SARTORIUS

Product Datasheet

BioPAT® Trace and BioPAT® Multi Trace

Online Measurement of Multiple Parameters From 1 to 4 Vessels

Benefits

- Real-time online monitoring of bioprocesses parameters
  - Glucose and lactate
  - Methanol or ethanol
- Enable automated parameter feed | bleed control capability
- Single-use sensor and fluidic elements
- Compact, space-saving design
- Room temperature stable biosensors
- Wide linear measuring range

Product Information

The control of nutrients and metabolites starts by monitoring the parameter concentration and its rate of change. Once known, then an actuator (e.g. feed pump) can affect a change and bring the parameter to the desired set-point. BioPAT® Trace and BioPAT® Multi Trace enables this control to be automated without the need for operator intervention during the bioprocess.

BioPAT® Trace analysis platform is designed for simultaneous online monitoring of up to two parameters in any given setup. The biosensor components measure either glucose and lactate or small-molecule alcohols, such as methanol and ethanol.
The system can be used for laboratory or industrial cultivations of microorganisms and mammalian cell lines.

BioPAT® Multi Trace has all the measurement functionality of the dedicated system yet is capable of sampling from up to four vessels without the need for operator intervention. The frequency, relative sample volume and accuracy of the parameter concentration data allows automated parameter control. This can be achieved by either actuating a feed pump or increasing the perfusion rate to influence parameter concentration and maintain a defined steady state.

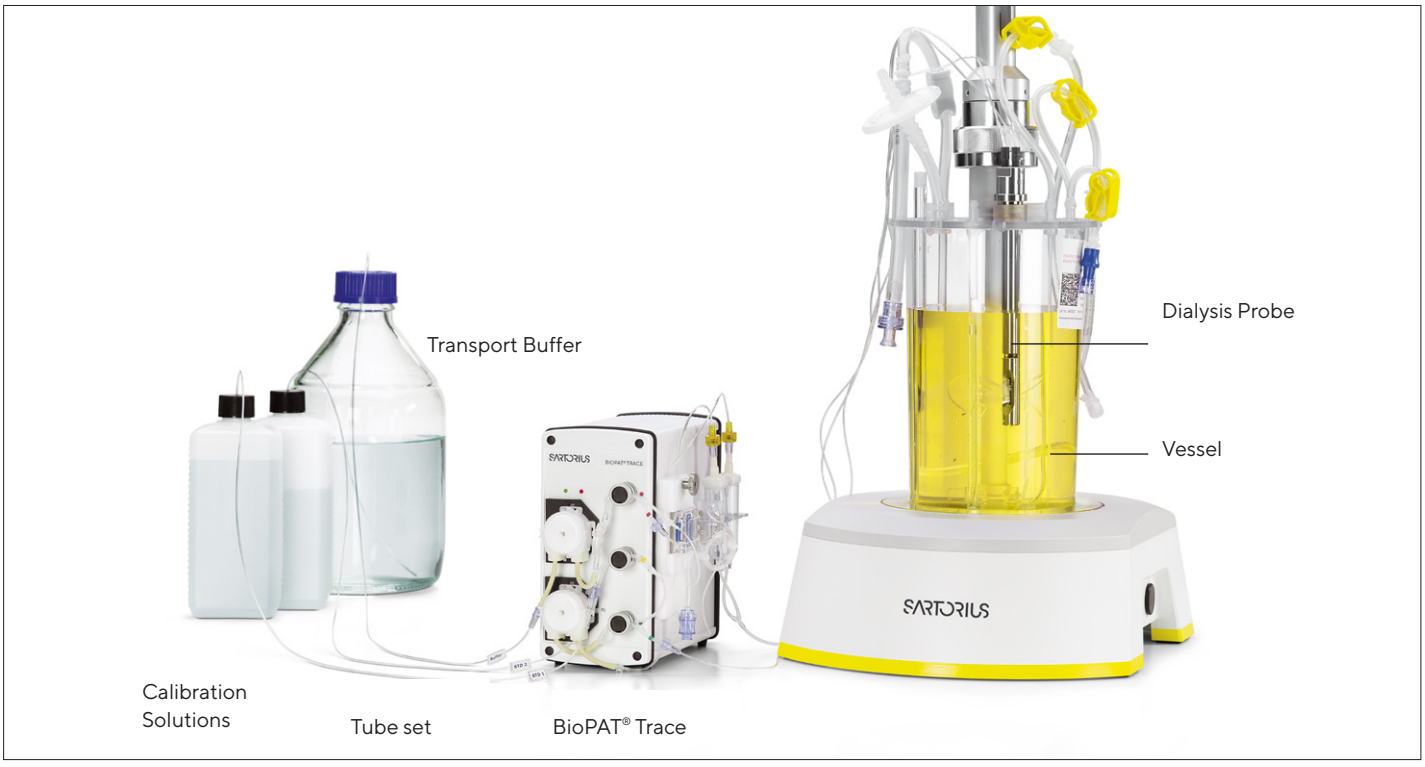


Figure 1: BioPAT® Trace practical setup with Univessel® SU

Biosensor

BioPAT® Trace sample analysis works by coupling an enzymatic reaction in combination with amperometric detection.
A two-channel enzyme electrode coated with an oxidase constitues the biosensor. The biosensor's platinum electrodes are coated with glucose oxidase and lactate oxidase and react with their corresponding substrates. Alternatively, the alcohol bio sensor utilizes alcohol oxidase to detect both ethanol and methanol concurrently.

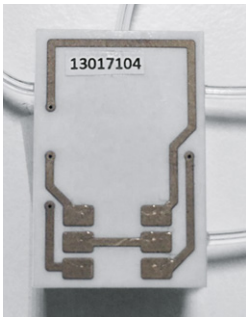


Figure 2: image of the back of the BioPAT® Trace biosensor

Fluidics Tube Set

To perform the sample analysis, a sample must be transported from the vessel to the biosensor. A complete fluidic setup consisting of 1–2 mm inner diameter tubing, peristaltic pump heads and ergonomically labeled connections is needed for every run. Each sampling method – dialysis or filtration – requires the corresponding Tube set to function correctly. The BioPAT® Multi Trace Tube set design has four sample lines which are controlled by automated pinch valves to sample from up to four different vessels. For easy identification, the back of the biosensor (Fig 2) has a unique serial number printed above the electronic contact points.

Continuous Analysis

The BioPAT® Trace provides continuous parameter analysis with up to one data point per minute during cultivation. It is independent of the type of cultivation (batch, fed-batch, continuous cultivation) and allows the setup of automated parameter control loops. In addition to the online analysis function, scheduled or manually activated parameter calibrations during a batch ensure measurement robustness without stoppage.

Range

The linear measuring range of the BioPAT® Trace extends from

1 to 40 g/L	(56 µM to 0.223 mM)	Glucose
0.5 to 10 g/L	(56 µM to 0.102 mM)	Lactate
0.01 to 10 g/L	(0.56 µM to 0.056 mM)	Low glucose
0.05 to 2.5 g/L	(0.56 µM to 0.026 mM)	Low lactate
0.5 to 20 g/L	(6.24 µM to 0.624 mM)	Methanol
1 to 40 g/L	(10.85 µM to 0.868 mM)	Ethanol

BioPAT® Trace and Multi Trace require a minimum two-point calibration with known traceable parameter solutions to generate the linear measuring range. These calibration solutions are available from Sartorius Stedim Biotech.

Frequency

The measurement frequency of the BioPAT® Trace filtration probe is up to 60 analyses per hour whereas; the dialysis setup yields 30 analyses per hour from a single vessel. The BioPAT® Multi Trace must perform additional flushing between vessel sampling and, therefore provides analyses every 6 (filtration)/7(dialysis) minutes, with four vessels connected. The next sequential data point generated for the first vessel is 24(filtration) or 28(dialysis) minutes later.

If the required glucose|lactate concentration measured is below 0.1 g/L in dialysis mode the accumulation time increases, resulting in biosensor data points every six minutes. This requires a BioPAT® Trace firmware update, with an optional change of the dialysis probe membrane to increase the permeability.

The BioPAT® Trace software can take scheduled samples at any given time point thus increasing or decreasing the sampling frequency to tailor it to specific process control requirements.

Duration

The service life of the biosensor is 14 days or 5000 analyses depending on the application. The ambient temperature of the BioPAT® Trace can lie between 5°C and 35°C due to internal temperature correction. The ambient humidity should not exceed 90%.

Refer to the Glucose | Lactate: Performance and Accuracy application note for more details.

Accuracy

The deviation from the average measurement value is less than 3% for a measurement of 5 g/L glucose and 2.5 g/L lactate. Dynamic vessel temperature compensation of the biosensor and membrane diffusion is included if BioPAT® Trace is used with BioPAT® MFCS data acquisition.

Communication Integration

BioPAT® DCU Analog Connection
BioPAT® Trace has standard analog outputs in either voltage or milliamp signal ranges in order to connect it to the BioPAT® DCU and to show the two measured parameters. The BioPAT® DCU is configured to interoperate the signal over the fixed calibration range and show the two concentration values on the Biostat® visual display.

BioPAT® Multi Trace is not designed for analog connection to obtain the relevant data from all four vessels. Instead, digital connection is required.

BioPAT® MFCS digital connection
BioPAT® Trace and BioPAT® Multi Trace can be digitally connected by Modbus|OPC® to BioPAT® MFCS 3.0 bioprocess management module with additional software from Sartorius Stedim Biotech. This option allows parameter data to be imputed directly into the supervisory control and data aquisition software for all sampled cultivations.

Mechanical Integration

Reliable Sampling
To analyze substrates in cultivation media, it is necessary for the sample to be taken from the vessel, while maintaining the sterile conditions within. The reproducibility and relevance of the sample taken must remain intact. The BioPAT® Trace has four sampling probe options available: filtration, dialysis single-use and by-pass loop. All probe designs ensure aseptic removal from the vessel and transport to the biosensor module.

Filtration Probe

Cell-free samples are removed from the vessel using the filtration sampling probe, which incorporates a 0.2 µm polypropylene filter. This hydrophilized probe is mounted inside the bioreactor and subsequently sterilized along with the medium. The concentration of the bulk sample is directly correlated to the linear calibration in the biosensor.

- Continuous sampling removes 1 mL from the sample vessel per sample reducing the overall vessel volume. If in interval mode 5 mL is removed for each initial measurement.

Dialysis Probe

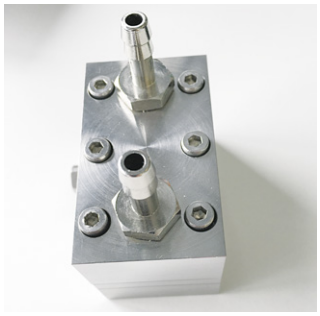
This probe functions by time-dependent diffusion ofsample across a 12 kDa permeable membrane. The transport buffer and vessel solution do not directly mix. However, during the BioPAT® Trace sampling cycle the transport buffer flow is paused and the concentration gradient drives small molecules from the bulk into the transport buffer. When flow is resumes after a set time period, this accumulated concentration is transported to the biosensor for analysis. This data is then correlated to the linear calibration to yield the bulk concentration.

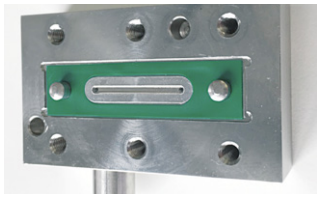
- This sampling method uses the diffusion of small molecules across the permeable membrane without any loss of vessel volume.

Single-Use Probe

The single-use probe functions on the same principles as the dialysis probe but is constructed from known traceable plastics and hollow fibers.

- This sampling method uses the diffusion of small molecules across the permeable membrane, without entailing any loss of vessel volume.





By-pass loop
The by-pass loop functions when sterilization or a technical limitation exists that a probe cannot be installed in the vessel. It functions on the same principles as the dialysis probe with the membrane contact surface installed into a flexible tubing line with a 6 or 9mm hose-barb connection.

Manual sample analysis
BioPAT® Trace systems enable a three-way stopcock to be conveniently integrated for manual sampling of off-line samples.

Calibration Solutions and Transport Buffer

BioPAT® Trace and BioPAT® Multi Trace require two calibration solutions and a transport buffer to function, and accurately determine the parameter concentration in a sampled vessel. These liquids are connected on the labeled end points of the Tube set and are automatically pumped within the system loop. The calibration solutions include expiration dates to ensure the accuracy and longevity of the system analysis. Upon request, test certificates can be provided for each calibration solution.

BPT0006	Transport buffer solution for CC Glc | Lac (20×);	0.5L
BPT0060	Transport buffer Glc|Lac (5x) for MO;	1.0L
BPT0046	Transport buffer for MeOH|EtOH (5×)	1.0L
BPT0007	Calibration solution 5 (10g/L Glc and 5g/L Lac);	0.5L
BPT0008	Calibration solution 4 (4g/L Glc and 2g/L Lac);	0.5L
BPT0009	Calibration solution 3 (2g/L Glc and 1g/L Lac);	0.5L
BPT0010	Calibration solution 2 (1g/L Glc and 0.5g/L Lac);	0.5L
BPT0011	Calibration solution 1 (0.5g/L Glc and 0.25g/L Lac);	0.5L
BPT0041	Calibration solution 6 (20g/L Glc and 10g/L Lac);	0.5L
BPT0043	Calibration solution 7 (0.1 g/L Glc and 0.05 g/L Lac);	0.5L
BPT0051	Calibration solution, 0.2 g/L Methanol	0.5L
BPT0052	Calibration solution, 1.0 g/L Methanol	0.5L
BPT0053	Calibration solution, 5.0 g/L Methanol	0.5L
BPT0054	Calibration solution, 20.0 g/L Methanol	0.5L
BPT0055	Calibration solution, 40.0 g/L Ethanol	0.5L
BPT0056	Calibration solution, 4.0 g/L Ethanol	0.5L
BPT0057	Calibration solution, 2.0 g/L Ethanol	0.5L
BPT0058	Calibration solution, 0.5 g/L Ethanol	0.5L
BPT0044	Concentrated (200×) cleaning | disinfection solution	1.0L

Technical Data

Specifications

BioPAT® Trace and BioPAT® Multi Trace

Measuring principle	Enzymatic amperometric		
Linear measuring range	Glucose Lactate low Glucose low Lactate Methanol Ethanol	1 to 40 g/L 0.5 to 10 g/L 0.01 to 10 g/L 0.05 to 2.5 g/L 0.5 to 20 g/L 1 to 40 g/L	(56 µM to 0.223 mM) (56 µM to 0.102 mM) (0.56 µM to 0.056 mM) (0.56 µM to 0.026 mM) (6.24 µM to 0.624 mM) (10.85 µM to 0.868 mM)
Measurement deviation	Glucose | Lactate Low Glucose | Lactate Methanol Ethanol	<1.5 % 1 to 20 g/L | <1.5% 1 to 10 g/L F.S. <2.5 % 0.5 to 1 g/L | <2.5% 1 to 0.5 g/L F.S. <2.0 % 0.5 to 20 g/L <2.0 % 1.0 to 40 g/L	
pH range of the medium	4.8 – 9.2		
Service life of the enzyme electrode	Glucose | Lactate Methanol or Ethanol	30 days or 5,000 analyses 15 days or 5,000 analyses	
Operating temperature	15 °C to 35 °C (59 °F to 95 °F)		
Operating humidity	10 to 90 %		
System storage conditions	5 °C to 60 °C (32 °F to 140 °F); 5% to 75% RH (non-condensing)		
Storage temperature Glucose | Lactate biosensor Alcohol biosensor	 5 °C to 25 °C (41 °F to 77 °F) 3 °C to 8 °C (37.4 °F to 46.4 °F)		

BioPAT® Multi Trace

Data frequency (with 4 vessel connected)	Filtration Dialysis	Up to 2 measurements/hr/vessel Up to 2 measurements/hr/vessel
Weight	2.0 kg	
Dimensions (W × H × D)	120 mm × 170 mm × 200 mm (4.7" × 6.7" × 7.9")	
Serial output	9-pin female connector to external pump	
USB interface	1 × USB port (software updates only)	

BioPAT® Trace

Data frequency	Filtration Dialysis	Up to 60 measurements/hr Up to 30 measurements/hr
Weight	1.8 kg	
Dimensions (W × H × D)	120 mm × 170 mm × 200 mm (4.7" × 6.7" × 7.9")	
Analog output options	0 to 10 V | 0 to 20 mA | 4 to 20 mA	
Serial output	9-pin female connector to external pump	
USB interface	1 × USB ports (software updates only)	

Connections

System communication interfaces	RS232, Ethernet
Communication cable length	Standard: 2 m (5 m and 10 m available)
Communication cable material	Non-metallic sheathed cable with finely stranded copper conductor; PVC insulation -40 °C to +70 °C (+40 °F to +158 °F)
Power supply	100 to 120 | 220 to 240 V ~; 50 | 60 Hz

Liquid | Waste Requirements

Transport buffer consumption	1.5 L/day to 2.0 L/day
Calibration solution consumption	5 mL/day to 145 mL/day
Fluid temperature	15 °C to 35 °C (59 °F to 95 °F)
Collection of waste liquid	Separate container required

BioPAT® Trace Filtration probe

Mechanical port connection | Insertion depth	12 mm[1] PG 13.5 | 130 mm 12 mm[1] PG 13.5 | 230 mm 25 mm[1] DN 25 | 130 mm 25 mm[1] DN 25 | 90 mm	BPT0021 BPT0022 BPT0023 BPT0036
Port adapter | insert depth reduction	19/12 mm | 49 mm 25/12 mm | 52 mm	BB-8848630 BB-34165225
Product contact materials	Construction material: 1.4404/AISI, 316L stainless steel – mechanically polished Filter: Polypropylene, 0.2 µm	
Pressure range	0.8 to 5 bar | 11.6 to 72.52 psi absolute pressure	
Port gasket	O-ring, 11.00 mm × 3.00 mm EPDM (FDA | USP Class VI)	
Vessel preparation requirements	filter install – hydrophilization - autoclave | steam sterilization	

[1] steel conduit armored thread

BioPAT® Trace Dialysis Probe

Mechanical port connection	Diameter: 12 mm thread: steel conduit, PG 13.5	
Insertion depth | Univessel® volume	132 mm | 0.5L	BPT0014
	165 mm	BPT0015
	212 mm | ½L	BPT0016
	232 mm | 2L	BPT0017
	332 mm | 5L	BPT0018
	362 mm | 5L	BPT0019
	432 mm | 10L	BPT0020
Port adapter | insert depth reduction	19/12 mm | 49 mm	BB-8848630
	25/12 mm | 52 mm	BB-34165225
Product contact materials	1.4404 AISI - 316L stainless steel – Mechanically polished	
Construction material	Dialysis membrane: Cellulose acetate, approx. 12 kDa MWCO[2] Pressure range: 0.8 bar to 3.4 bar | 11.6 psi to 49.91 psi absolute pressure	
Port gasket	O-ring, 11.00 mm × 3.00 mm EPDM (FDA | USP Class VI)	
Vessel preparation requirements	install membrane - fill buffer - autoclave | steam sterilization	

BioPAT® Trace Single-use Probe

Connection	Integrated into Flexsafe® STR® or RM bag sample port
Product contact materials	Flexsafe® RM or STR® Validation guide
Hollow-fiber membrane	Polyethersulfone PES, approx. 12 kDa MWCO[2]
Preparation requirements	Ready to use

[2] Molecular weight cut-off

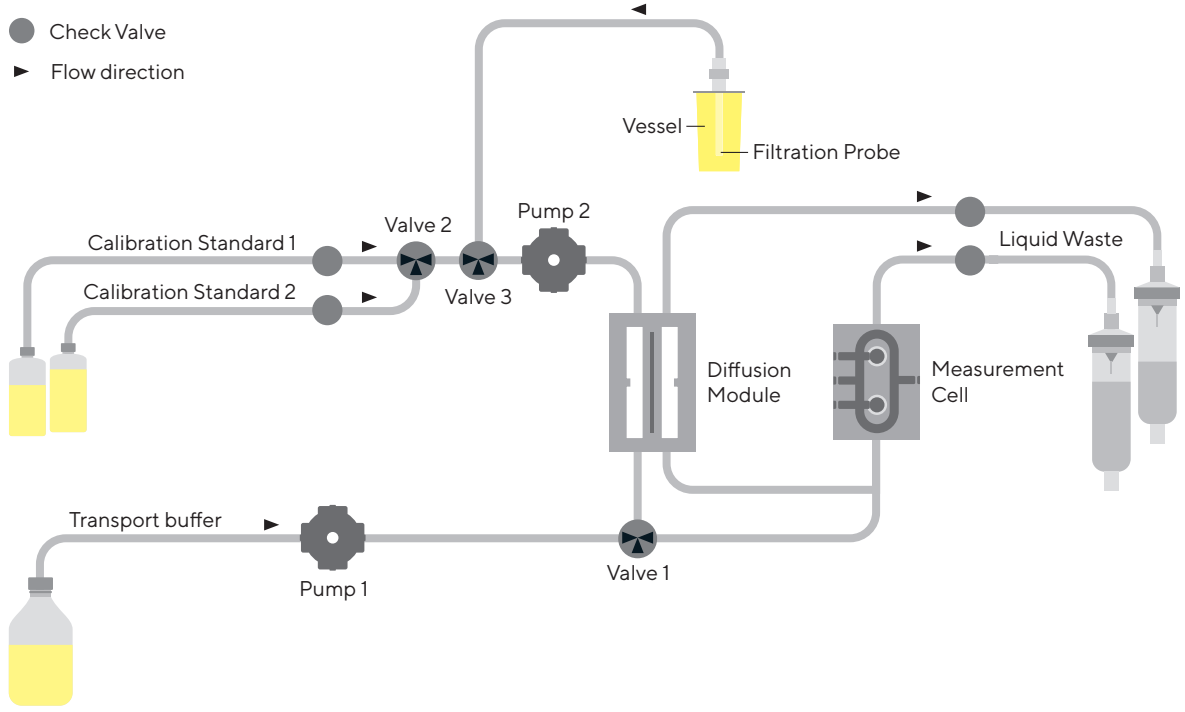
BioPAT® Trace Tube set for Filtration

BioPAT® Trace	
Inlets	4
Outlets	1
BioPAT® Multi Trace	
Inlet	7
Outlets	1
Tube sets for BioPAT® Trace	
Glc | Lac	BPT0004
Glc | Lac cellulase stable	BPT0005
MeOH | EtOH	BPT0049 and BPT0048
Tube sets for BioPAT® Multi Trace	
Glc | Lac	BPT0M02
Glc | Lac cellulase stable	BPT0M03
MeOH | EtOH	BPT0M04 and BPT0048

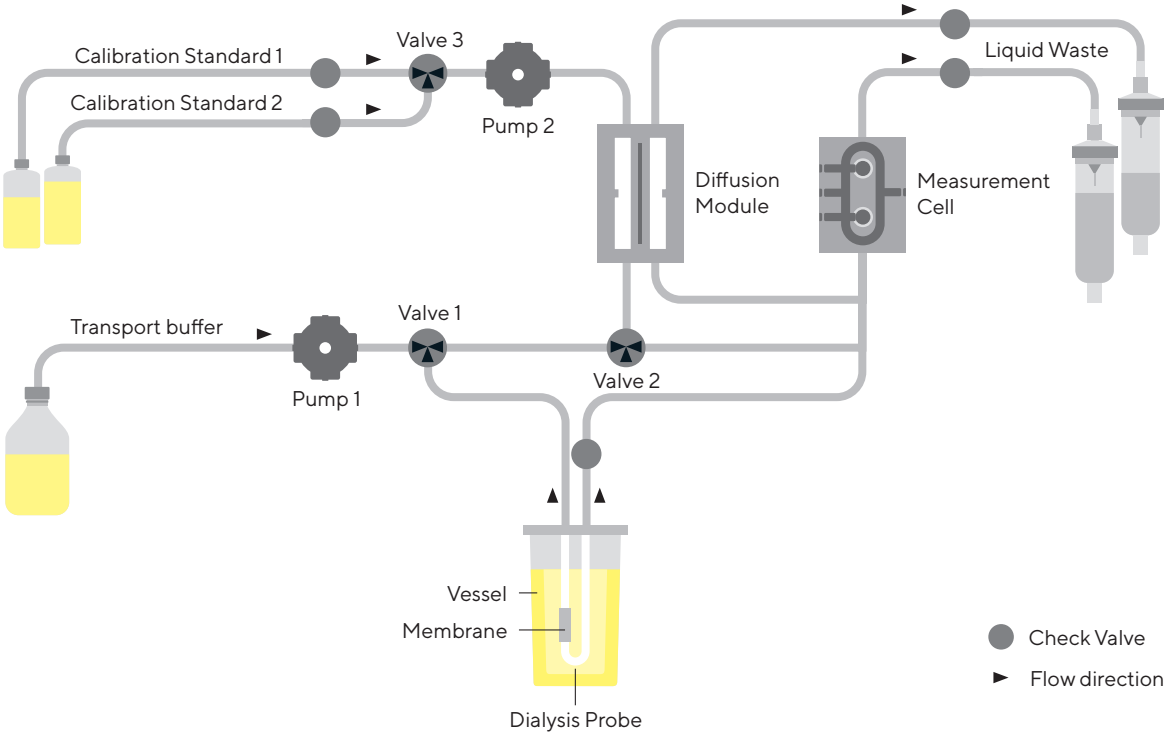
BioPAT® Trace Tube set for Dialysis

BioPAT® Trace	
Inlets	3
Sample return loops	1
Outlets	1
BioPAT® Multi Trace	
Inlet	3
Sample return loops	4
Outlets	1
Tube sets for BioPAT® Trace	
Glc | Lac	BPT0003
MeOH | EtOH	BPT0050 and BPT0048
Tube sets for BioPAT® Multi Trace	
Glc | Lac	BPT0M01
MeOH | EtOH	BPT0M05 and BPT0048

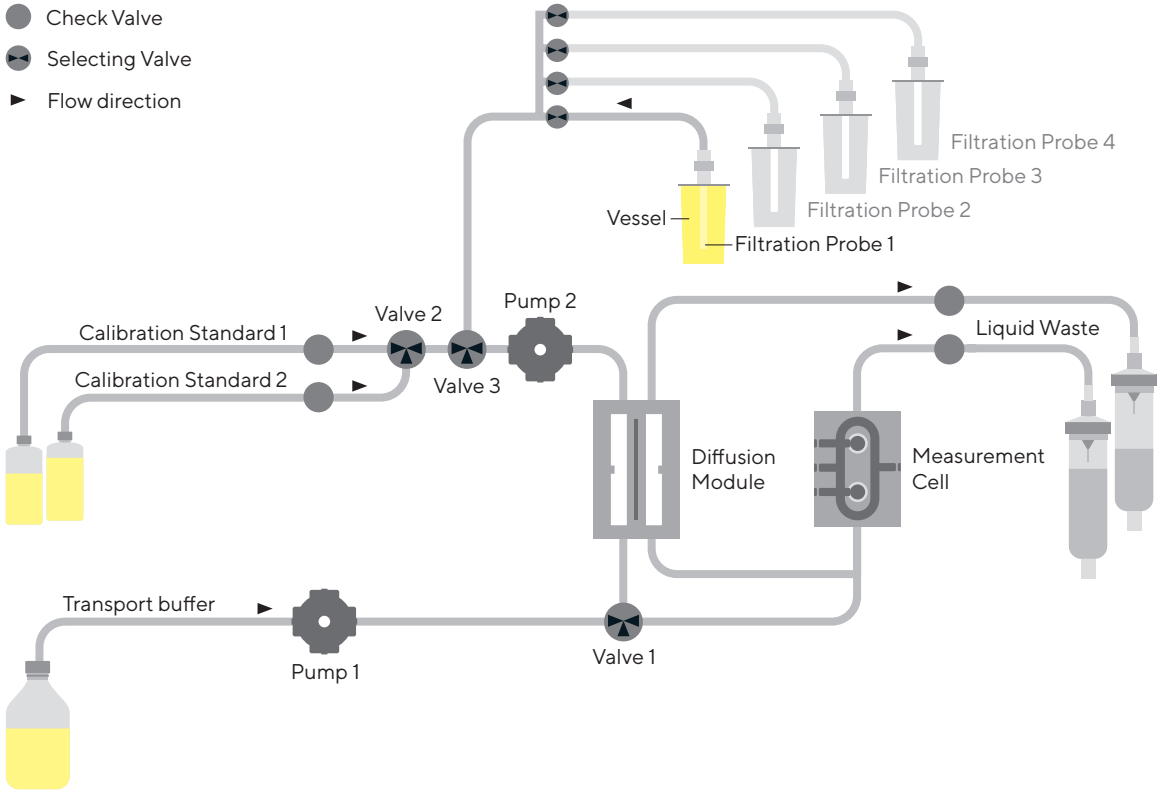
BioPAT® Trace
Tube set for Filtration



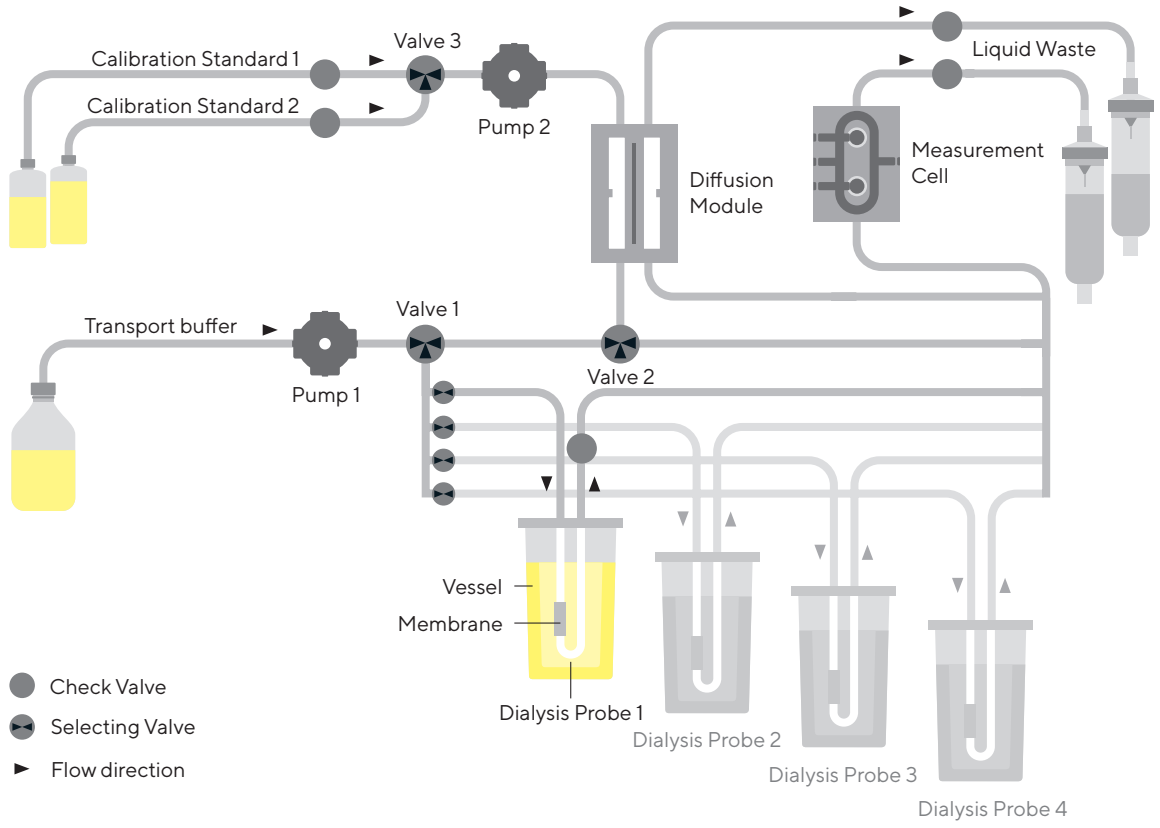
BioPAT® Trace
Tube set for Dialysis



BioPAT® Multi Trace
Tube set for Filtration



BioPAT® Multi Trace
Tube set for Dialysis



Certificates

Calibration certificates

Acceptance Report
Calibration Solution
4 g/l Glucose
2 g/l Lactate
Part.-No.: 850.305.003

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Phone: ++49-531-209008-0
Fax: ++49-531-209008-39
email: info@trace.de
www.trace.de

Certificate of Conformity:

We confirm the agreement of this acceptance report with the original examination report of arotop food environment GmbH, Mainz, December 19, 2011.

TRACE *Analytics GmbH*

Examination Report:

Calibration Solution 4 g/l Glucose / 2 g/l Lactate

Project-No.:	045369
Lot-No.:	2011-40376
Date of receive:	December 09, 2011
Parameter:	D-Glucose
Result:	3.97 g/l
Standard deviation:	± 0.014 g/l
Parameter:	L-Lactic Acid
Result:	2.007 g/l
Standard deviation:	± 0.066 g/l
Method:	R-Biopharm, Boehringer Mannheim, Enzymatic BioAnalysis / Food Analysis According to §64 LFGB, ASU L31.00-12 The detection limit of glucose is 4.0 mg/L The detection limit of Lactate is 5.0 mg/L

Date of Acceptance

Signature

The original report was performed by

arotop food environment GmbH
Institut für Geschmacksforschung. Lebensmittel- und Umweltanalytik
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Accredited in accordance with DIN EN ISO/IEC 17025.

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