

User Manual

Filtration probe 12 mm



Technical Documentation Filtration probe

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Important Note:

The data and information in this manual were compiled with the greatest of care. In spite of special care during creation of this document no warranty for an absolute accuracy can be given. If important information in this guidance are missed, if technical errors were found or if you would like to get more information about individual components, please notify us.

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1 General Instructions

1.1 About this document

These instructions provide all the information necessary for operation of the filtration probe. The instructions must be read, understood and used by all personnel using the filtration probe.

- These instructions are part of the filtration probe.
- Before working with the filtration probe, read the instructions carefully and completely.
- Keep them in safe and easily accessible place near the filtration probe site of installation.
- If the instructions are lost, request a replacement or download the latest instructions from our website.

Masculine or feminine forms are used to facilitate legibility in these instructions and always simultaneously denote the other gender as well.

1.2 Validity

These instructions apply to the filtration probe for the installation in 12/19 mm top port with PG 13.5.

1.3 Target groups

The instructions are designed for the target group „User“, who is familiar with the operation of the filtration probe and the associated working processes. The training takes place within the scope of start-up and is performed by TRACE Analytics GmbH or an authorized distributor.

1.4 Symbols used

The symbols used in the user manual are specifically intended to draw attention to the safety precautions! The symbol may not replace the text of the respective safety precaution. Therefore, the text must always be read completely!



Warning of potential consequential damage

1.5 Intended use

The filtration probe (in-line sampling probe) is intended for harvesting microbe-free filtrate from bioreactors/fermenters under sterile conditions.

The user must ensure, that

- the filtration probe is used for its intended purpose only, see chapter 2 – product description.
- the filtration probe is used only when functional and in proper working order.
- the user manual is always kept legible and complete at the place of use.

1.6 Disposal

Packaging

The packaging is made of environmentally friendly materials that can be used as secondary raw materials. If the packaging is no longer needed, it can be disposed of by local waste disposal authorities.

Filtration probe

The filtration probe including accessories does not belong in your regular household waste as this equipment is manufactured from high-grade materials which can be recycled and reused.

1.7 Hazardous materials

The filtration probes and accessories do not contain any hazardous materials that would necessitate special disposal measures.

Filtration probes contaminated with hazardous materials (NBC-contamination) will not be accepted for repair or disposal.

Decontamination Declaration

TRACE Analytics GmbH has a duty to protect its staff from hazardous substances. When returning the filtration probe, the sender must enclose a decontamination declaration as proof of compliance with the safety regulations governing the area of application for which they were used

- This declaration must detail the microorganisms, cells and media that the filtration probe/components have come into contact with and the measures taken to disinfect and decontaminate it.
- The recipient must be able to read this decontamination declaration before opening the packaging.

The form of a decontamination declaration is available on the website of TRACE Analytics at www.trace.de.

2 Product description

The filtration probe is intended for harvesting cell-free filtrate from bioreactors and fermenters under sterile conditions.

A tubular micro-filtration membrane made of polypropylene, positioned inside the bioreactor, serves as a sterile barrier.



The filtration probe is sterilized together with the bioreactor and installed in a 12 mm top port with PG 13.5 thread or in a 19 mm top port using a 19/12 mm reducing adapter.

Figure 1: Filtration probe 12 mm in two length

The membrane module of the probe is positioned in the turbulent zone of the reactor, near the agitator.

The microbe-free filtrate is sampled continuously or discontinuously at the probe head that is accessible outside the bioreactor.

For pumping the filtrate, the probe is connected to an external peristaltic pump. For manual sampling conventional single-use syringes can be used.

After sampling, the cell-free sample can be fed directly into the devices TRACE C2 Control and BioPAT[®] Trace for analysis.

Because of the consumption of fermenter medium, the filtration probe is better suitable for big fermenters above 100 liters (in particular for microbial processes). The filtration probe is also suited for small fermenters, if the sampling intervals are long (e.g. in cell cultures).

3 Function

The spiral tube made of stainless steel supports the polypropylene membrane (5). Permeate that is drawn through the membrane is led via a helical channel to 4 bore holes. From there, the filtrate flows the shortest route up to the head of the filtration unit (1), which prevents any remixing.

A PTFE ferrule (3) surrounds the end of the membrane and the exposed portion of the membrane mounting. By tightening the cap nut (2) into the filtration unit, the sealing ferrule distorts under pressure and securely seals the membrane end to the membrane mounting.

The thread of the filtration probe is sealed from penetrating microorganisms by an o-ring (4) and by tightening up to the limit stops.

The installation depth of the filtration probe is variable between 160 to 480 mm using the retaining nut of the mounting kit (6).

The blind plug which is part of the installation kit is used to close the filtration probe during the sterilization process.

4 Scope of delivery, consumables and spare parts

The filtration probe including accessories is delivered in protective packaging.

Please save this packaging; proper (return) shipping is only possible in the original packaging.

- Upon receipt, check the delivery for completeness and any possible damage that may have occurred in transit.
- Any transport damage must be reported within a week of delivery. Complaints made after this date will not be accepted.

4.1 Scope of delivery

The filtration probe for the installation in a 12 mm top port consists of a filtration unit with membrane mounting (1), cap nut (2), ferrule (3), o-ring (4), polypropylene membrane (5), mounting kit (retaining nut with sliding ring and o-ring) (6) and blind plug.

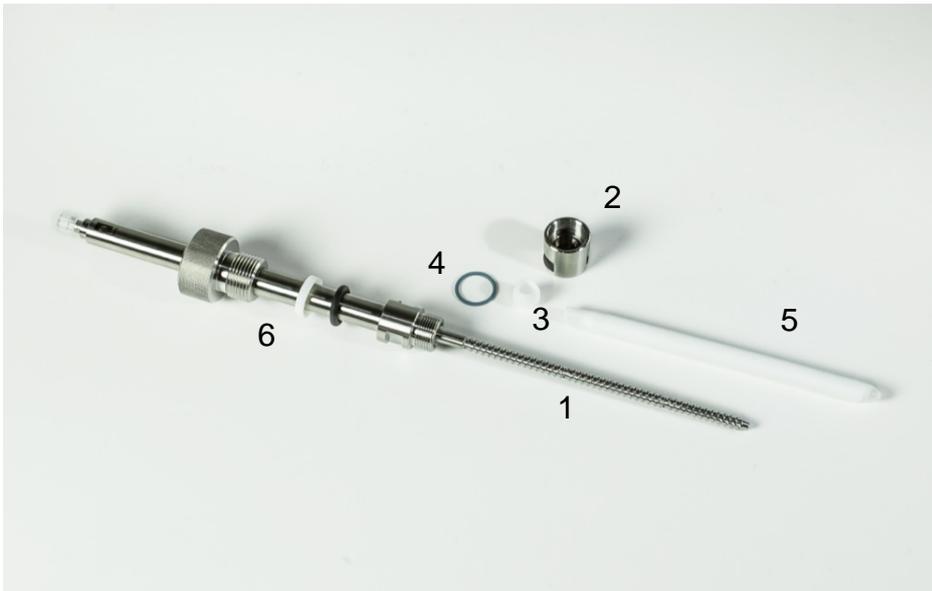


Figure 2: Parts of the filtration probe for the installation in a 12 mm top port with PG 13.5 thread

4.2 Optional spare parts

Two reducing adapter 19/12 (M26x1 with fine thread and RD 28x1/8" with coarse thread) are available for the installation of the filtration probe in a 19 mm top port.



Figure 3: Filtration probe with adapter M26x1

4.3 Order Information

4.3.1 Filtration probe

(Delivery with retaining nut, blind plug, o-ring, cap nut, membrane and user manual)

Description	Order No.
Standard version installation length ca. 160-230 mm	860.300.300
Extended version installation length ca. 160-330 mm	860.300.301
Extended version installation length ca. 160-480 mm	860.300.302

4.3.2 Membrane

Description	Order No.
Length: 130 mm	860.300.330

4.3.3 Accessories for the filtration probe

Description	Order No.
Blind plug (Locking the filtration probe)	816.000.150
Tubing set for the hydrophilization of the membranes	130.200.150
Installation kit (Connection to ProcessTRACE, external pump)	809.100.143
Retaining nut PG 13.5 with o-ring and sliding ring	860.300.012
Adapter 19/12 mm for the installation of the filtration probe in 19 mm top port (M26x1)	860.301.016
Adapter 19/12 mm for the installation of the filtration probe in 19 mm top port (RD28x1/8")	860.301.017

5 Design

The standard installation length of the filtration probe 12 mm in PG 13.5 respectively 19 mm top port is ca. 160-230 mm.

The filtration probe is also available with two extensions for high bioreactors/fermenters:

- Extension 100 mm (Installation length ca. 160-330 mm)
- Extension 250 mm (Installation length ca. 160-480 mm)

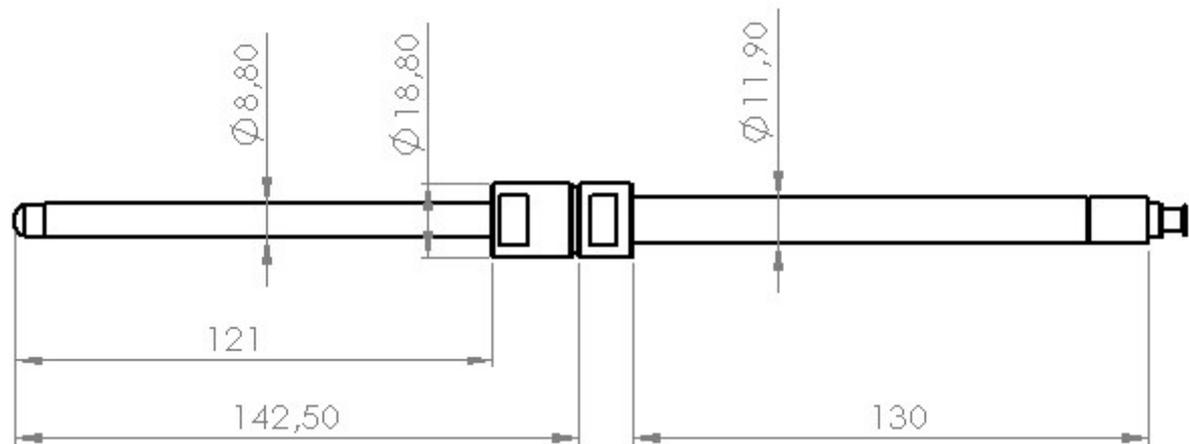


Figure 4: Drawing of the filtration probe standard version

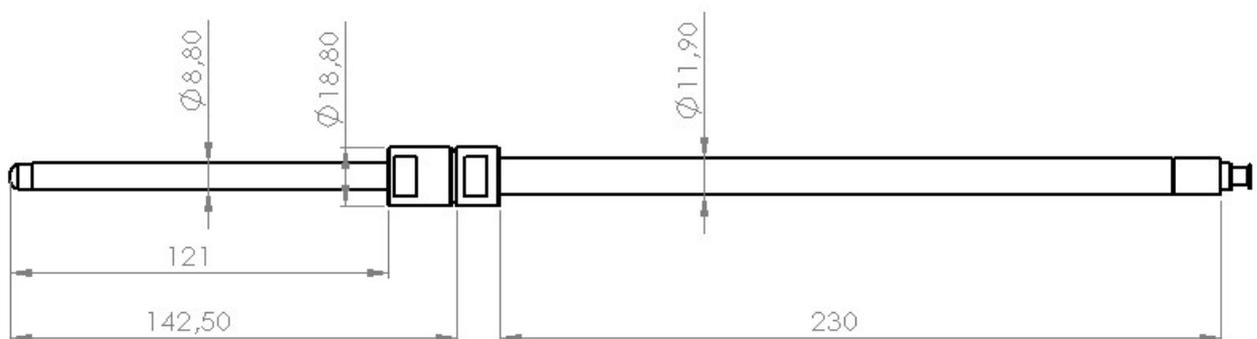


Figure 5: Drawing of the filtration probe with extension 100 mm

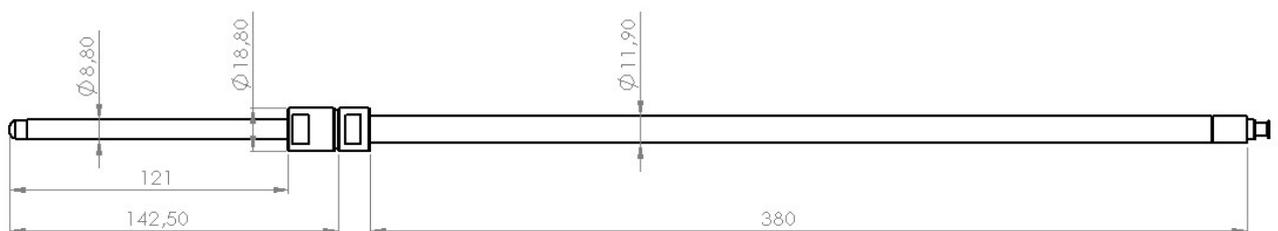


Figure 6: Drawing of the filtration probe with extension 250 mm

6 Getting started

6.1 Connecting the filtration probe

6.1.1 Mounting the filtration probe

Mount the o-ring over the external thread of the filtration unit. Then push the ferrule over the spiral tube (narrow opening first) up to the conical lower membrane mounting of the filtration probe (figure 7).

Take the polypropylene membrane out of its packaging. Place it carefully onto the spiral tube until it fits into the PTFE ferrule (figure 8).



Figure 7: Insertion of the ferrule



Figure 8: Mount the polypropylene membrane

Carefully screw the cap nut over the membrane and into the filtration unit. Tighten the cap nut using two wrenches up to the mechanical stop (figure 10).



Figure 9: Mounted polypropylene membrane



Figure 10: Tighten the cap nut



Before assembling the filtration probe, wet the external thread with demineralized water. Screw connection of the filtration probe is tightened up to the mechanical stop..

6.1.2 Hydrophilization of the polypropylene membrane

New polypropylene membranes are impervious to aqueous media (hydrophobic).

Therefore, the membrane must be hydrophilized after mounting into the filtration probe. Isopropanol 70 % (v/v) is used as hydrophilization solution.



The probe is immersed into the hydrophilization solution inside an upright cylinder of sufficient length that the membrane is entirely surrounded by liquid.

The alcohol is pumped through the probe into the closed system with a flow rate of 1– 2 ml/min by using a peristaltic pump connected to the sampling outlet of the probe. The hydrophilizing period lasts at least 2 hours. The probe can also be hydrophilized overnight without using the pump by storing it in 70% (v/v) Isopropanol.

If the filtration probe is used in connection with the online analyser TRACE C2 Control or BioPAT®Trace the hydrophilization and the leak test can also be performed with the hydrophilization set (see user manual of the analyser).

Figure 11: Setup hydrophilization of the 25 mm filtration probe

6.1.3 Leak test

Once hydrophilization has been completed, a leak test is carried out.

In order to do this, the hydrophilization setup described in chapter 6.1.2 is used.

Instead of drawing Isopropanol through the membrane of the probe, air is now pumped into the probe. The flow rate should be equal to the flow rate of the previous hydrophilization.

- Many small air bubbles should start to gradually escape from the membrane. Otherwise the membrane is hydrophilized insufficiently.
- The escape of large air bubbles from the screw connections is an indication for damaged gaskets.

In order to maintain the hydrophilic properties of the membrane until its installation into the bioreactor, it is recommended to store the membrane in a hydrophilization solution (Isopropanol 70%). Immediately before installation into the bioreactor, the Isopropanol must be replaced with water in order to avoid evaporation and the loss of hydrophilization.

6.1.4 Installing into the bioreactor

Before installing the filtration probe into a bioreactor, check that all couplings are securely fastened and tightened. Inspect the o-ring on the filtration probe and replace it if it is damaged.

Select a port of the bioreactor which will allow the filtration probe to be placed such that the membrane surface will always be completely immersed in fluid. The filtration probe should also be placed in an area of maximum turbulence (near an impeller) to maximize the filtering capacity of the filtration probe (crossflow-effect).



After installation, please ensure that the probe does not come into contact with moving parts (e.g. stirrer or agitator shaft) inside the bioreactor.

The polypropylene membrane must be completely covered with liquid during operation in the bioreactor. The membrane should never be allowed to dry out, as that could lead to loss of its hydrophilic characteristics. The filtration probe is also available with an extension of 100/250 mm for high bioreactors with long installation length.

A high hydrostatic pressure inside the bioreactor can be sufficient to provide sample flow.

Using the filtration probe with an on-line HPLC we recommend a feed pump (e.g. peristaltic pump) to limit the filtrate flow to max. 1.5 ml/min. Flow rates above 1.5 ml/min can lead to shortened service life due to filter pore clogging.

Always install the filtration probe just before filling the bioreactor. The membrane should never be allowed to dry out, as that could lead to loss of its hydrophilic characteristics.

6.1.4.1 Installation in 12 mm top port with PG 13.5 thread

Remove the plug of the top port and disassemble the cover of the bioreactor. Place the filtration probe carefully into the top port from the underside of the cover.

Push the o-ring and sliding ring over the exposed end of the filtration probe which is outside the top port. Screw the retaining nut onto the top port until you feel the resistance of the o-ring.



Figure 12: Installing the retaining nut

Adjust the immersion depth of the filtration probe by moving the exposed end of the filtration probe. Finally, tighten the retaining nut.

6.1.4.2 Installation in 19 mm top port with reducing adapter 19/12 mm

Push the reducing adapter, o-ring, sliding ring, and then the retaining nut over the end of the filtration probe. Fix the reducing adapter by screwing the retaining nut. Place the filtration probe from the top in a 19 mm port at the cover of the bioreactor. Finally tighten the retaining nut.



Figure 13: Filtration probe with reducing adapter

6.1.5 In-line sterilisation of the filtration probe

After installation into an appropriate port, the filtration probe has to be closed with a blind plug and sterilized along with the bioreactor. The filtration probe must be completely covered with liquid during the entire sterilization cycle.

After sterilization and reaching of operation temperature inside the bioreactor of max. 40°C the sample outlet must be opened so that a connected device (e.g. online analyser, online HPLC) can collect samples.

6.1.6 Connecting the filtration probe

The filtration probe is connected to the device (TRACE C2 Control and BioPAT® Trace) through the filtration tubing set. The male LUER connector of the tubing set can be directly attached to the female LUER connector at the outlet of the filtration probe as shown in figure 14.



Figure 14: Connection of the filtration probe to the tubing set

An installation kit (ferrule, fitting, connector, blind plug, adapter UNF/LUER) is available for the connection of the filtration probe e.g. to an external pump or the online analyser ProcessTRACE

6.2 Disassembly of the filtration probe

The filtration probe is disassembled by following the steps in chapter 6.1.1. In general, the PTFE ferrule has to be replaced, when opening the screws. If ferrules are re-used, proper sealing is no longer guaranteed.



The thread on the filtration unit is a lubricant free fastening thread. Repeated disassembly and reassembly can lead to metallic abrasion in the threads of the screws. Before reassembly the internal and external threads must be cleaned under running water to remove any deposits.

If you do not clean the threads there is a danger of thread seizing or cold welding and this makes the filtration probe unusable for the future.

6.3 Regeneration of the filtration probe after fermentation

Immediately after discharge and sterilization of the bioreactor, remove the filtration probe from the port. We recommend exchanging the membrane and PTFE ferrule after every fermentation.

However, in many cases reuse of the membrane (3 – 5 times) is possible after cleaning. For reuse of the probe, proceed as follows:

- Using a soft brush, remove all particulate matter from the outside of the filtration probe under flowing water.
- Clean the polypropylene membrane by circulating 0.5 N NaOH solution in filtrate direction through the filtration probe. The cleaning cycle requires 4 hours using the configuration described in chapter 6.1.2.
- Rinse the filtration probe thoroughly with demineralized water.
- Store the filtration probe in hydrophilizing solution (70% (v/v) Isopropanol) until the next fermentation to prevent the need to rehydrophilize the membrane.
- If the filtering performance of the filtration probe cannot be restored by thorough cleaning, a new membrane and PTFE ferrule should be installed

7 Data sheet filtration probe

Installation of the filtration probe:	Bioreactor with 12 mm top port with PG 13.5 thread Bioreactor with 19 mm top port using a reducing adapter 19/12 mm
Types / Installation length in the bioreactor:	Standard version / ca. 160-230 mm Extended version (+100 mm) / ca. 160-330 mm Extended version (+250 mm) / ca. 160-480 mm
Material:	Austenitic stainless steel
Quality of the material:	1.4404/AISI 316L
Filtration method:	Sterile in-line filtration
Membrane material:	Tubular micro filtration membrane out of polypropylene
Membrane length:	Ca. 130 mm
Pore size of the membrane:	0.2 µm
Flow rate:	1-1.5 ml / minute
Membrane sealing:	PTFE ferrule
Sterilisation in the bioreactor:	In liquid at 1.5 bar / 125°C
Mounting kit for the variable installation of the filtration probe:	Retaining nut PG13.5 with o-ring and sliding ring
Accessories for the installation in 19 mm top port:	Reducing adapter M26x1 with fine thread Reducing adapter RD28x1/8" with coarse thread
Installation kit (only for the connection of the filtration probe to an external pump or online analyser ProcessTRACE)	Ferrule, fitting, connector, blind plug and adapter UNF/LUER