Pure Process
CARL STUART GROUP

Single-Use Filtration and Mixing

Solutions for Cell Harvesting and Bioreactor Agitation

DrM LIFE SCIENCE

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Single-Use Filtration Technology

FUNDABAC® SU and CONTIBAC® SU

DrM's two new single-use filter types consist of large surface filter elements, packed into a fully contained plastic enclosure. It is a clever alternative to disposable filter cartridges for cell harvesting and purification in biopharmaceutical processes.

Additionally, the FUNDABAC® SU and CONTIBAC® SU design is ideally suited for handling toxic or otherwise hazardous substances in a fully enclosed environment. The filtered solids can be sent for disposal inside the closed plastic bag and do not need to be handled further.

The increased surface area boosts the filtration efficiency and results in high throughput. For pharma/biotech applications, plastic components in contact with the process medium can be pre-sterilised, making CIP/SIP redundant.

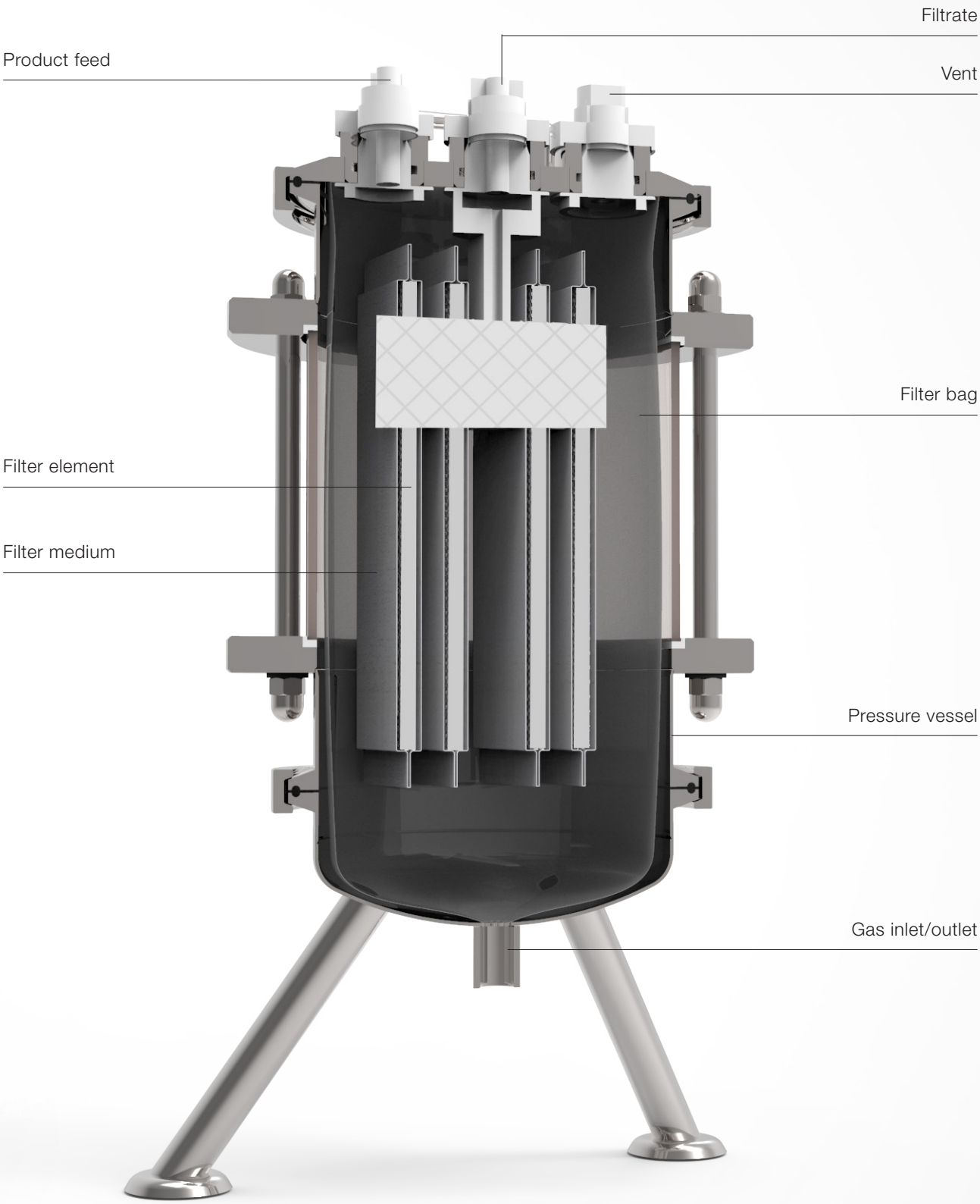
The filter bag is installed in a pressure vessel during filtration. This design opens up the possibility to compress the filter bag by applying an external pressure at the end of the filtration cycle, thus also allowing filtration of the liquid heel.

Both single-cycle and multi-cycle filtrations can be performed due to the unique filter design. The cake can either be back-flushed and accumulated on the bottom of the bag (FUNDABAC® SU), allowing for a safe disposal of the solid waste once the required filtration cycles are performed. Alternatively, the cake can be discharged out of the filter bag after each cycle (CONTIBAC® SU).

Key advantages

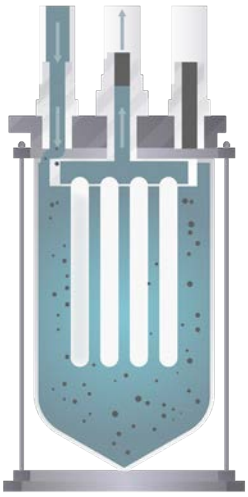
- High throughput
- Increased yield in cell recovery and enzyme recovery operations
- Shorter reactor downtime due to reduced cleaning and validation requirements
- Pre-sterilised and validated filter enclosure available for pharma/biotech applications
- Reduced heel volume and compaction of solid waste thanks to the external pressure
- Fully enclosed containment made completely with plastics ensuring safe handling and disposal of hazardous components
- Multilayered plastic bag providing superior robustness

FUNDABAC® SU Design

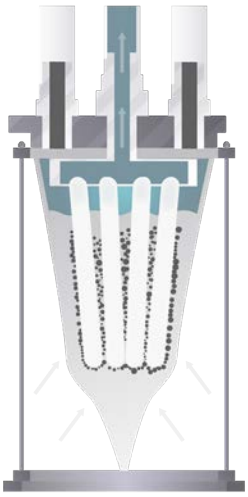


FUNDABAC® SU Operating Principles

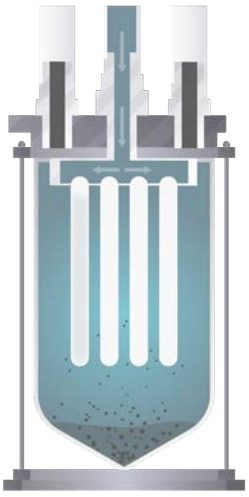
1 FUNDABAC® SU – Multicycle Filtration



Filtration



Heel Volume Filtration

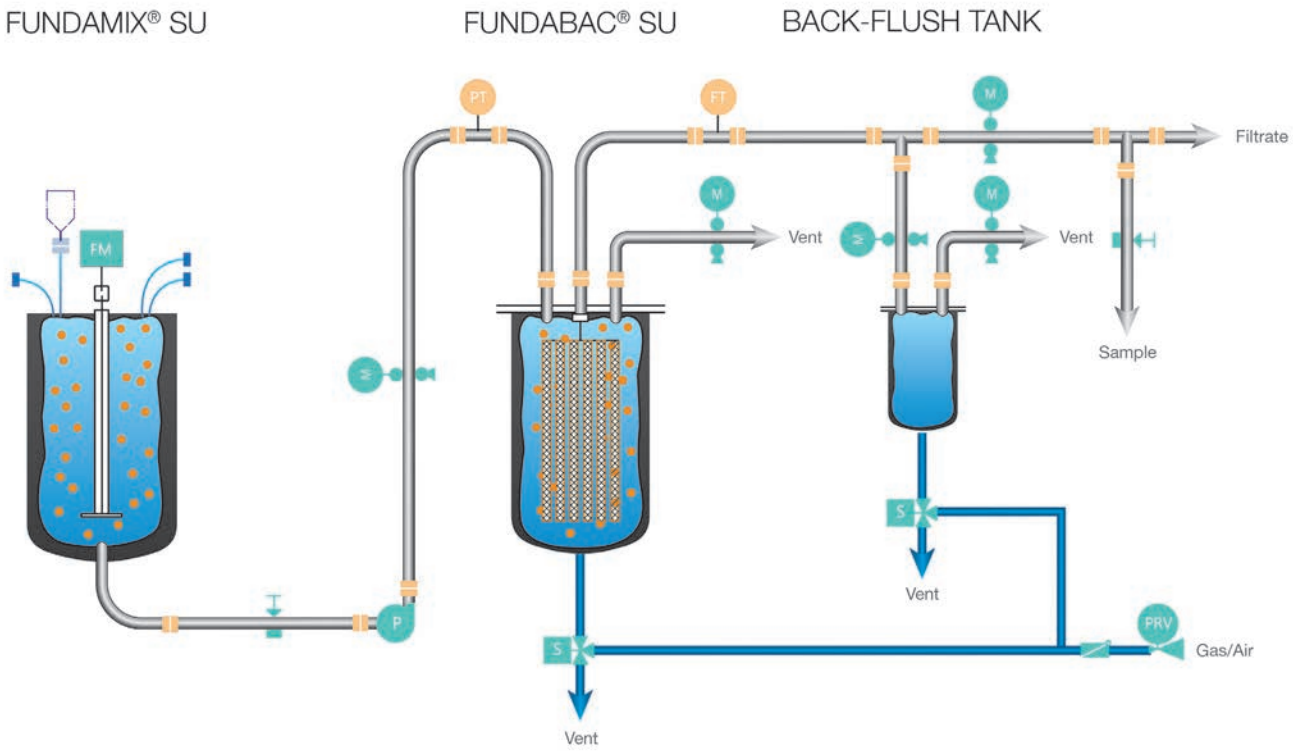


Back-Flush

The unique FUNDABAC® SU design allows for performing single-cycle and multi-cycle filtrations, where the cake can be back-flushed and accumulated on the bottom of the bag. Finally the compressed bag containing the solid waste is removed and safely disposed of in a very compacted form.

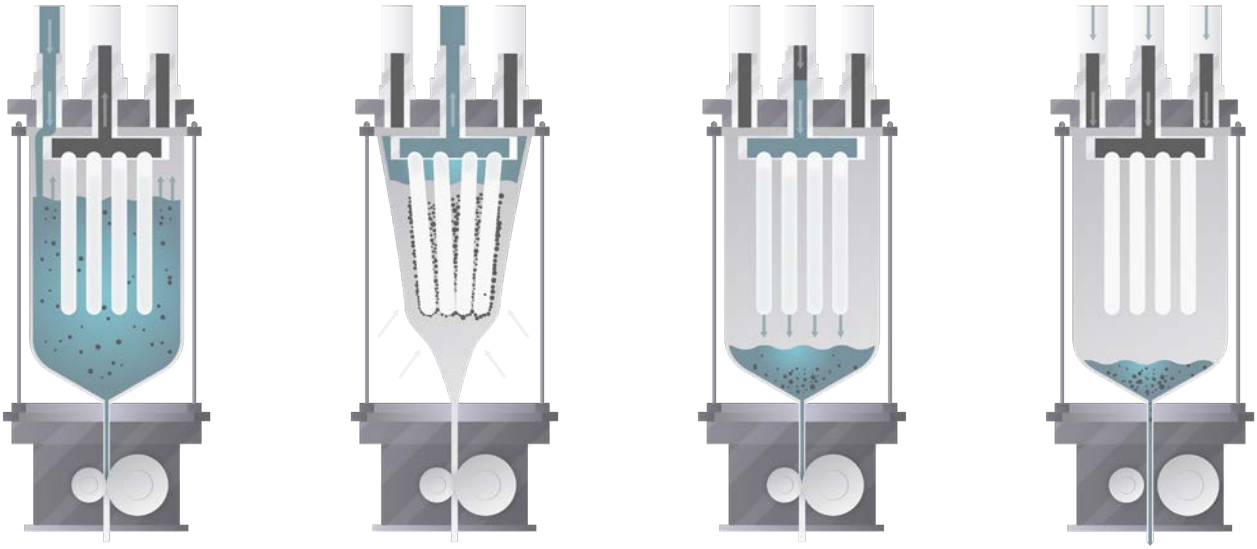
FUNDABAC® SU

Video



CONTIBAC® SU Operating Principles

2 CONTIBAC® SU – High Capacity Filtration



Filtration *Heel Volume Filtration* *Back-Flush* *Discharge*

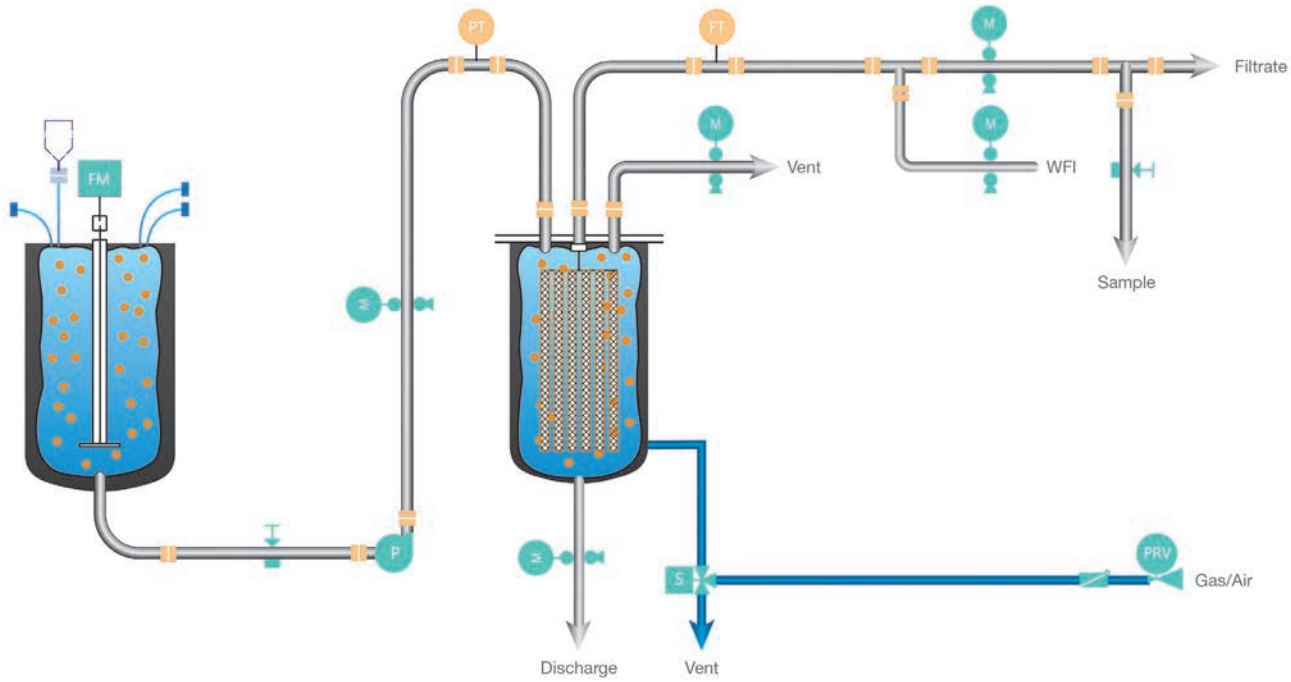
The unique CONTIBAC® SU design builds upon the FUNDABAC® SU with the same features. However, it additionally incorporates a discharge opening to allow almost unlimited filtration cycles. This significantly increases the capacity at minimum footprint and reduces operating cost.

CONTIBAC® SU

Video

FUNDAMIX® SU

CONTIBAC® SU



CHO Cell Harvest Test Results using the CONTIBAC® SU

CONTIBAC® SU Bag

A 2L CONTIBAC® SU filter with two elements was used to filter out Chinese Hamster Ovary (CHO) cells. The cell suspension was mixed with Cellpure C300 filter aid to enhance the filtration rate and quality. A highly permeable filter cake was formed during the filtration, which was subsequently back-flushed to regenerate the filter media. Once back-flushed, the cake was discharged through the bottom connector to regenerate the encapsulating plastic bag for the next cycle.

Flow Rate

- Cake filtration allows for high average flow rates to be achieved
- The flow rate increases with increasing amount of filter aid
- A pH reduction agglomerates impurities such as cell debris, DNA, and host cell proteins, thereby increasing the flow rate

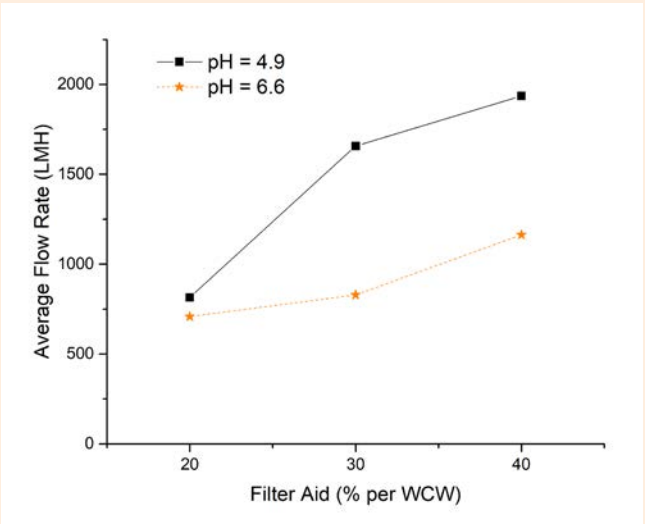


Figure 1: Average flow rates over 5 minutes of filtration at a pressure of 1.5 bar. The tested culture had 22 million cells per ml. The filter aid is given relative to the wet cell weight (WCW).

CHO Cell Harvest Test Results using the CONTIBAC® SU

Multi-Cycle

- After each cycle, the filter media is back-flushed, which removes the cake and regenerates the filter
- Due to the regeneration, a high average flow rate can be maintained over many cycles
- Other benefits of the cyclic operation are:
  - Smaller filter required
  - Lower footprint
  - Lower investment/operating cost
  - Less leachables/extractables
  - Suitable for large batches and high cell densities

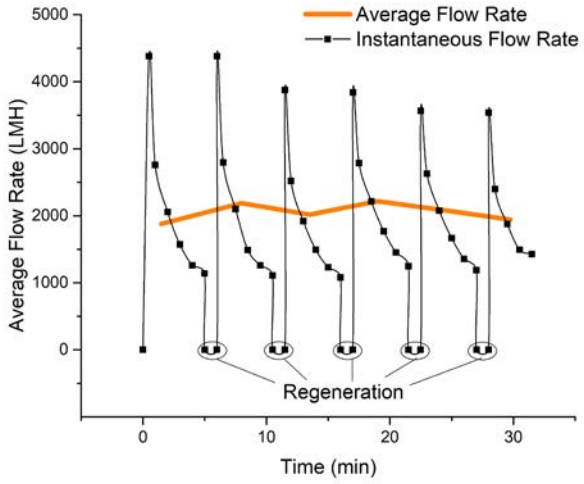


Figure 2: Instantaneous and average flow rates at a reduced pH, performed at a pressure of 1.5 bar and 40% filter aid per WCW. The tested culture had 22 million cells per ml.

Turbidity

- Regardless of the amount of filter aid and pH, turbidities below 15 FNU are achieved
- The turbidity is reduced by 98 – 99%
- The high filtrate quality extends the lifetime of downstream filters

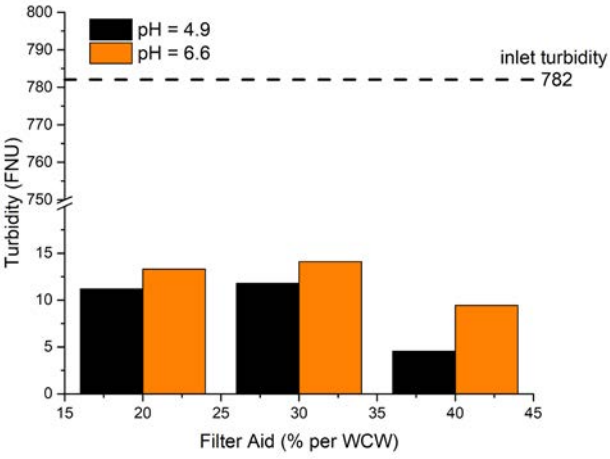


Figure 3: Turbidity measurements at the crude pH and a reduced pH for 20 – 40% filter aid per WCW. The tested culture had 11 million cells per ml. The dashed line shows the inlet turbidity.

FUNDAMIX® SU Mixer

FUNDAMIX® SU – Mixing Technology

DrM has developed a new type of single-use mixing device, the FUNDAMIX® SU system, which combines the proven FUNDAMIX® high performance mixing technology with the advantages of a closed and disposable plastic enclosure. A wide range of different connections allows for a modular and very flexible approach in the design of the production chain. For biotech applications the bags for our single-use mixer are delivered pre-sterilized and therefore cleaning/sterilization processes as CIP/SIP are no longer necessary.

The FUNDAMIX® SU offers many distinctive features of the standard FUNDAMIX® technology, such as low shear force but powerful mixing action, making it perfectly suited for homogenisation, powder suspension, pH adjustment, media preparation, fermentation and many other typical biotech process operations.

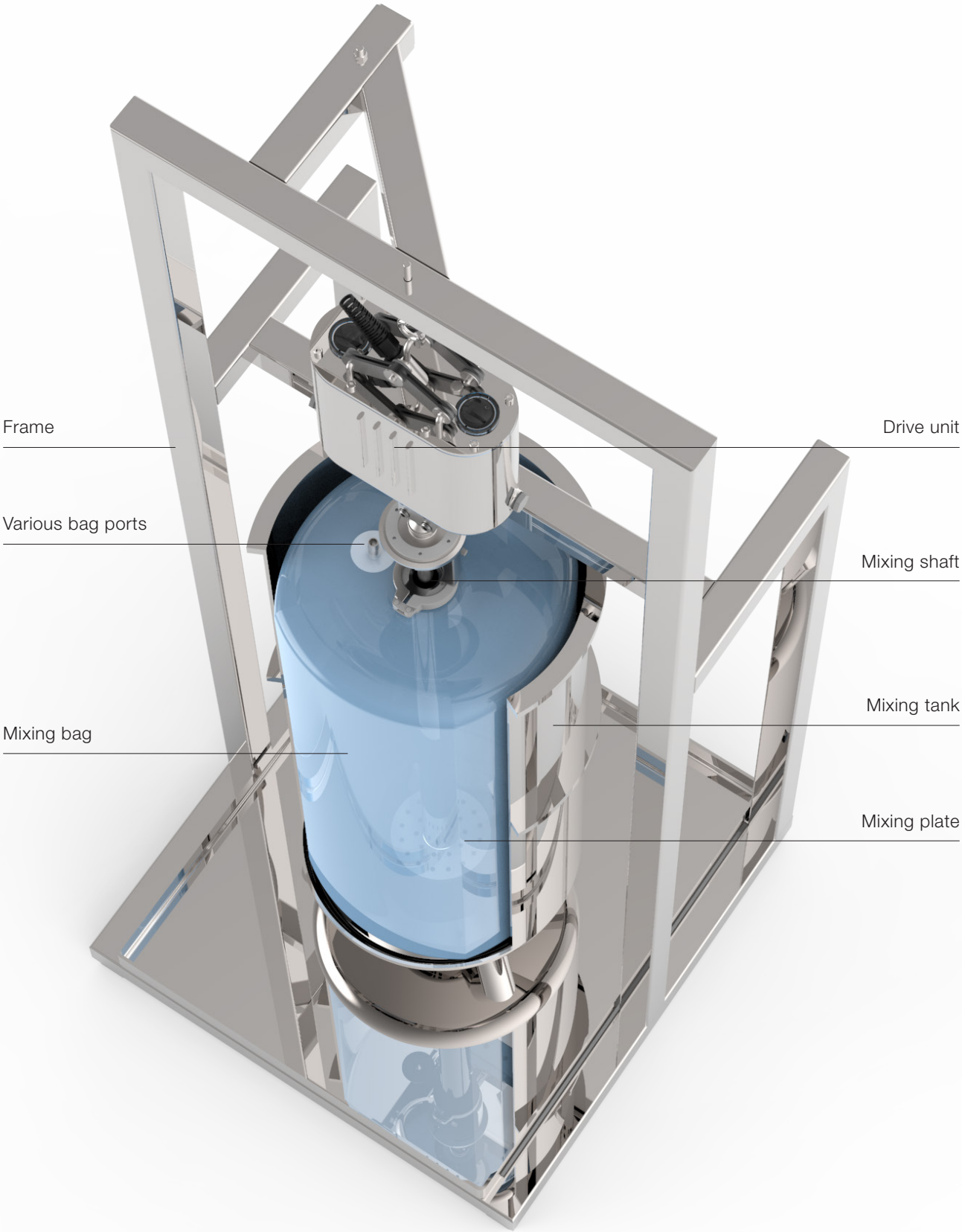
Key advantages

- Fully enclosed environment made from plastics ensures safe handling and disposal of components
- Robust and reusable steel shaft for efficient energy transfer to the mixing plate
- Strong multilayered bag film with gas barrier and high chemical resistance
- Various bag volumes available
- No dynamic sealing and thus no risk of particulate generation caused by plastic-on-plastic friction
- Easy connection to all FUNDAMIX® drive devices
- Completely sealed shaft connection for quick and easy bag assembly
- Chemically resistant and robust polymer plate for high mixing efficiency
- Bottom mounted outlet port allowing homogenization during draining

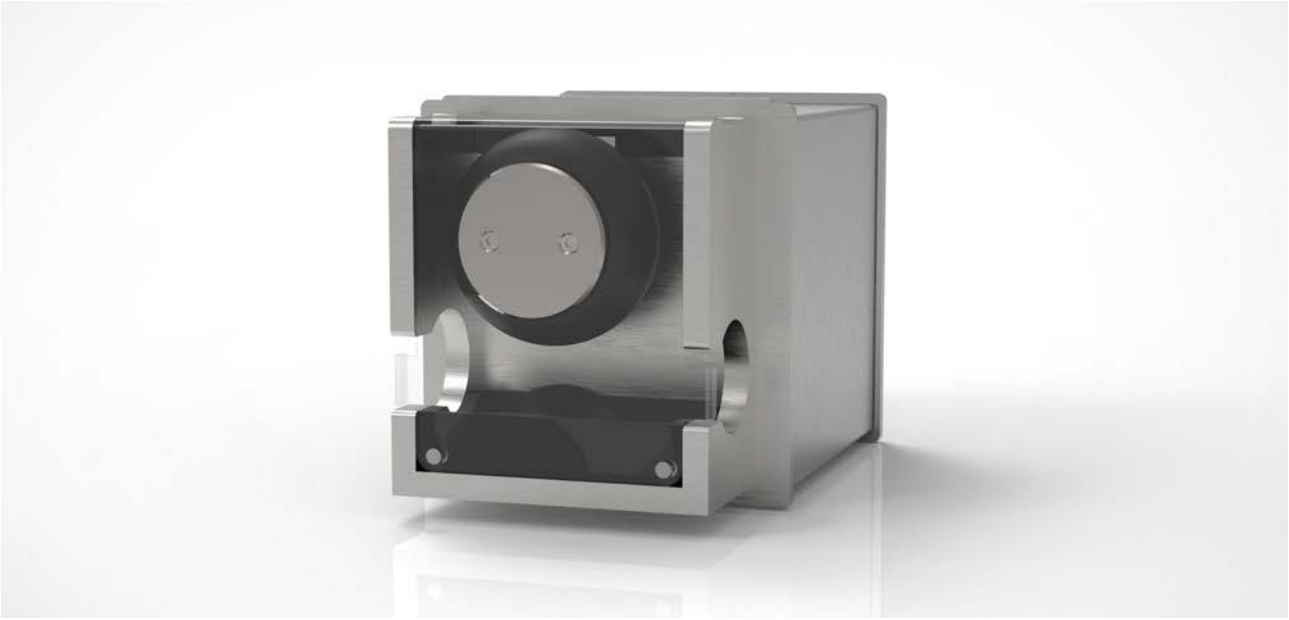
FUNDAMIX® SU

Video

FUNDAMIX® SU Design



Pinch Valve



Single-Use Pinch Valve

Pinch valves are often used in single-use applications for on/off flow control. As the valve does not get in contact with the process media it does not require replacement of any parts. Only the flexible tubing is being changed as a single use item. For non-pressure designs simple solenoid-driven pinch valves can be used, but when pressure needs to be applied, such as in filtration equipment the significantly tougher tubings together with the internal pressure pose a significant burden to the pinch valve and standard solenoids normally cannot do the job.

A newly developed design allows for on/off control of pressurized single-use tubings in a compact package. The electrically driven actuator is a microprocessor-controlled geared motor which opens and closes when an ON or OFF signal is received. The tubing firmly sits in a well-defined bed which guarantees uninterrupted operation for many cycles. The valve can either be supplied as stand-alone type or it can be easily installed within a cabinet with only the actuated part being visible.

The combination of this component with our single use filtration system is a perfect fit.

SU VALVE	
Type	Pinch, non-invasive
Model	SU Valve
Actuation	Electrical
Actuation Time	Opening: 3 sec Closing: 3 sec
Power Consumption	Idle position (closed or open): 0.1W During opening and closing (3 sec.): 5W
Power Supply	24 VDC / 12 VDC
Signal Input	OFF Position: 0VDC ON Position: 12...24VDC
Material	316L / Polyethylene
Max. Working Pressure (barg)	4
Max. Working Temperature	80 °C
Hose size	OD 6.35 - 25.4 mm OD 1/4” - 1”
Electrical Connection	Power, 12VDC: 2 wires Signal, 24VDC: 2 wires
Note	User interface via PLC or DCS

FundaStep Controller

FundaStep SU - The Customized Step Controller

Although it is possible to operate the Single-Use Filters manually, for improved experience and consistent quality it is recommended to run the filtration package automatically. The filtration is a batch operation and hence the operating sequence runs through a number of distinct process steps, such as Filling, Prefiltration, Heel Volume Filtration and Back-flushing. Various process parameters, such as pressures, flow or turbidity can be measured and logged. These can give valuable input to understand the performance of the filtration package, compare individual filtration batches and optimise the protocols.

To simplify installation and operation, the compact control panel not only houses the PLC but also the custom made SU valves, solenoid valves and air filter regulator for the instrument air supply. Pump, agitator, instruments and instrument air are connected and the flexible single use tubing is easily attached to the valves.

The FundaStep Controller comes in two sizes:
1. 400 x 300 x 200 mm (HxLxW)
2. 600 x 300 x 200 mm (HxLxW)

While both controllers provide a total of 6 SU valves and 2-3 solenoid valves which is more than enough to operate the complete system, the larger housing allows for additional space to install custom instruments which can be attached to an additional DIN rail inside the box. Both housings have the same compact foot print.

The process is visualised on an iPad which connects to the controller via Bluetooth and can be placed anywhere within reach of signal. Valve positions, steps, timers and instrument values are all shown on the high resolution touch screen which allows for complete operator control of the sequence to run in various operating modes:
1. Fully automatic loop filtration: The filtration cycle restarts automatically after reaching the end of the sequence
2. Automatic single pass filtration: The filtration cycle stops after reaching the end of the filtration
3. Step-by-step: The operator steps through the sequence manually
4. Manual: The operator opens and closes each individual valve from the touch screen

Key advantages

- Compact housing with small foot print to optimise valuable clean room space
- Simple installation
- Modern controller software with password protection and optional cloud connection for data logging and sequence management
- Controller can run automatically in offline mode without touch panel
- Edit mode allows complete customisation of sequence steps
- Inclusion of patented SU valves
- Flexible use of digital (DO) and analog (AO) outputs as well as analog inputs (AI). Maximum 32 DO, 4 AO, 8 AI with one low level and one high level trigger for each AI
- Analog inputs and outputs can be calibrated on the panel which increases flexibility to apply any custom instruments.
- Logging of all AI with protocol of steps and timers

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