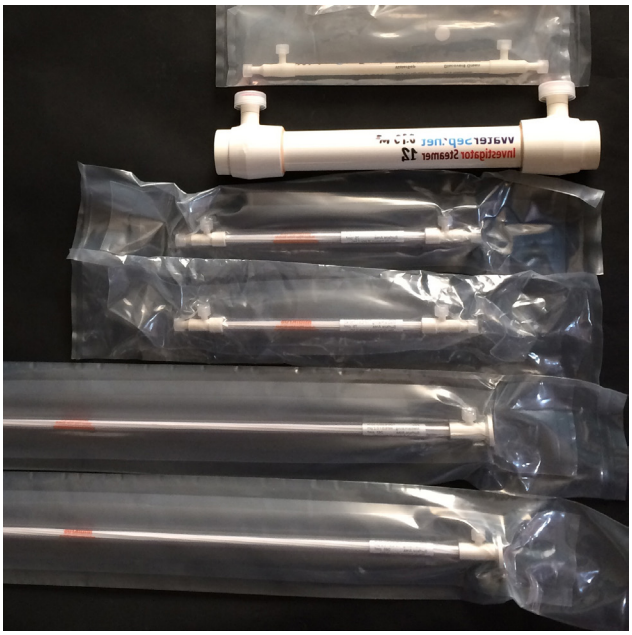
Selectable acessories for P-SUB's

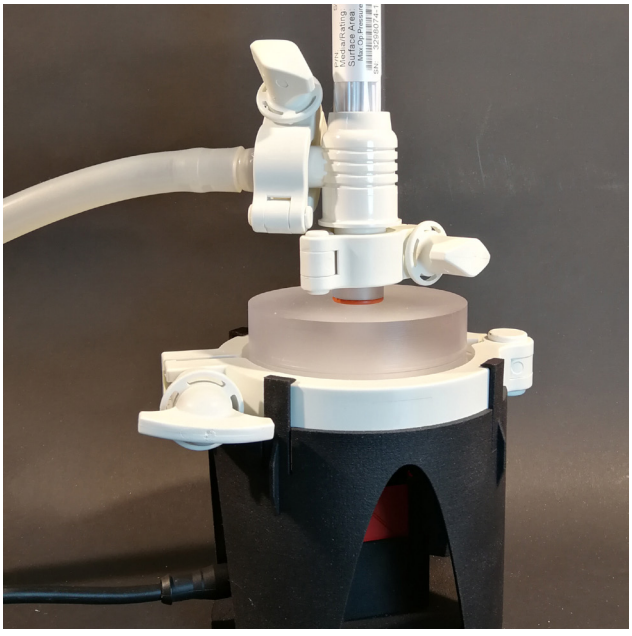
Connecting the HFF with sanitary couplings to the O-SUP or the A-SUE outlet/ inlet port and the SUB ports is easy. PerfuseCell as well as other suppliers offer various connection devices.

HFF – harvest continuously a cell free permeate. Choose from one of your preferred suppliers, such as:

- www.spectrumlabs.com
- www.watersep.net
- www.parker.com/dh-bioprocessing
- www.gelifesciences.com







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