

Customized Perfusion Single-Use-Bioreactor



Continuous Biomanufacturing

Lady Margaret Hall,
University of Oxford,
England

20-22 June 2018



Please let me explain ...
Per Stobbe
www.stobbepharma.ch

I PR - Intellectual-Property-Right's



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
 (19) World Intellectual Property Organization
 International Bureau
 (43) International Publication Date: 16 February 2017 (16.02.2017)
 WIPO PCT
 (11) International Publication Number: WO 2017/025210 A1

(51) International Patent Classification: C12M 1/00 (2006.01), C12M 1/34 (2006.01)
 (52) International Application Number: PCT/US2016/01000
 (53) Filing Date: 17 May 2016 (17.05.2016)
 (54) Publication Language: English
 (55) Priority Data: PACT010013 9 August 2015 (08.08.2015) DK; PCT/US2016/01000 17 May 2016 (17.05.2016) US

(71) Applicant: STORBE PHARMA TECH GmbH, 21100 Hamburg, Germany
 (72) Inventor: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (73) Agent: JPM AVIATION APG, London, GB, 31 Finsbury Square, London, EC2A 1DU, GB

(57) Abstract: The present invention relates to a bioreactor system comprising a single-use bioreactor, a single-use pump and a single-use membrane filter. The bioreactor system is configured to provide a liquid media of high oxygen concentration in a perfusion mode continuous process for expression of a protein in a single-use bioreactor through a liquid containing pump. The bioreactor system includes a pump system with a valve to a single-use bioreactor in a perfusion mode for operating and with a disposable bioreactor system in a perfusion mode for continuous processing.

(12) United States Patent Application Publication
 (11) Pub. No.: US 2017025210 A1
 (43) Pub. Date: Jun. 7, 2018

(54) RETENTION SYSTEM
 (71) Applicant: STORBE PHARMA TECH GmbH, Chiano (CI)
 (72) Inventor: Per STORBE, Chiano (CI)
 (73) Assignee: STORBE PHARMA TECH GmbH, Chiano (CI)
 (21) Appl. No.: 15586349
 (22) Filed: Nov. 6, 2017

Related U.S. Application Data
 (53) Continuation of application No. PCT/US2016/01000, filed on May 17, 2016.
 (51) Foreign Application Priority Data
 Aug. 8, 2015 (DK) PACT010013
 (52) International Classification: B01D 21/00 (2006.01), B01D 21/02 (2006.01), B01D 21/04 (2006.01)

(57) Abstract: The present invention relates to a system consisting of a single-use pump and a single-use micro-organism based mass culture for cultivating organisms in a liquid media at concentration in a perfusion mode expression of biological material. The inlet of the liquid media is a valve to the breath reservoir of the pumping single-use pump system. The inlet of the liquid media is a valve to the breath reservoir of the pumping single-use pump system continuously processing.

(54) THE DISPOSABLE ALTERNATING TANGENTIAL FLOW HARVESTING SYSTEM
 (57) Abstract: Methods and systems of harvesting a cell product from a cell culture by collecting cells in a fluid medium and the cells have produced a cell product at a harvest concentration are disclosed. The cells are cultured in a cell culture system including a bioreactor connected to an ATP device. The methods include draining fluid medium from the bioreactor through the outlet and the ATP system yields a cell product in a liquid containing cell product and a waste stream with a concentration of cell product that is lower than the harvest concentration based on the bioreactor, extracting the liquid containing cell product from the ATP tank, settling the bioreactor with sterile phosphate buffered saline or fluid medium without any cell product, and repeating steps with a desired amount of cell product has been removed.

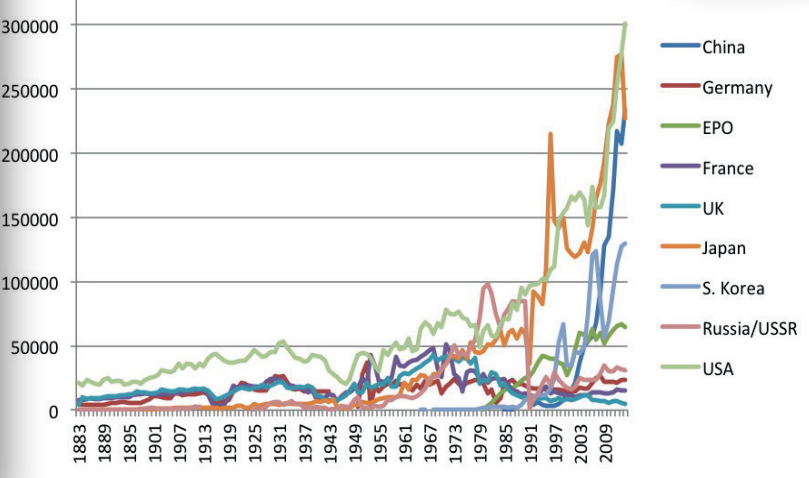
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
 (19) World Intellectual Property Organization
 International Bureau
 (43) International Publication Date: 24 June 2010 (24.06.2010)
 WIPO PCT
 (11) International Publication Number: WO 2010/069321 A2

(51) International Patent Classification: B01D 21/00 (2006.01)
 (52) International Application Number: PCT/DE2009/002621
 (53) International Filing Date: 14 December 2009 (14.12.2009)
 (54) Publication Language: English
 (55) Priority Data: PACT090115 19 December 2009 (19.12.2009) DK; PACT090111 19 October 2009 (19.10.2009) DK; PACT090142 25 October 2009 (25.10.2009) DK; PACT090165 29 October 2009 (29.10.2009) DK

(71) Applicant: Per STORBE, Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (72) Inventor and Assignee: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (73) Common Representative: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy

(57) Abstract: An electronically controlled diaphragm pump system is provided. The pump system comprises a pump housing with a drive gas chamber and a fluid chamber separated by a diaphragm. The drive gas chamber is connected to one or more gas ports for injecting and/or sucking a gas into and out of the gas chamber. The fluid chamber is connected to a least one port for fluid inlet and at least one port for fluid outlet, where the fluid port has a valve adapted to open for fluid inlet when it is sucked out of the gas chamber and the outlet port has a valve adapted to open for fluid outlet when gas is injected into the gas chamber. The pump system further has a pressure means connected to a gas inlet port for providing a drive gas pressure in response to a control signal, and an under-pressure means connected to a gas outlet port for providing a gas under-pressure or sucking of gas in response to a control signal. Furthermore, the pump system has a displacement sensor for detecting displacement of position of the diaphragm, and control circuitry connected to the displacement sensor for determining the displacement or position of the diaphragm and adapted for supplying the control signals to the gas pressure means and the gas under-pressure means. It is preferred that the means for providing a drive gas pressure comprise a gas pressure proportional control valve being connected to the gas inlet and the control circuitry, whereby the drive gas pressure is varied as a function of the control signal supplied by the control circuitry. Also, the means for providing a gas under-pressure may comprise a gas under-pressure control valve being connected to the gas outlet and the control circuitry, whereby the gas under-pressure is varied as a function of the control signal supplied by the control circuitry.

Patents Granted Worldwide by Country



(12) United States Patent
 (11) Pub. No.: US 6,544,424 B1
 (43) Date of Patent: June 8, 2003

(54) FLUID FILTRATION SYSTEM
 (71) Inventor: Jerry Shultz, Livingston, NJ (US)
 (73) Assignee: Redwood Technology Company, East Hanover, NJ (US)

(57) Abstract: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 3549(a) by days.

(51) Int. Cl. 7: B01D 61/00
 (52) U.S. Cl.: 210/237.2, 210/192.2, 210/132.3
 (53) Field of Search: 210/237.2, 210/192, 210/132, 210/131, 210/130, 210/129, 210/128, 210/127, 210/126, 210/125, 210/124, 210/123, 210/122, 210/121, 210/120, 210/119, 210/118, 210/117, 210/116, 210/115, 210/114, 210/113, 210/112, 210/111, 210/110, 210/109, 210/108, 210/107, 210/106, 210/105, 210/104, 210/103, 210/102, 210/101, 210/100, 210/99, 210/98, 210/97, 210/96, 210/95, 210/94, 210/93, 210/92, 210/91, 210/90, 210/89, 210/88, 210/87, 210/86, 210/85, 210/84, 210/83, 210/82, 210/81, 210/80, 210/79, 210/78, 210/77, 210/76, 210/75, 210/74, 210/73, 210/72, 210/71, 210/70, 210/69, 210/68, 210/67, 210/66, 210/65, 210/64, 210/63, 210/62, 210/61, 210/60, 210/59, 210/58, 210/57, 210/56, 210/55, 210/54, 210/53, 210/52, 210/51, 210/50, 210/49, 210/48, 210/47, 210/46, 210/45, 210/44, 210/43, 210/42, 210/41, 210/40, 210/39, 210/38, 210/37, 210/36, 210/35, 210/34, 210/33, 210/32, 210/31, 210/30, 210/29, 210/28, 210/27, 210/26, 210/25, 210/24, 210/23, 210/22, 210/21, 210/20, 210/19, 210/18, 210/17, 210/16, 210/15, 210/14, 210/13, 210/12, 210/11, 210/10, 210/9, 210/8, 210/7, 210/6, 210/5, 210/4, 210/3, 210/2, 210/1

(57) Abstract: A filtration system for fluids, particularly biological fluids. The filtration system includes a filter container, compressor connected to one end to a storage vessel and at the other end to a diaphragm pump. The filter container is a hollow filter medium or a screen filter. The vessel serves as a storage container for a process stream to be filtered. The diaphragm pump provides the means for generating rapid, alternating low water potential flow between the vessel and pump and through the filter or screen filter. The system allows easy removal of waste from the filter and the addition of fresh fluid to replenish the filtered fluid.

(3) Claims, 8 Drawing Sheets

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
 (19) World Intellectual Property Organization
 International Bureau
 (43) International Publication Date: 01 February 2018 (01.02.2018)
 WIPO PCT
 (11) International Publication Number: WO 2018/022661 A1

(51) International Patent Classification: B01D 21/00 (2006.01), B01D 21/02 (2006.01), B01D 21/04 (2006.01)
 (52) International Application Number: PCT/US2016/01000
 (53) International Filing Date: 17 May 2016 (17.05.2016)
 (54) Publication Language: English
 (55) Priority Data: PACT010013 9 August 2015 (08.08.2015) DK; PCT/US2016/01000 17 May 2016 (17.05.2016) US

(71) Applicant: STORBE PHARMA TECH GmbH, 21100 Hamburg, Germany
 (72) Inventor: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (73) Agent: JPM AVIATION APG, London, GB, 31 Finsbury Square, London, EC2A 1DU, GB

(57) Abstract: Methods and systems of harvesting a cell product from a cell culture by collecting cells in a fluid medium and the cells have produced a cell product at a harvest concentration are disclosed. The cells are cultured in a cell culture system including a bioreactor connected to an ATP device. The methods include draining fluid medium from the bioreactor through the outlet and the ATP system yields a cell product in a liquid containing cell product and a waste stream with a concentration of cell product that is lower than the harvest concentration based on the bioreactor, extracting the liquid containing cell product from the ATP tank, settling the bioreactor with sterile phosphate buffered saline or fluid medium without any cell product, and repeating steps with a desired amount of cell product has been removed.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)
 (19) World Intellectual Property Organization
 International Bureau
 (43) International Publication Date: 24 June 2010 (24.06.2010)
 WIPO PCT
 (11) International Publication Number: WO 2010/069321 A2

(51) International Patent Classification: B01D 21/00 (2006.01)
 (52) International Application Number: PCT/US2009/002621
 (53) International Filing Date: 14 December 2009 (14.12.2009)
 (54) Publication Language: English
 (55) Priority Data: PACT090115 19 December 2009 (19.12.2009) DK; PACT090111 19 October 2009 (19.10.2009) DK; PACT090142 25 October 2009 (25.10.2009) DK; PACT090165 29 October 2009 (29.10.2009) DK

(71) Applicant: Per STORBE, Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (72) Inventor and Assignee: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy
 (73) Common Representative: STORBE, Per: Via Luigi Leonardo 12, 69300 Chiano (CI), Italy

(57) Abstract: An electronically controlled diaphragm pump system is provided. The pump system comprises a pump housing with a drive gas chamber and a fluid chamber separated by a diaphragm. The drive gas chamber is connected to one or more gas ports for injecting and/or sucking a gas into and out of the gas chamber. The fluid chamber is connected to a least one port for fluid inlet and at least one port for fluid outlet, where the fluid port has a valve adapted to open for fluid inlet when it is sucked out of the gas chamber and the outlet port has a valve adapted to open for fluid outlet when gas is injected into the gas chamber. The pump system further has a pressure means connected to a gas inlet port for providing a drive gas pressure in response to a control signal, and an under-pressure means connected to a gas outlet port for providing a gas under-pressure or sucking of gas in response to a control signal. Furthermore, the pump system has a displacement sensor for detecting displacement of position of the diaphragm, and control circuitry connected to the displacement sensor for determining the displacement or position of the diaphragm and adapted for supplying the control signals to the gas pressure means and the gas under-pressure means. It is preferred that the means for providing a drive gas pressure comprise a gas pressure proportional control valve being connected to the gas inlet and the control circuitry, whereby the drive gas pressure is varied as a function of the control signal supplied by the control circuitry. Also, the means for providing a gas under-pressure may comprise a gas under-pressure control valve being connected to the gas outlet and the control circuitry, whereby the gas under-pressure is varied as a function of the control signal supplied by the control circuitry.

Ready to use
"right out of
the box"

The building block's for Perfusion-SUB's

1 SUB Single-Use-Bioreactor

A SUB specifically designed for your application. Adaptable Working Volume, special impeller and aerator, desired length and hose brand, fit your existing PCS, etc.



2 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.



3 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 broth exchanger fully controlled.



4 SUS Single-Use-Sensor's

Single-Use-Sensor's which fit your existing Process-Control-System connections. Parameters measured with VisiFerm, OneFerm, PICO biomass and level.



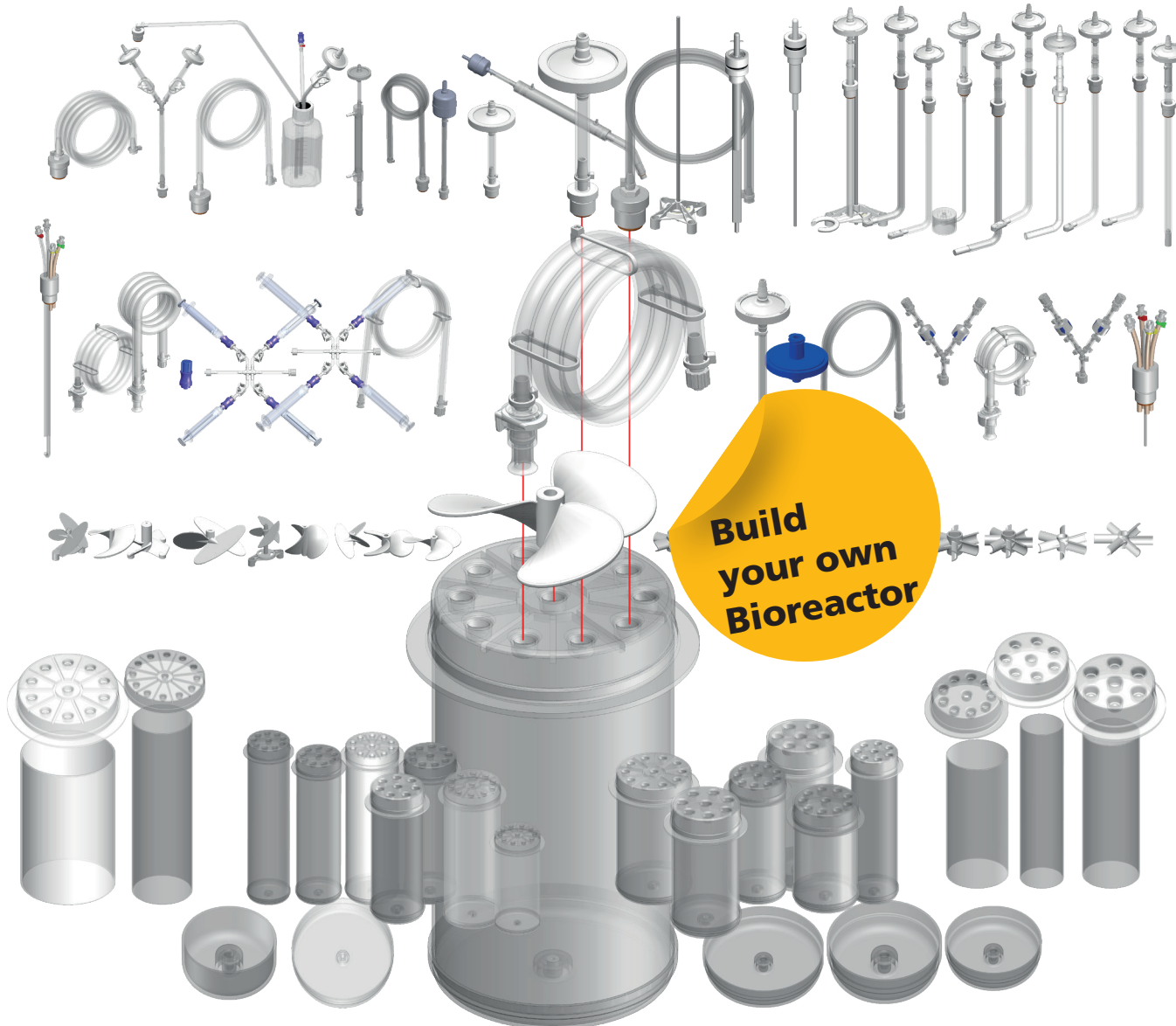
5 HFF Hollow-Fiber-Filter

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.

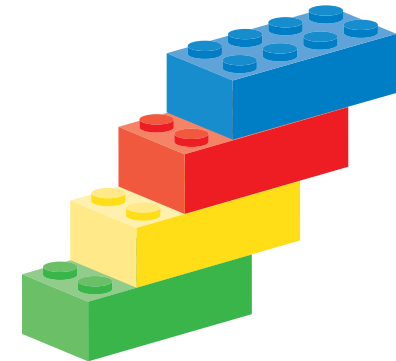


① What does “Customized” really mean?



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 !



If you know Lego® you will like to
build with us.

It's all Plug & Play!

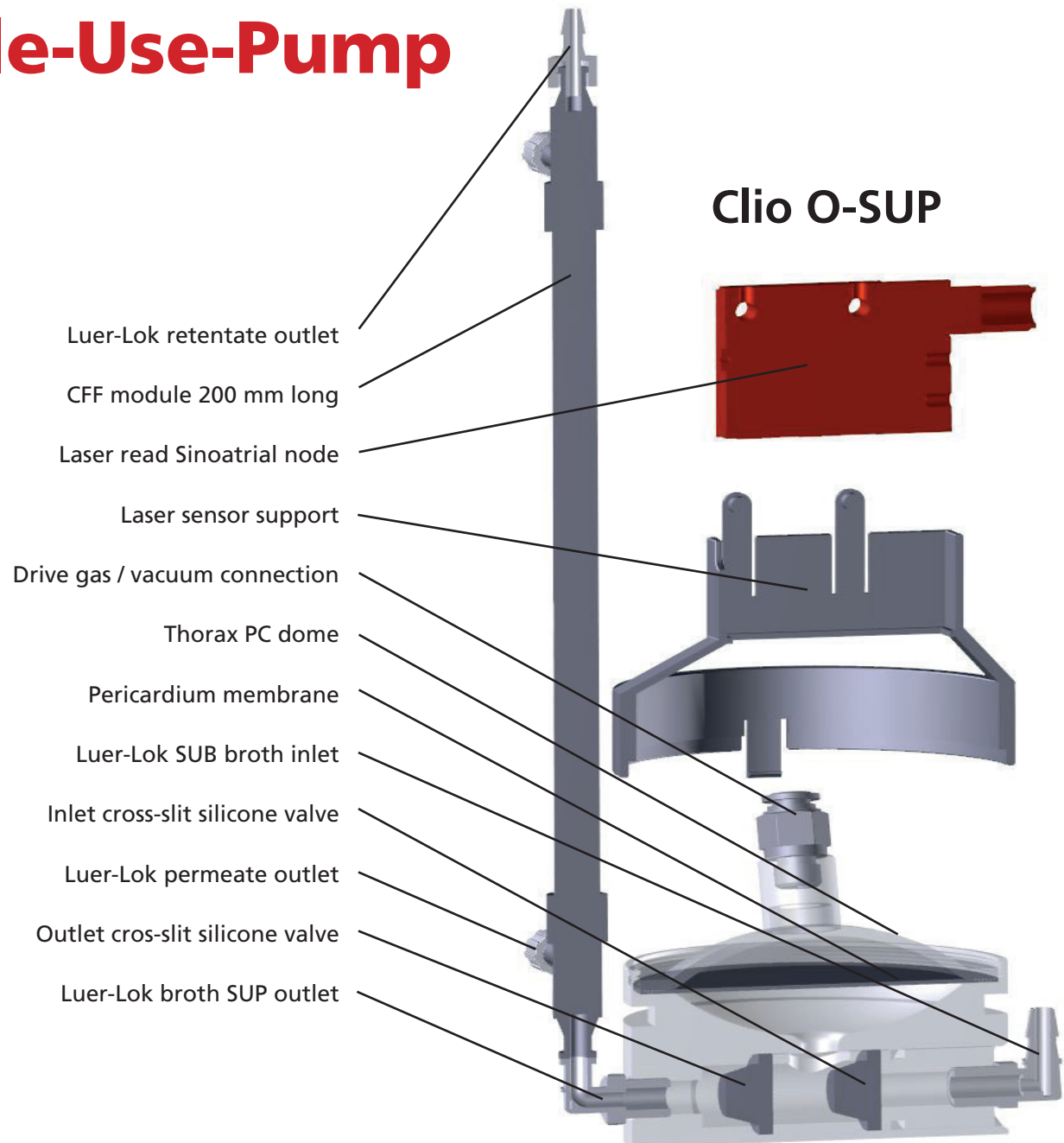
② The **One-way-Single-Use-Pump** for accurate measurement of both volume and velocity

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 stroke is measured accurately independent of the ever dynamic stroke volume. Each stroke duration can vary between seconds and multiple minutes.



3 The unique

Alternating-Single-Use-Exchanger

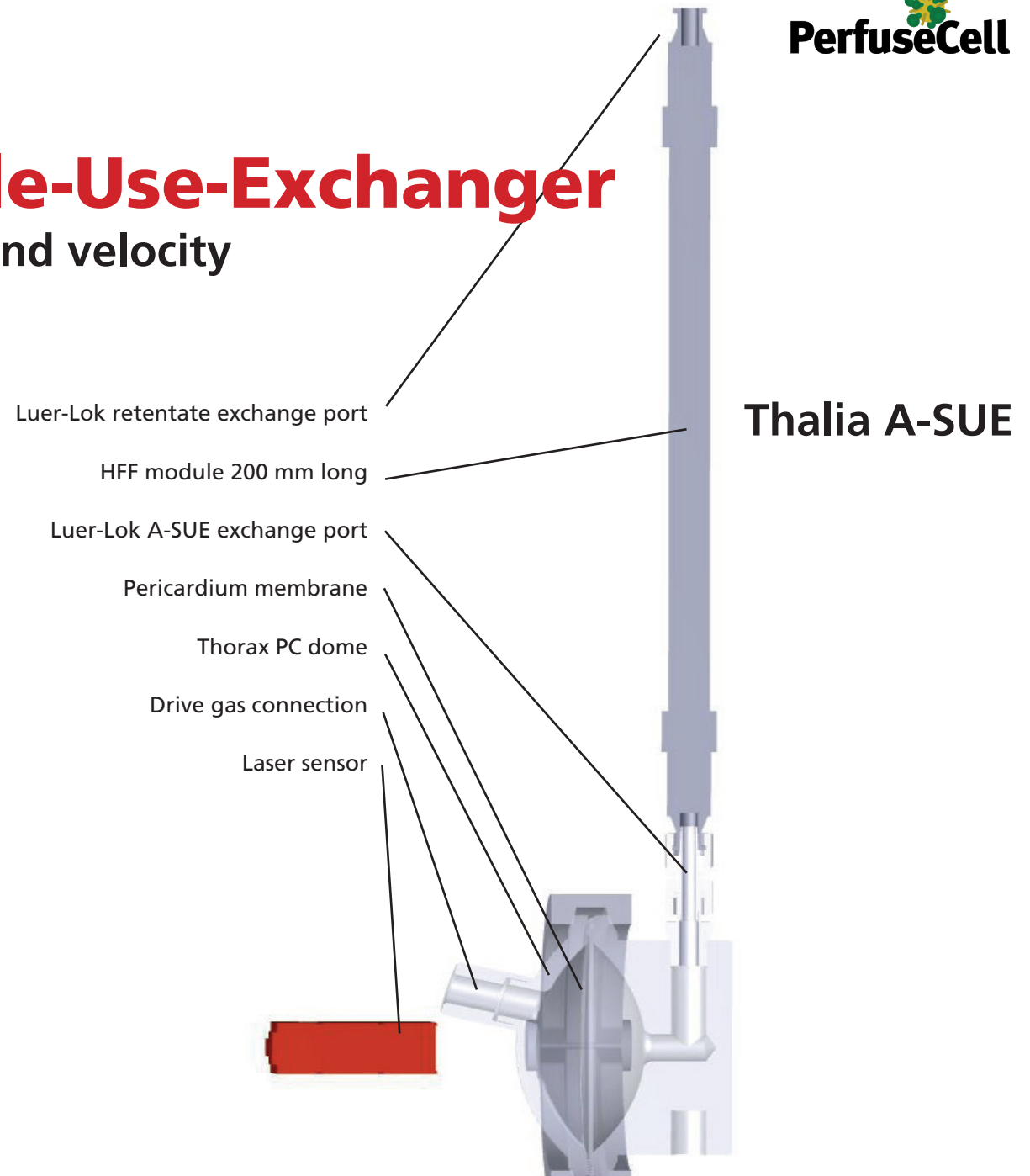
Thalia measure both volume and velocity

The A-SUE is arranged inside a Polycarbonate housing with no connected 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 stroke is measured accurately independent of the ever dynamic stroke volume. Each stroke duration can vary between seconds and multiple minutes.



④ The unique **Single-Use-Sensor's** measures DO, pH, bio-mass, level



CellMembra-500 and CellRetention-500 as standard include pre-installed Single-Use-Sensor's (SUS) for DO, pH, bio-mass and level. The DO, pH and bio-mass SUS is mounted for lowest possible point of sensing in the broth. Photo show mounted vertically through the head-plate.

CellMembra-3200 and CellRetention-3200 as standard include pre-installed vertically mounted Single-Use-Sensor's (SUS) for DO, pH and level. Bio-mass as a horizontal option at bottom.

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.

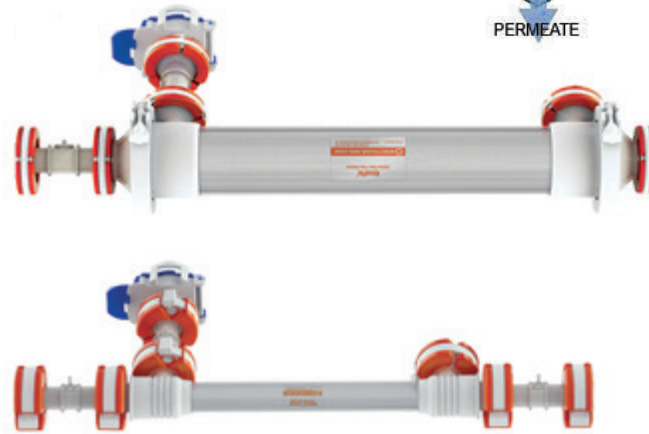
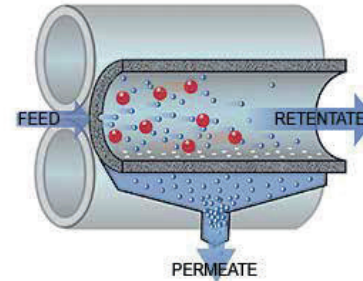
⑤ The Hollow-Fiber-Filter

separates at 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, broth and effectively concentrated in the SUB.



Mini P-SUB

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

CellMembra-500

Mini 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

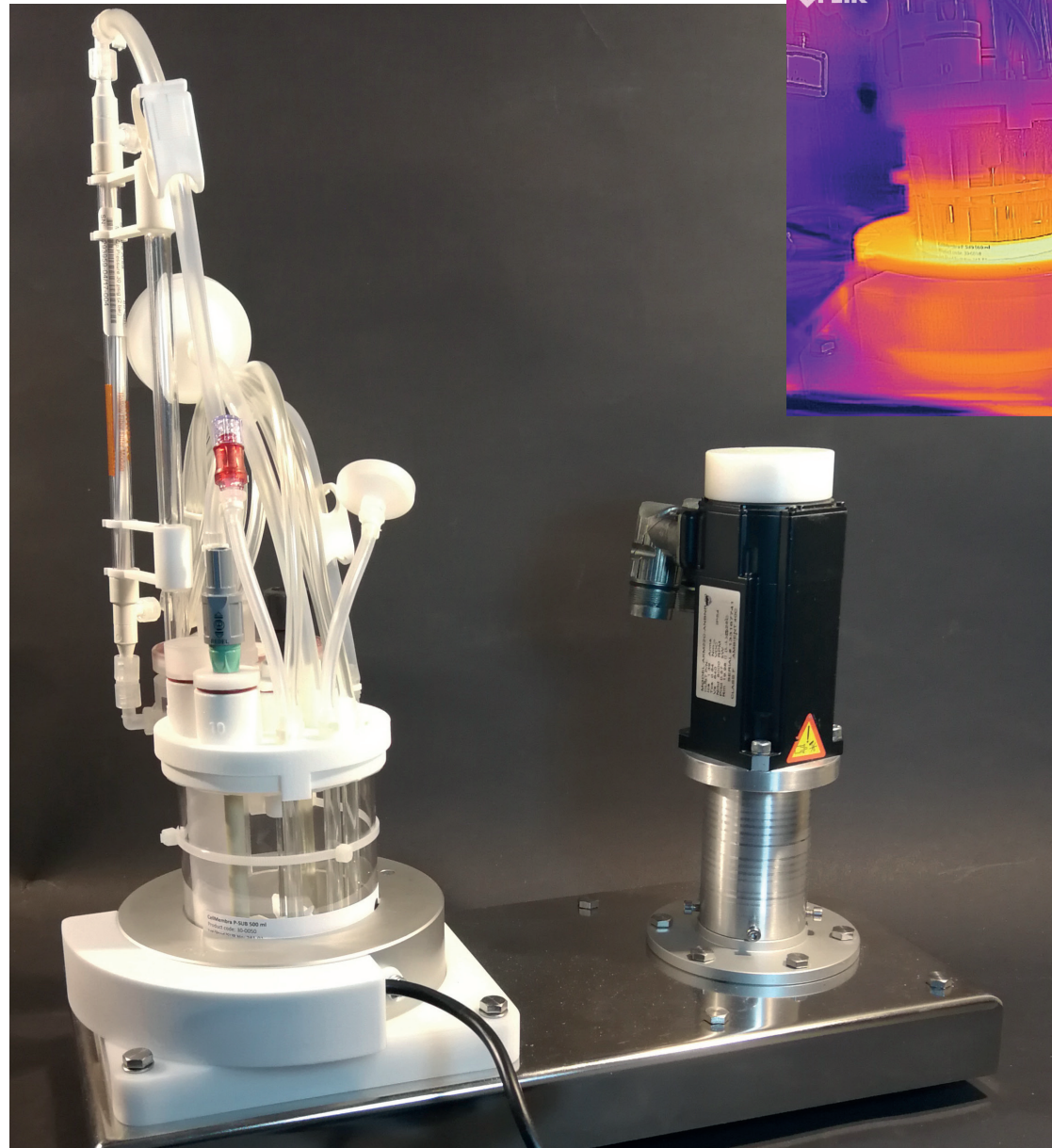
driven by standard PCS

CellMembra-500

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

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).
- 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.



Mini P-SUB

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

CellRetention-500

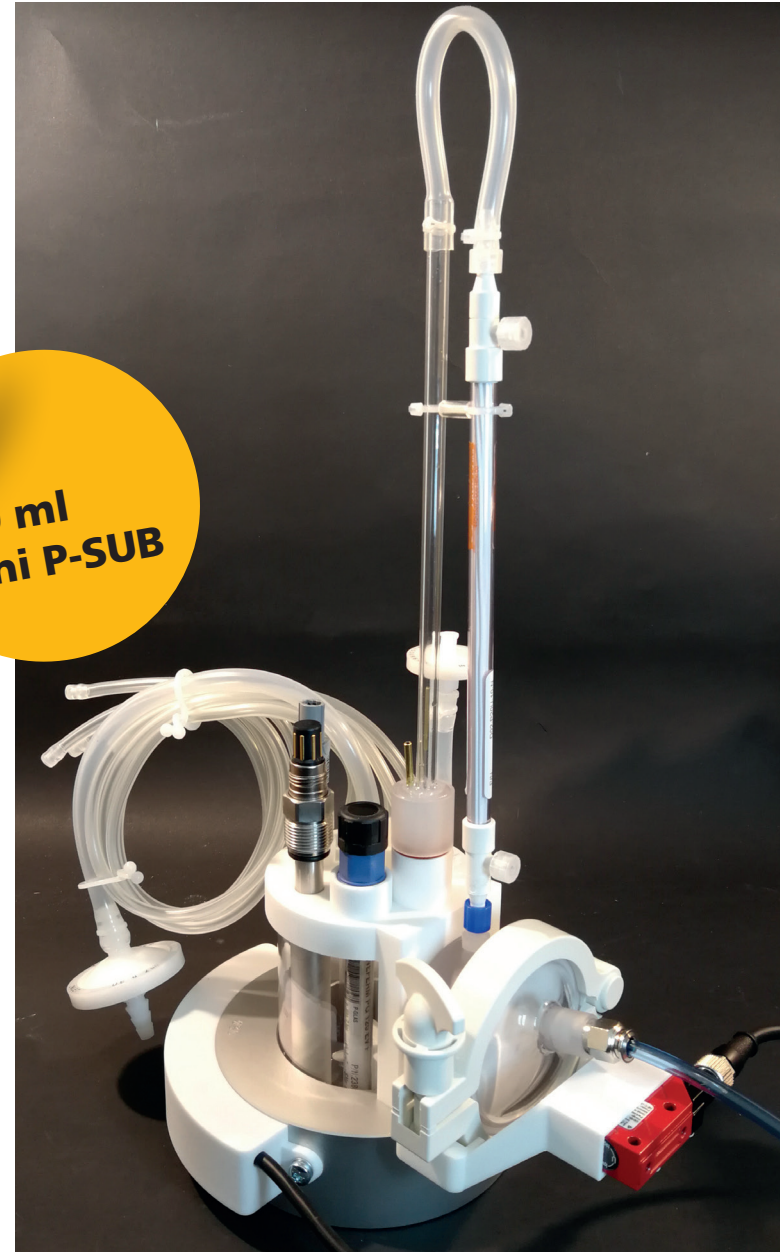
Mini P-SUB for cell retention in perfusion cultivation setup in a fully single-use setup. CellRetention-500 integrates customized CellVessel Single-Use-Bioreactor (SUB), Alternating-Single-Use-Exchanger (A-SUE), and 4 x Single-Use-Sensor's with the HFF (Hollow-Fiber-Filter).

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.



**100 ml
mini P-SUB**



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 3200 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



Medium size P-SUB

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

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

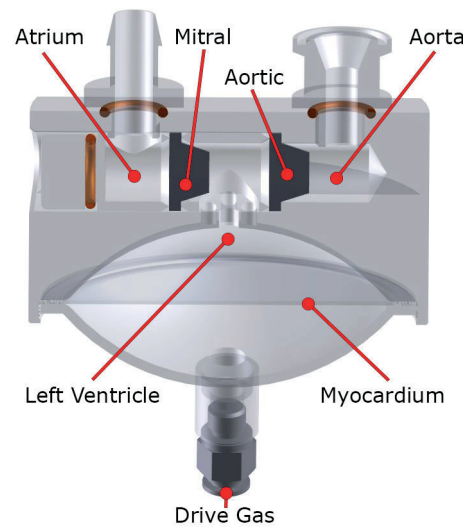
CellMembra-3200

- 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 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 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



Medium size P-SUB

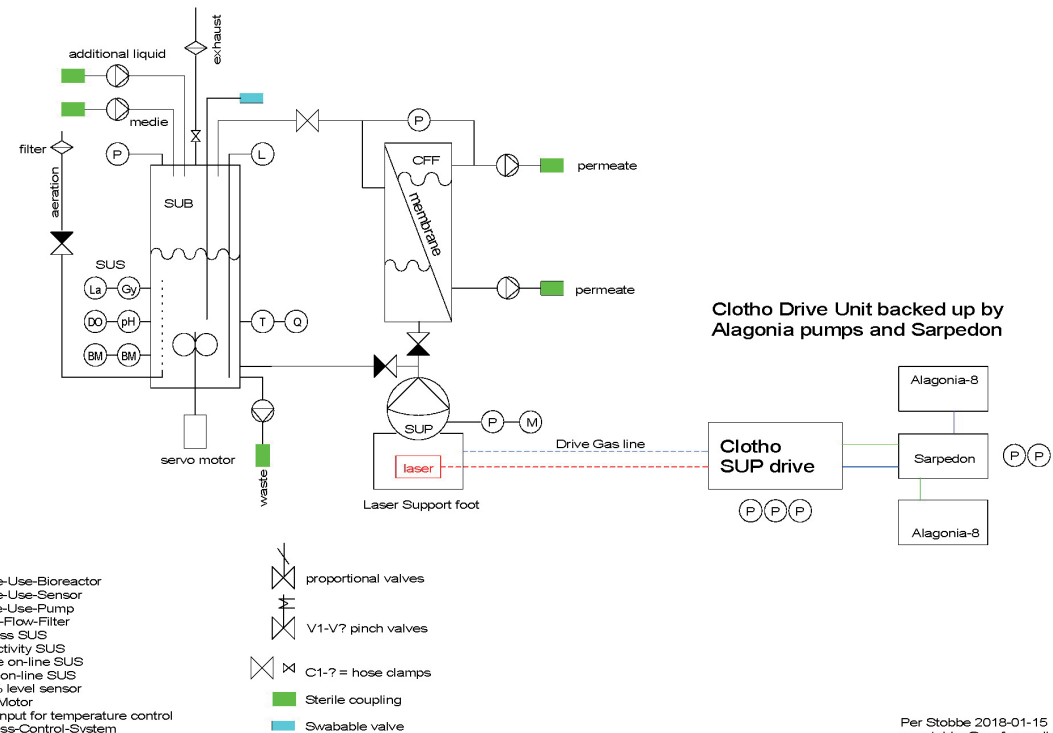
with Single-Use-Pump,
Single-Use-Sensor's,
Hollow-Fiber-Filter



CellMembra-3200

- CellMembra-3200 is all pre-assembled and ready to use
- O-SUP is Clío-100 with selectable 0 – 100 ml volume per stroke
- O-SUP fully controlled volume and velocity by Clotho
- 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 Clío O-SUP pump, sensors, valves
Perfusion, cell retention, one direction pulsating flow through CFF



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

Medium size P-SUB

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

CellRetention-3200

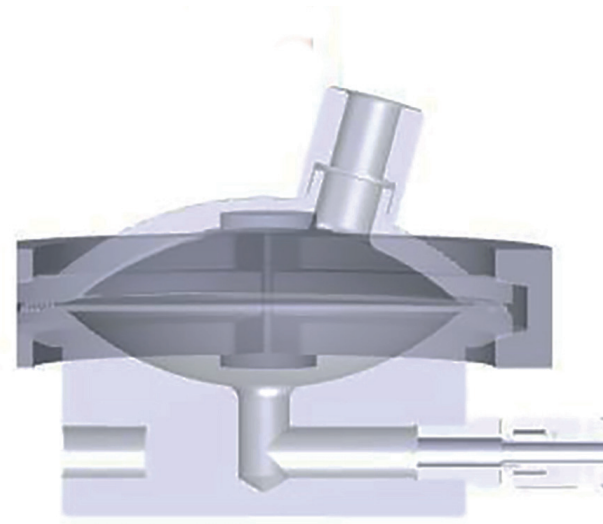
- CellVessel SUB with 3,2 liter Vessel Volume (VV)
- CellVessel ranging 400 ml – 2.000 ml Working Volume (WV)
- Integrated Thalia-100 A-SUE fully controlled and measured 0 - 100 ml volume per stroke
- Any available HFF can be specified and pre-installed and as many as needed
- SUB with any type of impeller and as many as needed
- Agitation from top (HPD) facilitates a range of servo motors with a variety of adaptor's
- 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

World
smallest
parallel
P-SUB



Medium size P-SUB

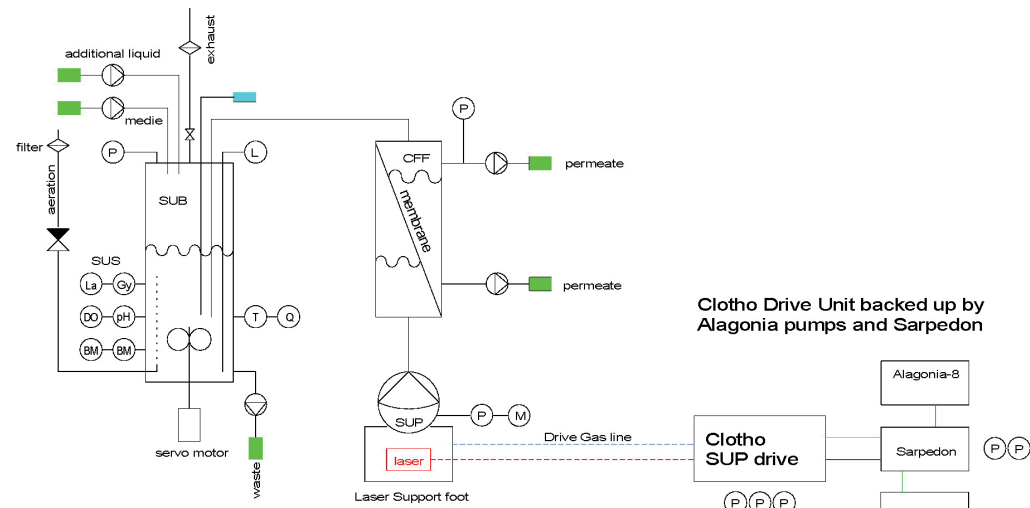
with Single-Use-Exchanger,
Single-Use-Sensor's, single-use
Hollow-Fiber-Filter








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
- 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 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-V7 pinch valves
 C1-7 = hose clamps
 Sterile coupling
 Swabable valve

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

Ultra compact Clotho-2 Drive Unit

for CellMembra / CellRetention / CellBLU



The portfolio of CellMembra and CellRetention and CellBLU Perfusion-SUB's are all driven by the green Clotho / blue Lachesis 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):

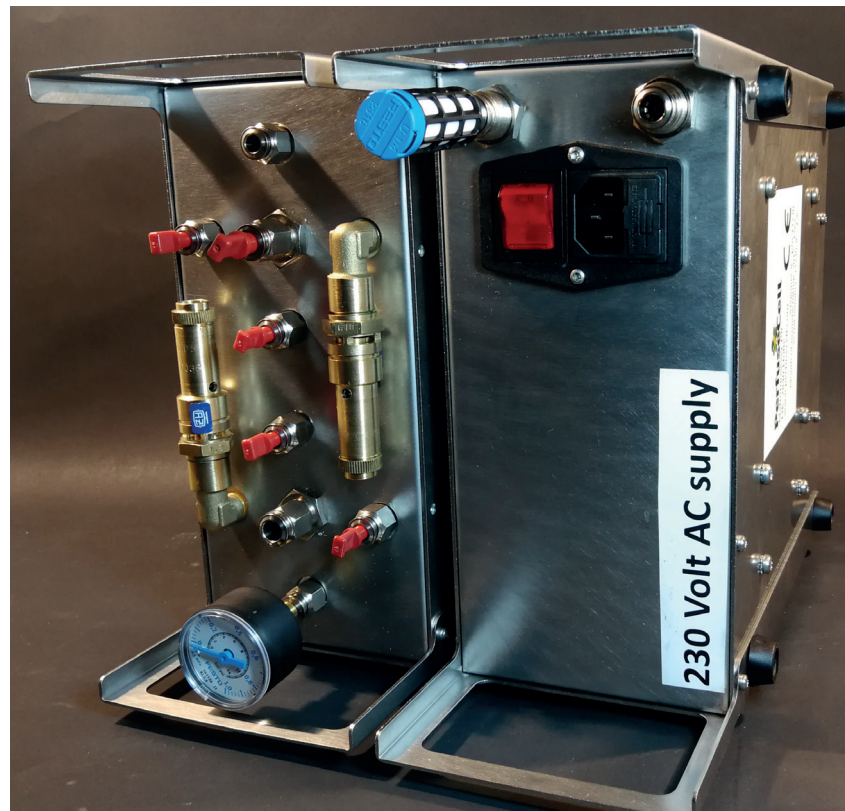
- W: 230
- D: 230
- TD: 295
- H: 110

Clotho Drive Unit and possible 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 / reservoir.



Clotho software

drive both O-SUP and A-SUE

Clotho Drive Unit's contain a webserver displaying online information on the build-in display. The webserver allow the enduser with a smartphone or a PAD 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 Linux firmware.

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

Ver. C.70

Cleaning/Harvest relation	Set point conveyed volume	Velocity calc straws & diameter		Configuration
1 : 5	200 ml/min	1	1.0 mm	Close
Automatic device control		Manual device control		
Run	Stop	Vacuumize	Pressurise	

Clotho-2

Year Month Day Hour Min. Sec.
Time: 2018 2 12 14 21 22



Adjust Time

Wanted 0 Y 0 M 0 D 0 h 0 m 0 s

Set Time

Device selection:

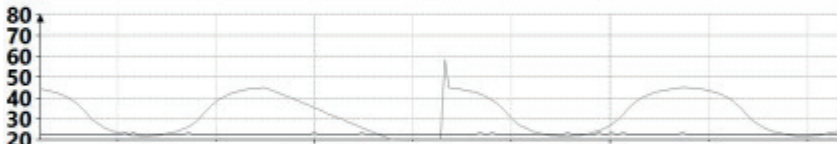
O-SUP

A-SUE

Thalia-30

Clio-30

Clio-100



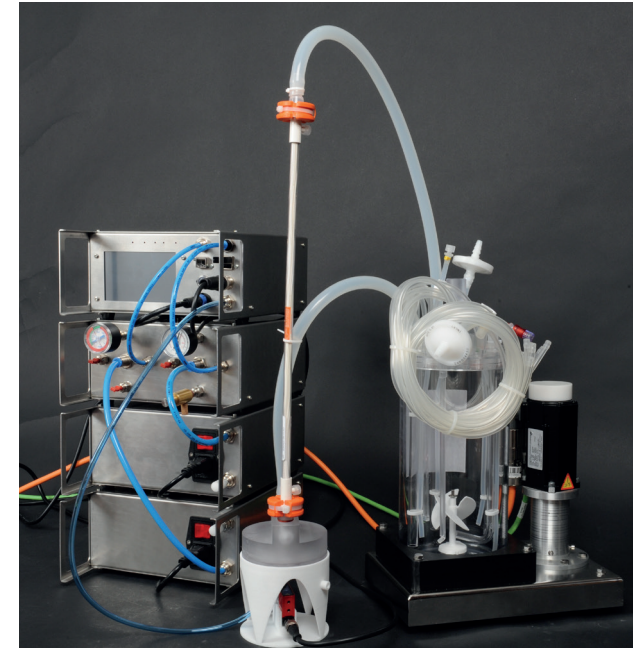
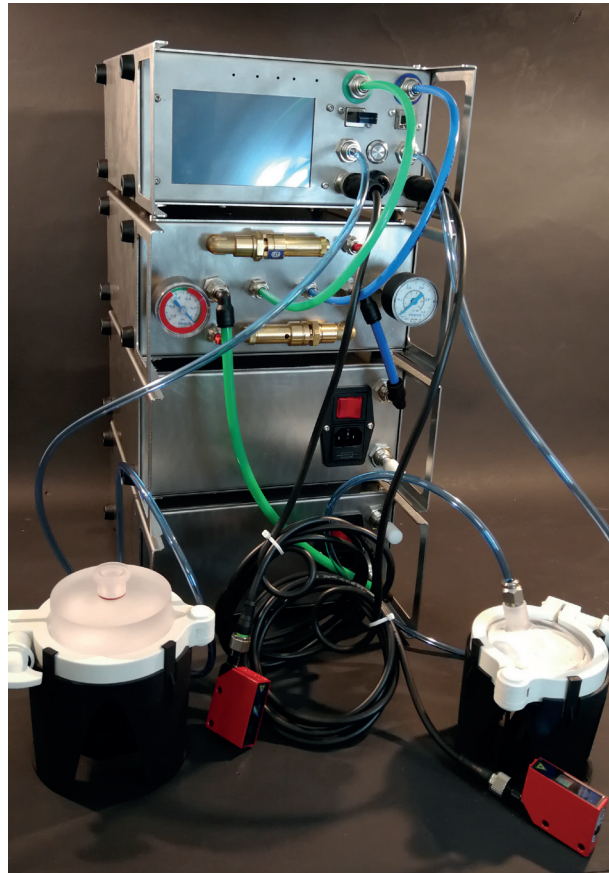
	3m30s	4m	
Drive Gas▲P	Real time vol. (ml/min sec)	Device stroke per min	Last harvest avg. velocity:
-0.011 Bar	2.2 ml/min	5	- 0.0 m/s
Supply▲P	Avg. volume conveyed	Device stroke before cleaning:	Last cleaning avg. velocity:
-0.012 Bar	59.3 ml/min	3	- 0.0 m/s
Vacuum▲P	Total volume conveyed	Total device stroke:	Total run time:
-0.014 Bar	13.0 ml	31	4.2 min

Clotho-2 Drive Unit **setup** for CellMembra & CellRetention & CellBLU

Dual channel fully independent operated by Clotho-2 Drive Unit.

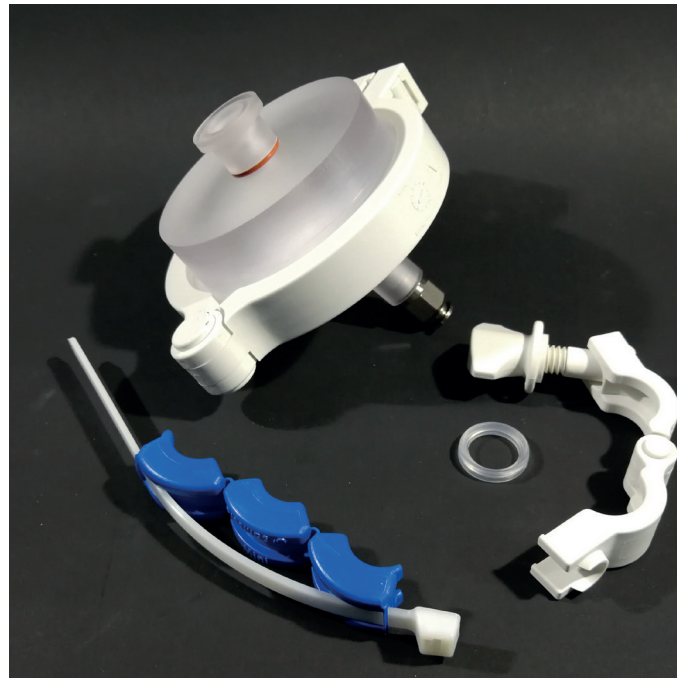
Clotho-2 designed for control of two in parallel operating Single-Use-Pump's and / or Single-Use-Exchanger's.

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



Accessories for P-SUB's

Connecting the HFF 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.

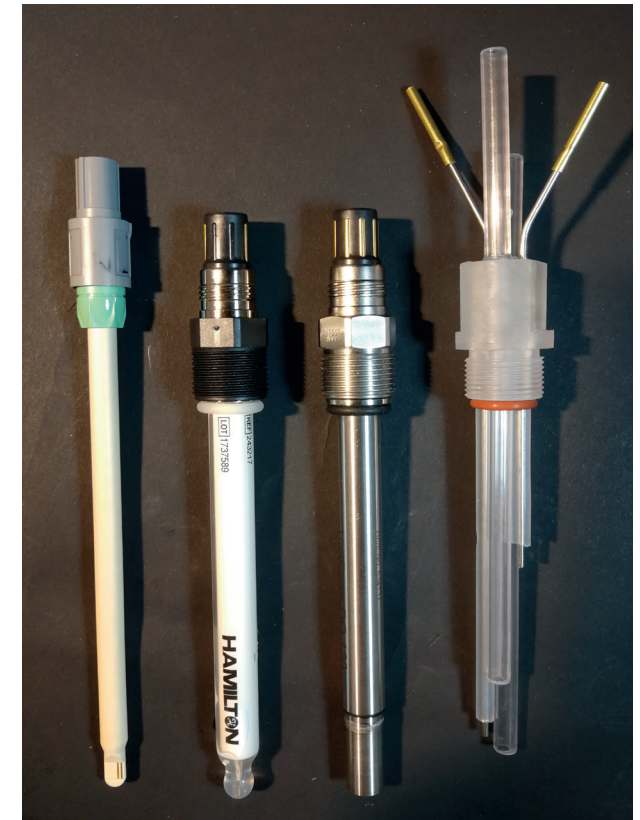


HFF – harvest continuously a cell free permeate. Choose from one of your preferred suppliers, such as:

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



Capacitance bio-mass, pH and DO and level - all Single-Use-Sensor's – all pre-installed in one package. Here shown in lenght for the 500 ml P-SUBs.



Thank you for your attention

