PATsmart™ MAVEN® Glucose/Lactate On-line Analysis System

User Guide

Software v7.6.22
MAVEN Remote 1.1.1.5

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1. Safety

The equipment described in this user guide were designed and built with a high level of consideration given to hazard analysis and regulatory standards. However, safety can only be achieved when operators take all necessary measures. It is thus the operator's responsibility to be aware of and execute proper safety measures.

The following safety instructions do not release the operator(s) from the responsibility to observe other relevant safety measures that may apply to the equipment.

1.1 Intended Use

The device is a 2-channel on-line analyzer to determine glucose and lactate concentrations in laboratory or industrial cultivations of microorganisms and cell lines.

The operator must ensure that

- the device is used only for its intended purpose and only when functional and in proper working order,
- the device is used only indoors, on a flat, horizontal surface or mounted on the included stand, and
- the user manuals are kept legible and intact near the place of operation.

Any use beyond the intended use of the device can cause severe, unforeseeable hazards and is the sole responsibility of the operator.

1.2 Intended Personnel / Target Groups

This user guide is intended for the following target groups. All personnel must possess the knowledge listed.

Target Group	Knowledge and Responsibilities
User (Operator)	User is familiar with the operation of the device and the associated work processes. User knows the dangers that can occur when working with the device and can avoid these dangers. User has been trained on the operation of the device. The training takes place within the scope of startup and is carried out by the Operating Engineer/Laboratory Manager or the Administrator (see below).
Operating Engineer / Laboratory Manager (OE/LM)	OE/LM makes decisions about the use and parameterization of the device. OE/LM is trained on the operation of the device. The training takes place within the scope of startup and is performed by Repligen or an Authorized Service Provider.
Administrator	Administrator is responsible for compliance with safety requirements and workplace safety regulations. Administrator ensures that all individuals who work with the device have access to the relevant information and have been properly trained on the operation of the device.

1.3 General Safety Instructions

Warning: Risk of injury if instructions are not followed.

High Voltage: Dangerous electrical voltage present.

- Read this section before starting the device.
- Only operate the device when it is functional and in good working order.
- Follow recommended maintenance practices (chapter 7).
- Have any damage repaired as soon as possible by Repligen or an Authorized Service Provider.

1.3.1 Electrical

Electrical switching elements are present in the device. Damage to the insulation or individual components can be life threatening. Contact with parts under voltage poses a direct danger of death.

Repairs and modifications to the electrical components of the device may only be carried out by Repligen or an Authorized Service Provider.

The device may only be opened by Repligen or an Authorized Service Provider.

The system owner is responsible for the following:

- Check the device regularly for defects, such as loose connections or damage to the insulation.
- Note the device's ingress protection (IP) rating. The IP rating specifies its suitability for various ambient conditions, namely the levels of moisture and particulates.
- Do not use incorrectly sized power cords.
- Keep live parts away from moisture.
- If the electrical equipment is defective, immediately turn off the power supply and contact Repligen.

1.3.2 Energy Release

Energy supply lines must be correctly sized and protected against accidental fluctuations and faults, which can cause unintended energy release, i.e. power surges.

The device must be used with power supplies as described in section 10.1. Connections must be fitted with fully functional safety equipment, such as an earth-leakage circuit breaker for mains connections.

1.3.3 Accessories, Consumables, Spare Parts

All accessories, consumables, and spare parts used with the device must be supplied by Repligen. Only use accessories, consumables, and spare parts that are in good condition. Using unsuitable accessories, consumables, or spare parts may result in malfunction, damage, or total failure of the device.

1.4 In Case of Emergency

Malfunction may result in injury or property damage. If there is immediate danger of personal injury or equipment damage, take the device out of operation immediately:

- Unplug the power cord from the device.
- Have any malfunctions repaired immediately by Repligen or an Authorized Service Provider.

The solutions (buffer concentration, cleaning, and calibration solution) used for the operation of the devices are not strongly corrosive, poisonous, or seriously harmful to skin. If skin contact occurs, rinsing with water for several minutes is sufficient. You can find more information on this in the safety data sheet for each solution.

2. Product Description

The PATsmart™ MAVEN® System from Repligen is a highly versatile, on-line, sample-free monitor of glucose and lactate in bioreactors and fermenters with optional automated feed control. The device's compact housing contains all the necessary mechanical, fluidic, and modular electronics. The MAVEN System may be operated using a diffusion probe or diffusion module, both of which allow for sterile and safe measurement from the bioreactor/fermenter. Transport buffer, control solution, and waste can be suspended in bags and attached to the supplied stand hook to save space.

Analyses are performed in a biosensor module that uses a combination of enzymatic conversion and electrochemical detection. A two-channel electrode, coated with immobilized oxidase enzymes, serves as the biosensor. System control is performed via an external computer with an easy-to-use software interface.

In addition to measuring glucose and lactate concentrations, the MAVEN System also offers accurate control of substrate feeding for improved product titer, quality, and process robustness.

Figure 1. The MAVEN System

3. Components

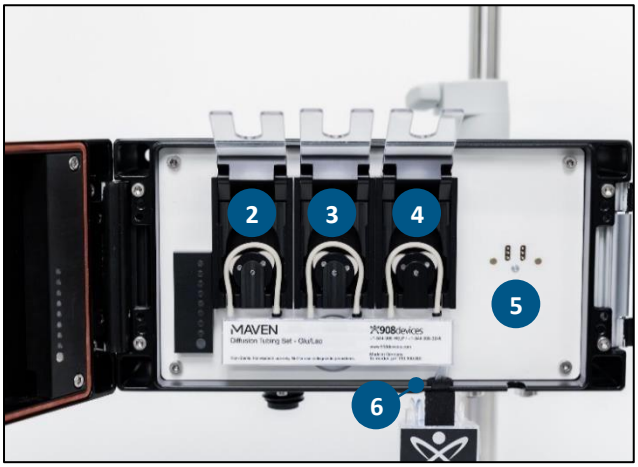
3.1 Main Body

1. Hook for control solution

Figure 2. MAVEN System Main Body Components

3.2 Pump and sensor interface

2. Pump 1: transports buffer to probe and then to sensor
3. Pump 2: transports buffer to sensor
4. Pump 3: transports calibration standard to sensor
5. Biosensor connection (magnetic)
6. Fluidics box mounting point



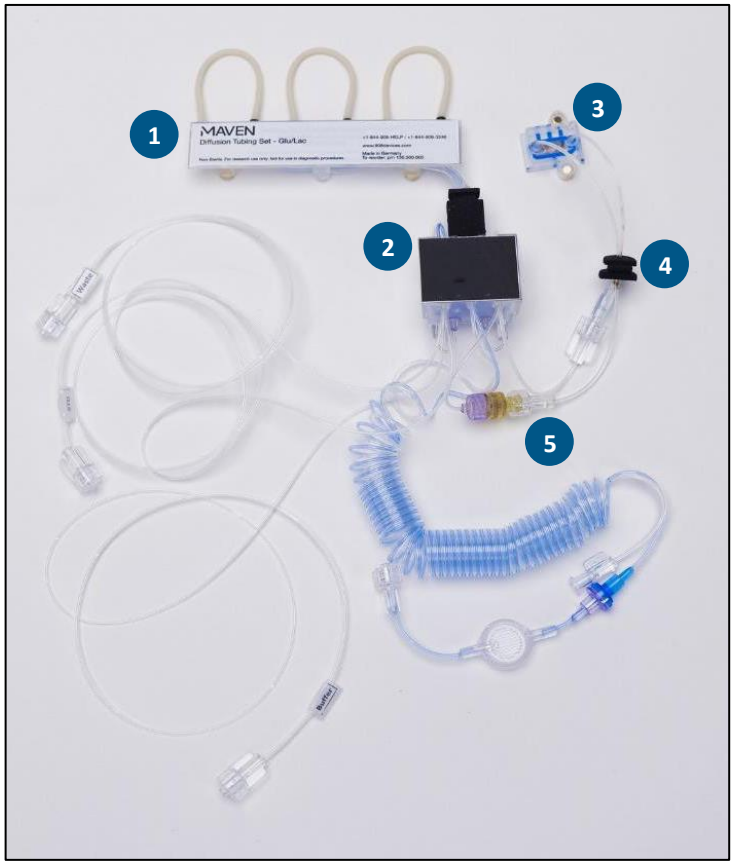
3.3 Bottom of device

7. Analog output connection socket
8. Serial interface connection socket
9. Ethernet connection socket
10. Power supply connection socket
11. Power switch

A power supply unit is included with the system. The MAVEN System can be switched on or off via the power switch. The electrochemical signal from the biosensor is automatically converted to a concentration value and sent to the analysis software on the associated PC via the ethernet port. The MAVEN System also features several additional options for signal output. Analyte concentrations may be output as analog voltage (0–10 V) or current (0–20 mA of 4–20 mA) or sent via RS232 serial interface.

3.4 Tubing Set

Figure 3. MAVEN System Tubing Set Components



Components

1. Retaining plate
2. Fluidics box
3. Biosensor
4. Mounting gasket
5. Luer connector

The MAVEN Tubing Set consists of all the components required for analysis:

- A retaining plate with peristaltic pump tubing loops ensures continuous flow of solutions (Figure 3, #1)
- A fluidics box organizes the connection lines for buffer, control solution, waste, and sampling (Figure 3, #2)
- A biosensor contains enzyme-coated electrodes for detecting glucose and lactate and attaches to the device panel with magnets (Figure 3, #3)

Table 1. Operational Checklist

Item	Action	Section Reference	☑
0	**Initial Setup**		
	Set the IP address of your MAVEN System	3. Network Setup	
1	**Assemble diffusion probe**		
	Install diffusion membrane	5.1. Assemble Diffusion Probe	
	Install probe in reactor	5.2. Connect Diffusion Probe to Bioreactor	
	Sterilize if necessary	5.3. Sterilize Diffusion Probe	
2	**Prepare transport buffer and waste container**		
	Dilute transport buffer concentrate	4.6. Prepare Buffer Solution	
	Provide waste container with disinfectant, if needed	6.4. Preventing Contamination	
3	**Mount tubing set**	5.4. Mount Tubing Set	
4	**Connect supply and discharge lines**	4.5. Connect Supply and Discharge Lines to Diffusion Probe	
	Connect transport buffer, control solution, and waste container	5.7. Connect Buffer, Control Solution, and Waste Container	
5	**Switch on the device**	7.1. Startup	
6	**Launch PC software**	7.1. Startup	
7	**Set operating parameters**		
	Enter project information	7.1.1. Project Information	
	Set measurement parameters	7.1.2. Measurement Parameters	
	Set controller settings (if using)	7.1.3. Controller Parameters	
	Initialize tubing set	7.1.4. Initialization	
8	**Start measurements**	7.2. Main Screen	
9	**Check biosensor for air bubbles**	4.5. Connect Supply and Discharge Lines to Diffusion Probe	
10	**Perform reference measurement/calibration**	7.3. Calibration	
11	**Optional: connect analog outputs to process control system**	8.1. Analog and Serial Outputs 8.2. Open Platform Communications Unified Architecture (OPC UA)—Data Transfer Via TCP/IP Feed Pump Control: 7.1.3. Controller Parameters	

4. Network Setup

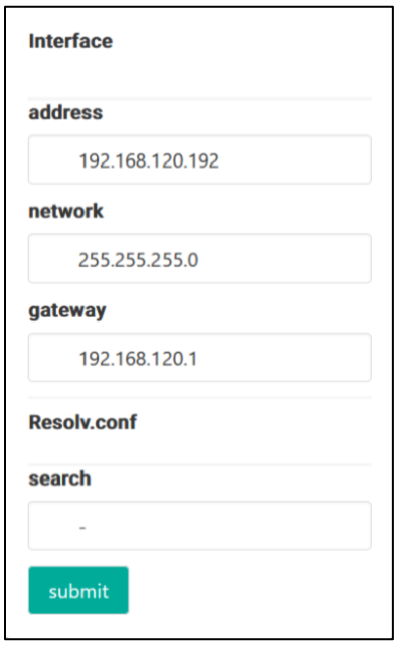
4.1 Connecting to a Company Network

Before you start, decide whether you will:

A. Connect the MAVEN System to your company network (preferred)
B. Or connect the MAVEN System to a gateway PC via an ethernet cable.

Option A: Connect the MAVEN System to a network:

1. Contact your IT department to assign a new IP address to the MAVEN System. The factory IP address may not be compatible with your corporate network.
2. Connect the MAVEN System to the network using an Ethernet cable.
3. Open a web browser and type in the factory IP address 192.168.120.234 to configure the network settings on the MAVEN System.
4. Choose “Network settings” in the menu.
5. Enter the new IP address assigned by your IT department in the address field and click submit.
6. Reboot the MAVEN System.



Note: *After changing the network address, the device can only be accessed via this new IP address. If using the Trace_mon app (see Appendix 2), the last 3 digits of the IP address (here 192) will be displayed in the upper left corner. The asterisk indicates a successful connection.*

Option B: Connect the MAVEN System to the gateway PC

1. The MAVEN System will not function as a DHCP client. Contact your IT department to configure the MAVEN System PC from an automatic DHCP server to a static IP address.
2. Connect the MAVEN System directly to the PC via a crossover Ethernet cable. In this case, the device will work with the factory IP address (192.168.120.234).
3. Edit Ethernet adapter properties to direct connect to the MAVEN System with default IP 192.168.120.234.

4.2 Network Troubleshooting

If you have entered an incorrect IP address on the device's website during installation, no connection will be established. Follow these steps to remedy:

1. First, try to connect to the MAVEN System internal website (default IP address 192.168.120.234) using a direct PC connection and a crossover Ethernet cable.
2. If this is not possible, you may reboot the MAVEN System into a preconfigured network safe mode with the IP_set boot file. First, switch off the MAVEN System. Copy the IP_set boot file (available from the Replgen Customer Support Portal) to a USB drive, plug the drive into the front USB port, and switch on the device. After the boot process, the MAVEN System will have the IP address 192.168.120.232. Open a web browser and type in IP address 192.168.120.232. After establishing a connection to the MAVEN System, you can reset the network address via your web browser as described above. Remove the USB drive and restart the MAVEN System as normal.

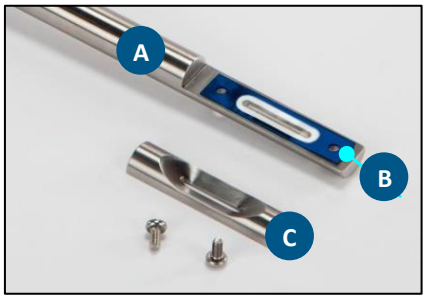
5. Hardware Setup

5.1 Assemble Diffusion Probe

The diffusion probe consists of a probe body, a disposable membrane, and a lunette that holds the membrane in place. Follow these steps for proper assembly of the probe before use.

1. Place the diffusion membrane onto the bottom of the probe, with the colored/silver side facing the lunette.

Figure 4. Diffusion Probe Components



Components

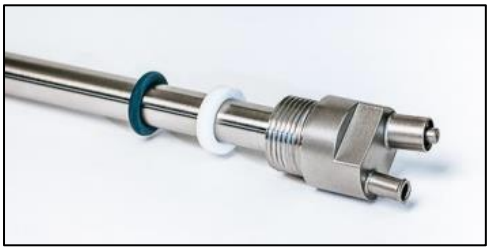
A. Probe
B. Membrane
C. Lunette

2. Hold the lunette against the membrane and tighten the screws to secure the lunette onto the probe.

Important:

- *The membrane must sit flush against the sides of the probe. Inserting the membrane at an angle can result in leaks at the diffusion probe head and jeopardize sterility.*
- *The white side of the membrane must face the diffusion probe.*
- *The colored/silver side of the membrane must face the lunette.*

3. Before installation and sterilization, slide the white compression washer onto the probe body as shown; note that the flat side should contact the bottom of the probe threads. Slide the o-ring onto the probe body and up against the compression washer, as shown.



5.2 Connect Diffusion Probe to Bioreactor

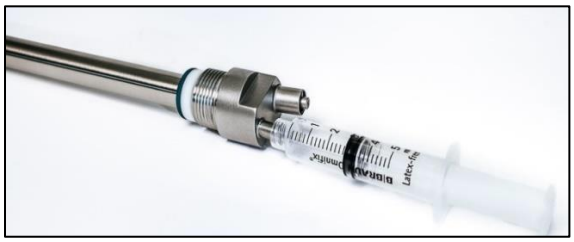
The minimum immersion depth for the diffusion probe is 53 mm (or 25 mm with low immersion depth membrane).

Notes:

- *A special membrane is available for small bioreactors (<200 mL), featuring a diffusion probe immersion depth of only 2.5 cm.*
- *Different port adapters may decrease the minimum immersion depth. Please make sure to use a probe long enough to maintain total submersion of the diffusion membrane (49–53 mm).*

5.3 Sterilize Diffusion Probe

1. Connect the diffusion probe to a disposable Luer syringe, as shown.
2. Fill the diffusion probe with enough deionized water until fluid exits the discharge port.
3. Check that no water is leaking from around the membrane at the probe tip.



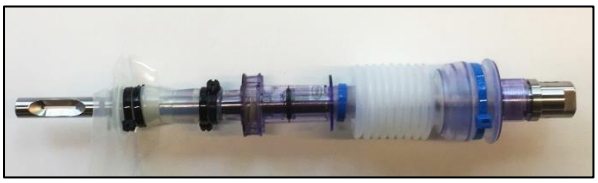
4. Close the diffusion probe with the sealing caps.

5. Utilize steam sterilization at 1 bar, 121°C.

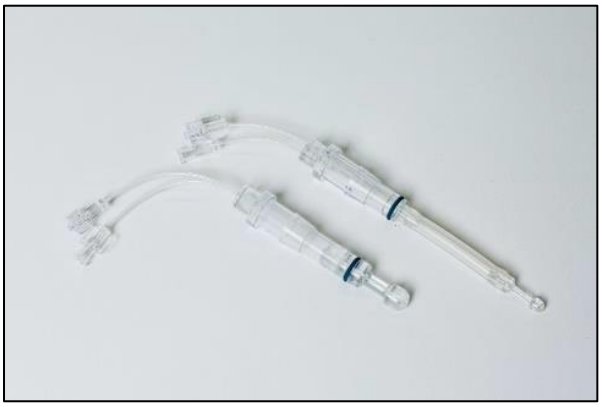
Important: *During sterilization, the diffusion probe must be filled with deionized water and closed with the included caps to prevent damage to the membrane.*

5.3.1 Accessories Also Available

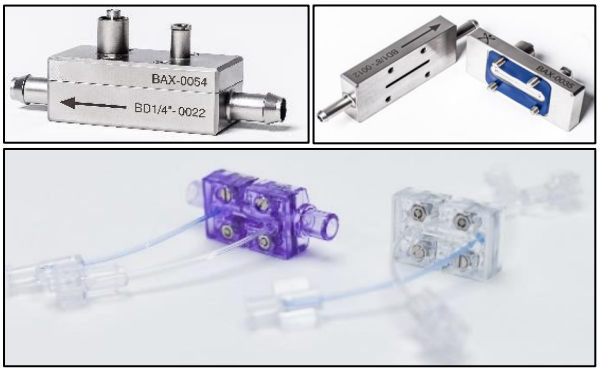
For single-use applications, the diffusion probe (length 300 mm) can be installed using a Kleenpak™ adapter, available from Thermo Scientific™—Bioreactor Probe Assembly, Order No. SH3B12122.01.



Single-use plastic probes can be integrated into reactor bags via common ½" ports. Separate designs are available for stirred and wave reactors.

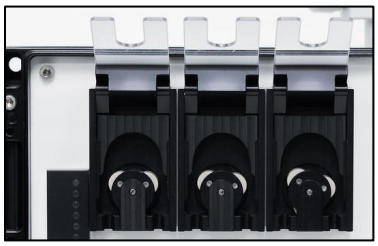


Reusable or single-use diffusion modules are available for instances when a probe geometry is not suitable. The reusable modules are made entirely of stainless steel or PEEK to ensure high sterility assurance. A diffusion module may be installed in any line accessing the medium and the reusable versions may be sterilized *in situ* with the bioreactor.



5.4 Mount Tubing Set

1. Use the latch on the right side of the MAVEN System to open the front door.
2. Lift the three flaps to reveal the peristaltic pump rollers.



3. Hold the tubing set by the retaining plate and loop the tubes over the peristaltic rollers.
4. Carefully fold the flaps back down to press the rollers against the tubing.

5. Use the supplied Luer connectors to hook up the biosensor module.
6. The biosensor attaches to the sensor contact panel via a pair of magnets. Make sure the electrical contacts on the panel are aligned with the contacts on the biosensor.
7. Firmly insert both mounting gaskets into the corresponding notches in the case to maintain integrity of tubing when the door is closed.

8. Close and latch the door.

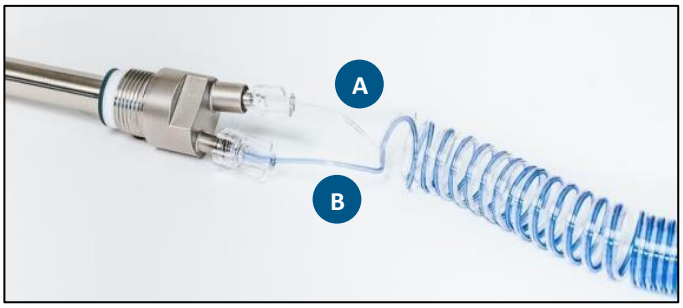
Note: *The MAVEN System is intended to be calibrated and run with the door closed.*

5.5 Connect Supply and Discharge Lines to Diffusion Probe

After sterilization, connect the probe to the tubing set, ensuring that as little air as possible is introduced. Air bubbles from the tubing set that become trapped in the biosensor can cause fluctuations in glucose and lactate measurements.

1. Remove sealing caps and set aside for later use.
2. Connect the supply line (blue tubing) and discharge line (colorless tubing) to the corresponding Luer connections on the probe.

Figure 5. Probe Supply and Discharge Lines



Components
A. Discharge (Colorless)
B. Supply (Blue)

5.6 Prepare Buffer Solution

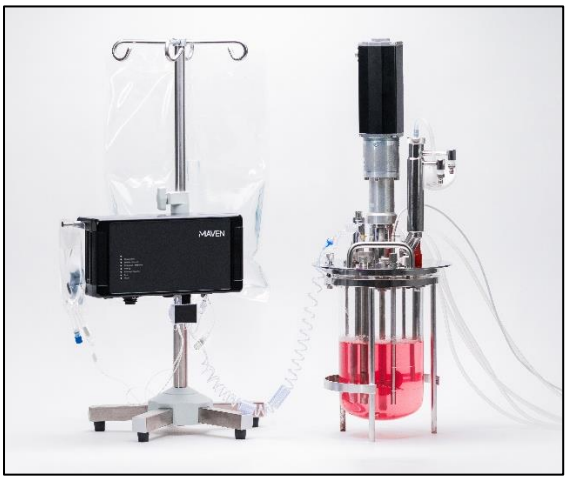
Mix the transport buffer according to package instructions and sterile filter into the provided hanging bag labeled “Buffer.”

- The included hook stand provides convenient storage for buffer solution during your bioprocess.
- If bottles are required by your lab, make sure the tubing is fully inserted into the bottle and that the bottle is covered (Parafilm M or a similar product is ideal) to prevent foreign matter from entering the solution.

Tips

- *Proper dilution can be verified by measuring the conductivity of an aliquot. Correctly diluted buffer has a conductivity of 5–15 mS/cm.*
- *The hanging stand is a convenient place to keep hardware for later use, such as the screwdriver, sealing caps, and spare membranes for the diffusion probe.*

5.7 Connect Buffer, Control Solution, and Waste Container



1. Connect the control solution, transport buffer, and waste lines to the fluidics box.

Note: *Lines are pre-assembled and come in labeled foil bags. To maintain sterility, we recommend these packets remain sealed until the tubing set has been mounted on the instrument.*

- *"BUFFER": to transport buffer*
- *"WASTE": to waste container*
- *"STD": to calibration solution*

2. After inserting tube into control solution, you may hang the bag on the convenient hook on the side of the main device housing.
3. Connect waste tubing to the provided hanging bag labeled "Waste". See the section on Preventing Contamination in this guide to maintain the sterility of your bioprocess.

Hardware setup is complete.

6. Consumables Information

The **transport buffer** consists of a salt mixture (for cell cultures) or a concentrate (for microbial cultures) that must be dissolved/diluted with water (deionized or distilled) according to the instructions. Proper dilution can be verified by measuring the conductivity of an aliquot. Correctly diluted buffer has a conductivity of 5–15 mS/cm.

The consumption of transport buffer depends on the measuring interval and the number of measuring points in operation. For typical measurement, the expected consumption rates are given in Table 2.

Table 2. Consumables Consumption

Interval	Buffer Consumption			2 L Will Last…		5 L Will Last…	
Minutes	mL/min	mL/h	mL/d	Hours	Days	Hours	Days
2*	0.850	51.0	1224.0	39.2	1.6	98.0	4.1
5*	0.850	51.0	1224.0	39.2	1.6	98.0	4.1
10	0.769	46.1	1107.0	43.4	1.8	108.4	4.5
20	0.531	31.9	764.6	62.7	2.6	156.9	6.5
30	0.447	26.8	643.2	74.6	3.1	186.6	7.8
60	0.350	21.0	503.8	95.2	4.0	238.2	9.9
120	0.287	17.2	412.8	116.3	4.8	290.7	12.1
180	0.260	15.6	374.8	128.2	5.3	320.2	13.3
360	0.231	13.8	332.2	144.9	6.0	361.2	15.1

*When a measurement interval is set to 2 minutes, the system does not have sufficient time to conduct a flushing cycle, so it uses the same amount of buffer as the five-minute measurement interval.

7. Cleaning and Maintenance

7.1 General Notes

- The lifetime of the sensor is at least 5,000 measurements. In continuous operation, this lasts at least 14 days. The lifetime of the tubing set is 30 days.
- Clogged or damaged tubing sets must be replaced to prevent measurement errors.
- If measurements are interrupted for a short time (maximum two days), you may continue to use the system without replacing the tubing set. However, during the interruption, the system must be kept in “Standby” mode, with all tubing remaining in contact with liquid.

7.2 Cleaning the System

If the system will be idle for longer than two days, follow the instructions below to ensure that all tubing remains clean and free of buildup:

1. Fill a clean flask with 250 mL of Cleaning Solution
2. Immerse the ends of all tubing lines from the tubing set (Buffer, Control) into the Cleaning Solution.
3. If possible, the diffusion probe should remain connected during cleaning. If this is not possible, e.g., due to the sterilization of the reactor, the Luer fittings on the tubes that connect to the diffusion probe should be connected to each other.
4. In the MAVEN Remote web app, click the **Clean** button, or in trace_mon.exe software, navigate to **Device > Clean** to begin the cleaning cycle.
5. Allow the unit to run until the Cleaning Solution is depleted.
6. Repeat steps 1–5 with one (1) liter of deionized water.

7.3 Cleaning the Diffusion Probe After Use

1. Remove the Luer connections between the tubing set and the probe.
2. After appropriate clean-in-place (CIP) procedures and/or sterilization, remove the diffusion probe from the bioreactor.
3. Clean the probe surface and caps with a soft brush and water.
4. Check the sealing rings of the diffusion probe for cleanliness and correct seating.
5. Remove the two TORX screws on the diffusion probe to remove the lunette and membrane.
6. Discard the membrane and clean the diffusion probe and lunette with a soft brush and water.
7. Flush cleaning solution followed by deionized water through the probe with the supplied syringe.
8. Dry the probe by flushing air with the supplied syringe.

7.4 Preventing Contamination

In longer, multi-week cultivation processes, it is possible for biofilm to develop in the tubing set, which can lead to clogged lines and inconsistent results. Below are some recommendations to keep both the instrument and your bioprocess running trouble-free.

Table 3. Contamination Problems and Recommendations

Common Problems and Contamination Sources	Recommendation
Transport buffer is diluted in a contaminated vessel or stored in a frequently refilled bottle	Always use clean containers/bottles for the transport buffer. Do not refill an empty buffer container but replace it with a clean one. Ideally, the buffer should be sterile filtered (this is typical for cell culture and GMP facilities).
Waste line is immersed in the waste liquid, allowing contaminants to spread into the tubing set	Replace waste containers regularly and do not allow the waste line to be immersed in the waste mixture.
Tubing set (reused) insufficiently cleaned/disinfected	Clean the tubing set according to the Cleaning & Maintenance section in this manual.
No disinfectant in the waste container	Add a disinfectant, such as KOH or NaOH pellets or chemical disinfectant to the waste container.
Waste container left open to the air	For best results, use the provided hanging bags to hold buffer solution and waste. If bottles are required by your lab, make sure the tubing is fully inserted into the bottle and that the bottle is covered (Parafilm M or similar product is ideal) to prevent foreign matter from entering the solution.
Insufficient sterilization of the probe or subsequent contamination when rinsing with the syringe	Check whether contamination has occurred after sterilization. A typical error is the use of a non-sterile liquid to rinse the probe after sterilization.
The probe does not show a signal while the calibration is unaffected	This is a typical sign of contamination inside the probe. Disassemble probe, discard membrane and tubing set, and re-sterilize system according to the Cleaning & Maintenance section in this manual.

8. Software: MAVEN Remote

The MAVEN Remote web interface allows you to control the MAVEN System from any computer on the same network. Follow these steps to set up your device.

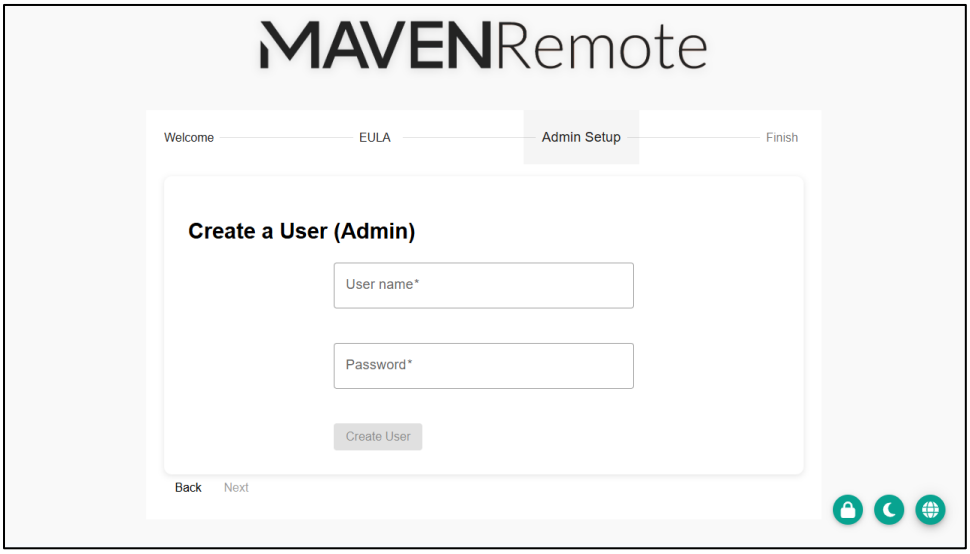
8.1 Startup

1. Activate the power switch at the bottom of the device.

2. Open a web browser and type in the IP address obtained in the network setup step (see chapter 3) followed by "/maven-remote".

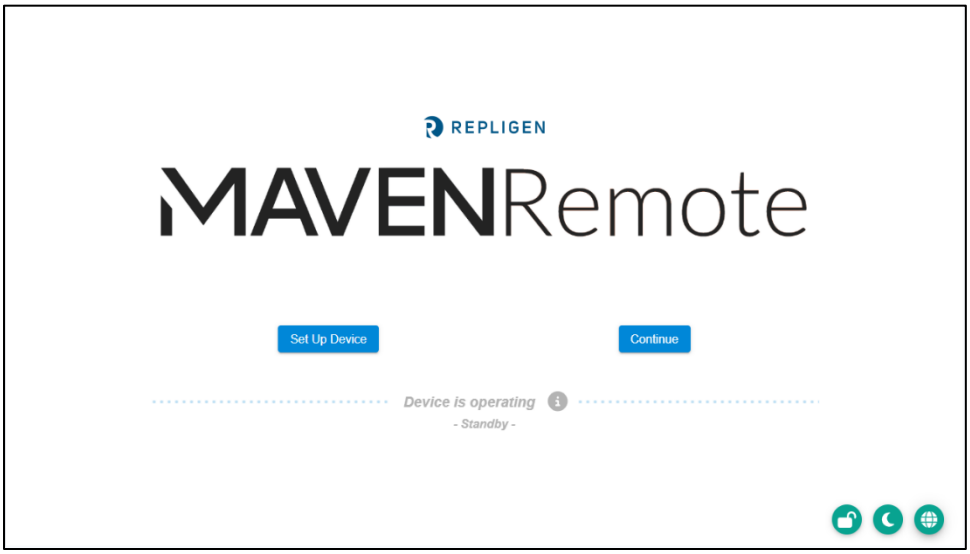
3. The first time using MAVEN Remote, an installation wizard will guide the user through setup. The wizard will only appear if there is no Admin account on the device and/or the End User License Agreement must be accepted (e.g., after a software update).
    a. Otherwise, skip to step 6.

4. Create the first Admin account during setup. More users (admin or non-admin) can be created later in the Users settings menu (section 8.4).



5. Click Finish to proceed.
6. Log in with your user credentials.
7. On the home screen:
    a. To initialize a new tubing set, click Set Up Device. When the pop-up appears, click Start Setup. This will overwrite previously saved calibration factors and other settings.
    b. To use previous settings and go to the home screen, click Continue Measurement. See section 8.2.

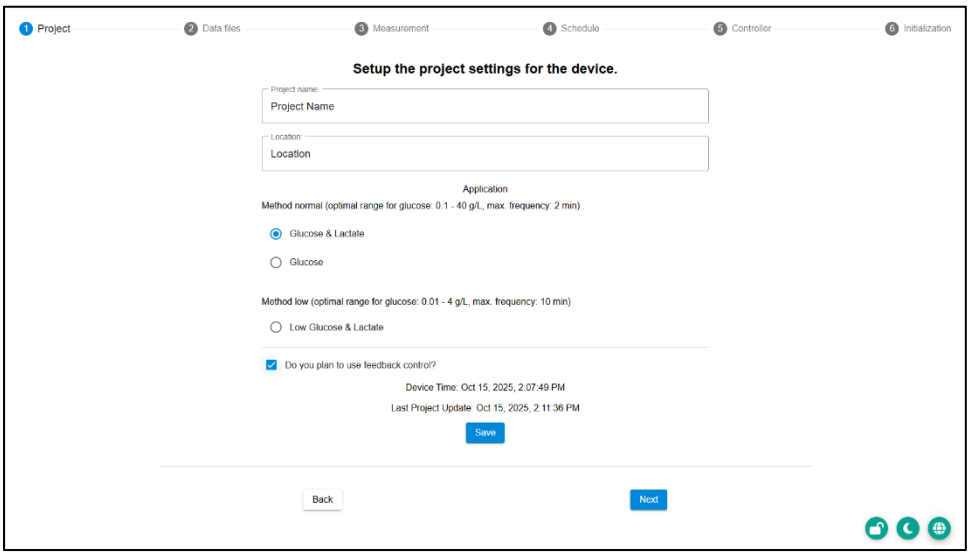
Note: *Make sure there is no active run before choosing Set Up Device. This will terminate all current activity and start the workflow to set up a new run.*



8.1.1 Project Information

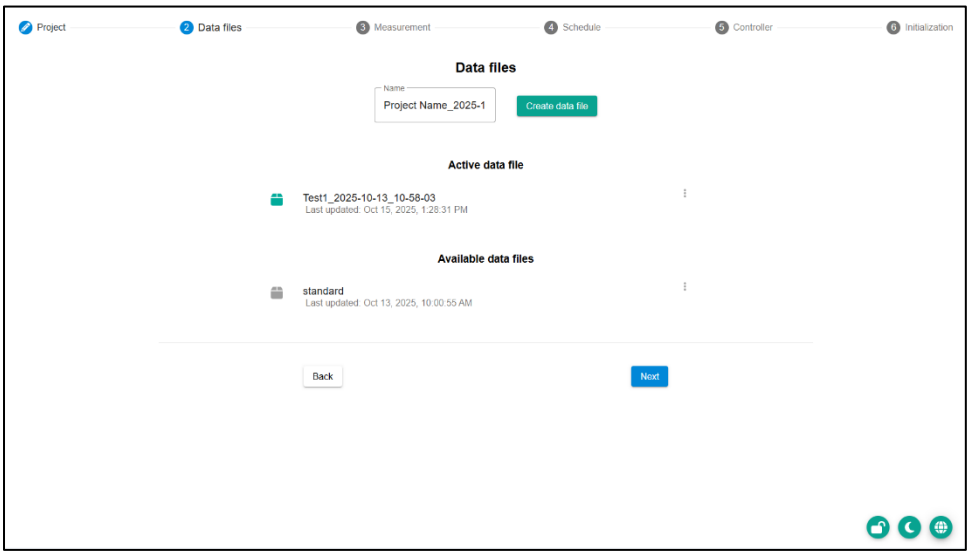
- Enter a Project Name and Location for easy file identification later.
- Select an Application based on glucose/lactate concentration.
- Click the checkbox next to “Do you plan to use feedback control?” if you are planning to use the MAVEN System to control a feed pump.

These settings can be changed later if needed. Click Save, then click Next to continue.



8.1.2 Data Files

Data may be downloaded as a .txt, .csv, or .xlsx file. If downloaded as .xlsx, the file displays an automatically generated chart that can be modified in Excel. The currently active save file appears in green at the top of the list. Use the three-dots menu (⋮) for additional file functions. It is highly recommeneded to create a new Data file prior to every run.

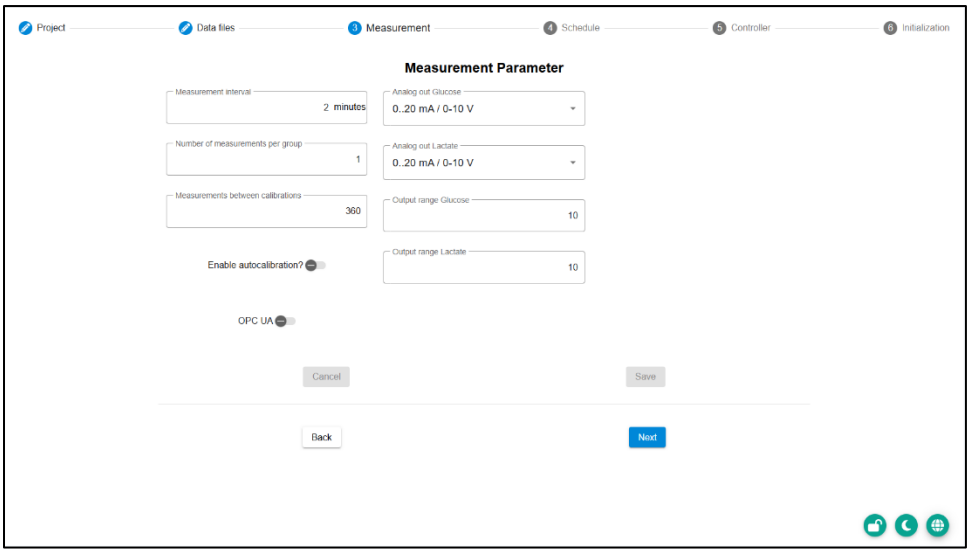


8.1.3 Measurement Parameters

These can be changed later as needed. Hints appear at the right side of the screen to help you determine the right settings.

- **Measurement Interval:** In minutes
- **Number of measurements per group**
- **Measurements between calibrations**
- **Enable autocalibration?** (on/off) It is recommended to turn this feature off. Instead, use the Schedule function (see section 8.1.4) to set up daily calibration.
- **OPC UA** (on/off)
- **Analog out Glucose, Analog out Lactate:** (Select the output of the signals for the analog port.)
- **Output range Glucose, Output range Lactate:** Set the value of the upper limit. For example, for a measurement range of 0–10 g/L of analyte, set this value to 10. The lower limit is preset to 0. For a voltage range of 0 – 10 V, 10 volts equals 10 g/L of analyte).

Click **Save** and then click **Next**.



8.1.4 Schedule

The Schedule function allows you to program calendar-based events (e.g., “run a sensor calibration next Monday at 8:30 am; standby every Friday at 1:00 pm”). Use the dropdown menus to set a date and time for the event. It is recommended to set up daily calibration (e.g. at 6:00 am) for every day of the run.

After creating an event, click Save to add it to the schedule. You may still use the measurement parameters to control the normal workflow for the MAVEN System (i.e., Measurement Interval and Number of measurements per group).

8.1.5 Controller Parameters

This screen appears when “Do you plan to use feedback control?” is activated in the Project screen. Under Type of Controller, you may choose between PID Controller and Minimum-Maximum Controller; each controller type offers different options. Under "Control by," select whether the control acts on an external pump via the serial interface or the analog output (section 8.1).

For PID control, click on the individual options to set the ideal glucose levels, proportional gain, integral time, and derivative time.

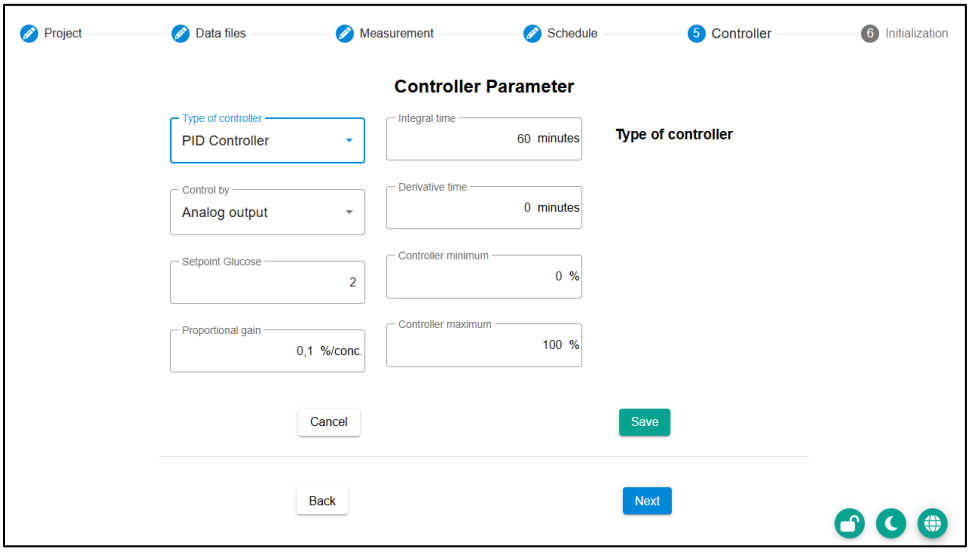


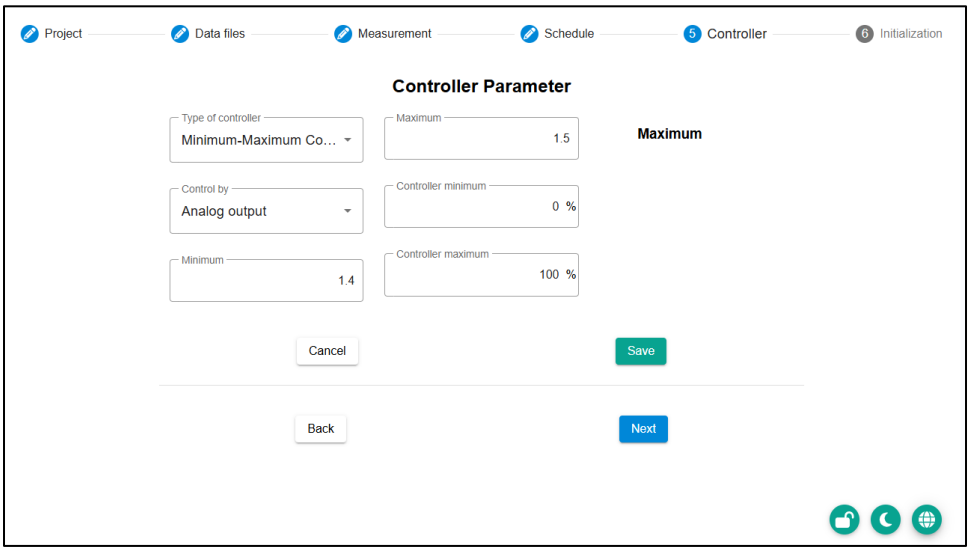
Table 4. Recommended PID Controller Settings

Parameter	Microbial Culture	Cell Culture
Proportional gain	0.1 – 0.5 %/conc.	0.01 – 0.1 %/conc.
Integral time (reset time)	45 min	60 min
Derivative time (lead time)	2 min	1 min

Notes:

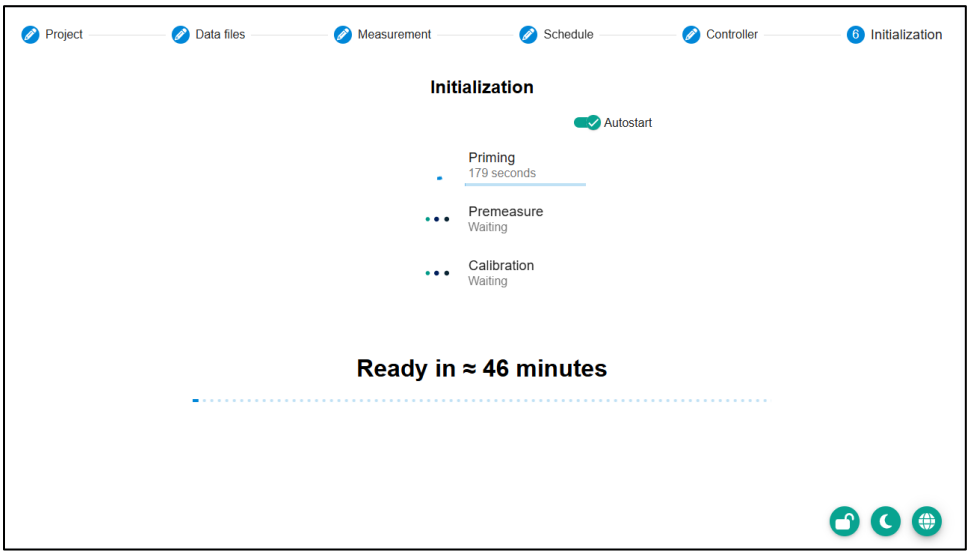
- The ideal proportional gain (P setting) depends on the feed concentration, maximum delivery rate of the pump, pump tube diameter, reactor volume, etc.
- In most cases, adjustment of the P setting is sufficient, and the integral (I) and deritivative (D) times can be maintained at the recommended values. If the feeding rate is too high, reduce the P setting. If the feeding rate is too low, increase the P setting.
- To avoid a too high integral gain (I-component) of the PID controller at the beginning, the I-component of the controller can be reset to the default I-component at any time with the "Reset controller" command.
- It is recommended to always reset the controller after filling the feeding line or in case of unknown history to avoid overdosing.

The Minimum-Maximum Controller switches the feeding pump to the minimum delivery rate when the analyte exceeds the maximum limit value and switches to the maximum delivery rate when the analyte falls below the minimum limit value. “Minimum” and “Maximum” determine the analyte values at which the controller will adjust the delivery rate; values should be entered in units matching the last reference calibration (section 7.3). “Controller minimum” and “Controller maximum” set the minimum and maximum delivery rates of the pump; the default settings are 0% and 100%.



8.1.6 Initialization

- **Start initialization:** It takes approximately 45 minutes to perform the Priming, Premeasure, and Calibration.
- **Autostart:** If activated, the MAVEN System will start measurement automatically.



8.2 Main Screen

The graph updates in real time as measurements occur, delivering insights into your bioprocess as they happen.

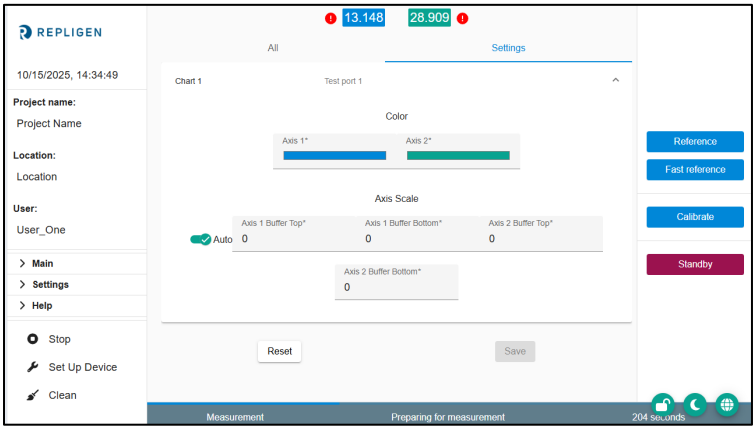
- Hovering over an individual data point shows the numerical values.
- The numbers in the top middle always show the latest measured values.
- The x- and y-axes may be adjusted by the sliders or within the Settings tab above the graph.
- The legend in the upper left can be used to show/hide data points for individual measurements (e.g., hide all the lactate data points)

- The colors assigned to the graph points may be changed in the Settings tab above the graph.

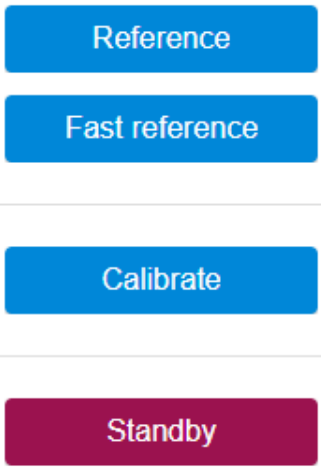
The current status of the system appears under the graph. The buttons in the upper-right corner allow for further manipulation of the graph:

	Data View	View measurements in a table format. Return to the graph by pressing the Close button.
	Zoom	Specify an area of the graph to enlarge.
	Zoom Reset	Return to the default view of the graph.
	Save as Image	Save the current state of the graph as a PNG.

The settings tab lets you change the colors used in the graph and adjust the axes.



Basic commands for your MAVEN System are located the right of the graph:



(See Calibration section, below)

(See Calibration section, below)

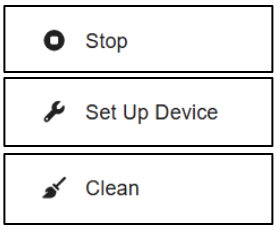
Switch device to standby mode to reduce buffer consumption if no measurements are taken.

Log out of the current session.

Switch to dark mode.

Change language settings.

Additional commands are located in the lower-left corner:



Halts all measurements and pauses both the workflow and scheduled event. The MAVEN System is placed on standby until further commands are issued.

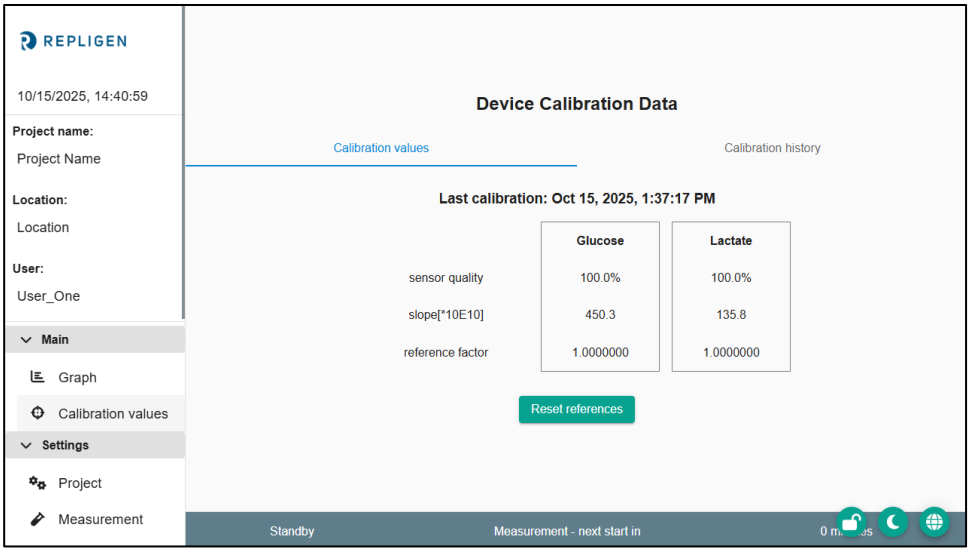
Begins the initialization process with previous settings.

Begins a cleaning cycle. See chapter 7. Cleaning and Maintenance.

8.3 Calibration

The MAVEN System is calibrated by a two-step process: referencing and then calibration. For details on referencing, see Appendix 1.

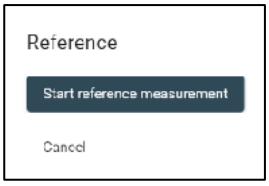
1. The sensor is calibrated using the MAVEN Calibration Standard Solution. Click the Calibrate button to begin. It is recommended to calibrate the MAVEN System once per day. The Calibration Values screen displays current and historical values.

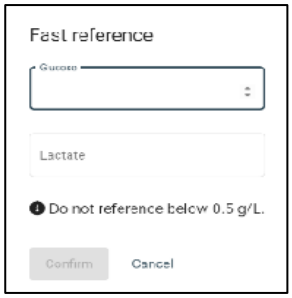


2. The probe membrane diffusion factor must be calibrated to account for the environmental conditions inside the bioreactor. This process is accomplished through the Reference or Fast Reference buttons.

   Reference should be used when you plan to take samples to confirm measurements from the MAVEN System with off-line analysis. After clicking the Reference button, a dialog box pops up, displaying current measurements. After you enter confirmed measurements from off-line analysis and click Apply, the MAVEN System will calculate a new reference factor based on the two values.

   Fast Reference allows you to enter known concentration values of the medium before the reference measurement is made.





The Calibration History screen shows all calibration values and reference factors acquired during the run.

Tips

After starting your process, it is recommended run another sensor calibration and reference factor after 12 hours and 36 hours. Afterwards, continue to calibrate daily.

(0h): Calibration + Reference → Start
(12h): Calibration + Reference
(36h): Calibration + Reference
(After, daily): Calibration

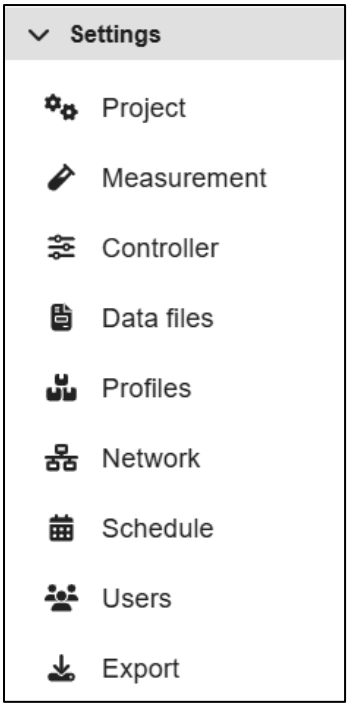
Do not overwrite low lactate reference measurements at the start of your culture.

At the start of cultivation, the culture typically has abundant glucose and no lactate. When performing a reference, the device suggests a value after the reference measurement, which is usually overwritten by entering a known value. If the existing lactate concentration is still very low, do not overwrite this value at first (the reference factor for lactate then remains at 1.0). As cultivation

continues, an increase in lactate concentration becomes more evident, and a normal reference, in which both values are overwritten, can be performed at the appropriate time.

8.4 Settings

Figure 6. Settings menu



Project

See section 8.1.1 Project Information.

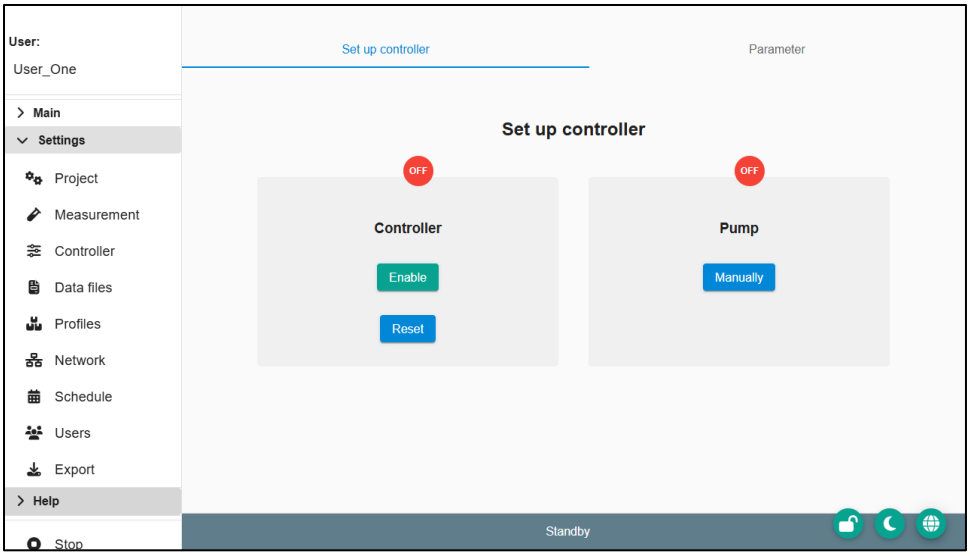
Measurement

See section 8.1.2 Measurement Parameters.

Controller

The MAVEN System can control an external feed pump via serial interface or analog output on the bottom of the device. When the controller function is enabled, a **green** field appears in upper right corner indicating the current delivery rate (0–100%) of the feed pump. If the controller is disabled, the background turns **red.**

- While the controller function is enabled, the feed pump cannot be switched off or operated manually.
- When the controller is enabled, the pump will continue to run at the last rate set by the controller until it is disabled.
- The controller reset button can be used to bring the integral gain back to the default value for the PID controller.
- The pump rate can also be manually set.
- See also section 8.1.5 Controller Parameters.

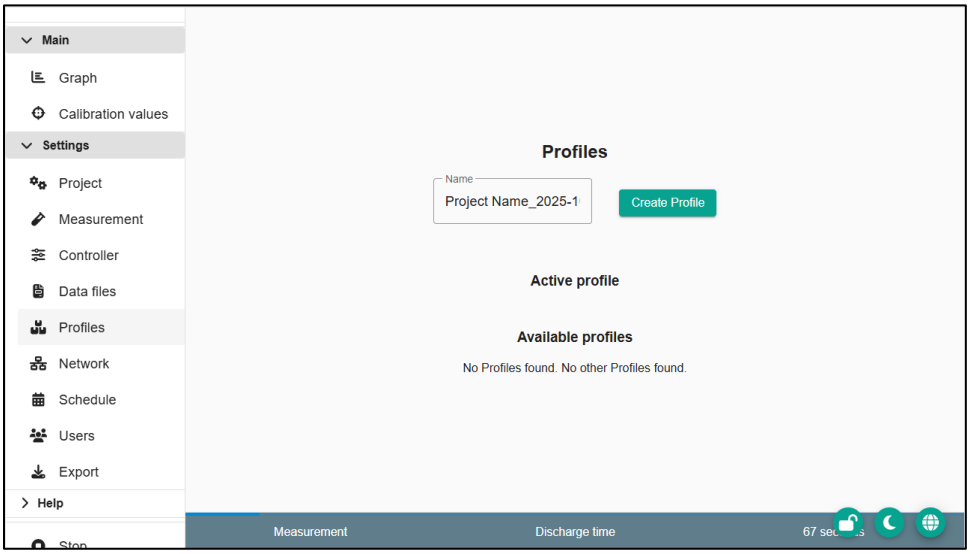


Data files

See section 8.1.2 Data Files.

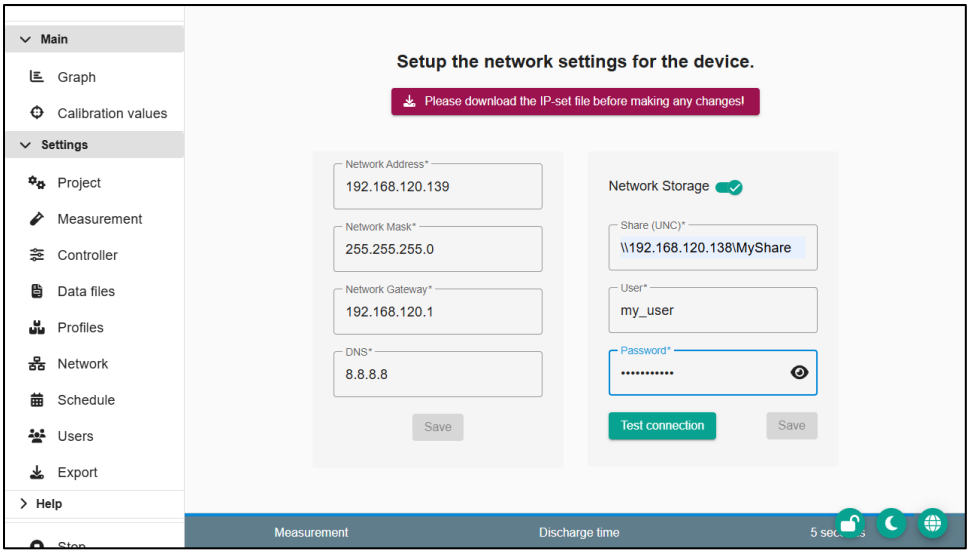
Profiles

A profile includes measurement parameters and other settings for a project type. For example, you may find it convenient to save profiles for different cell types or media, and then download the file to recreate the setup over multiple MAVEN Systems.



Network

Network settings should only be changed under supervision from your organization's IT department. Use the "Please download…" button at the top to export the backup IP settings to a USB drive before making changes. The USB drive can then be used to re-establish IP parameters if network changes make the MAVEN System inaccessible. See chapter 4 for more information.



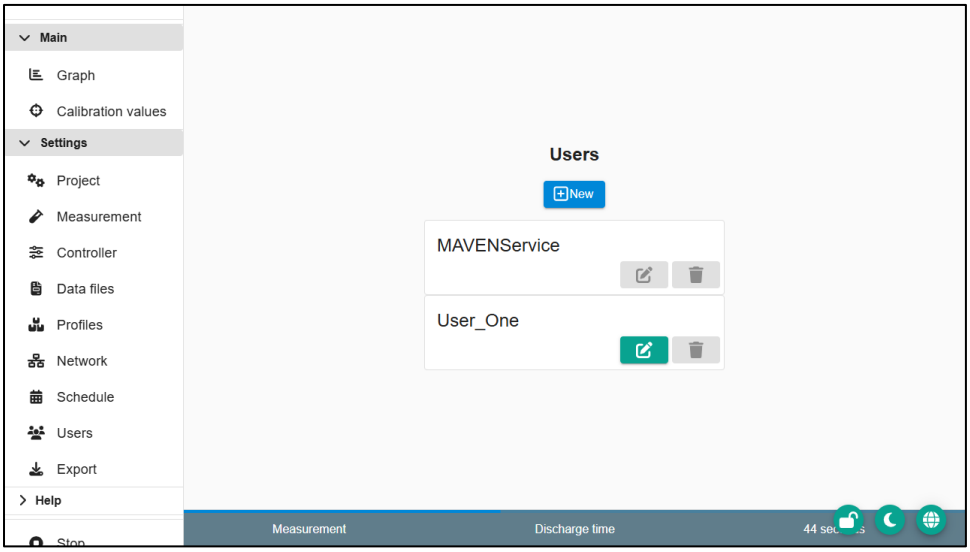
Schedule

See section 8.1.4 Schedule.

Users

A new user can be created by clicking +New.

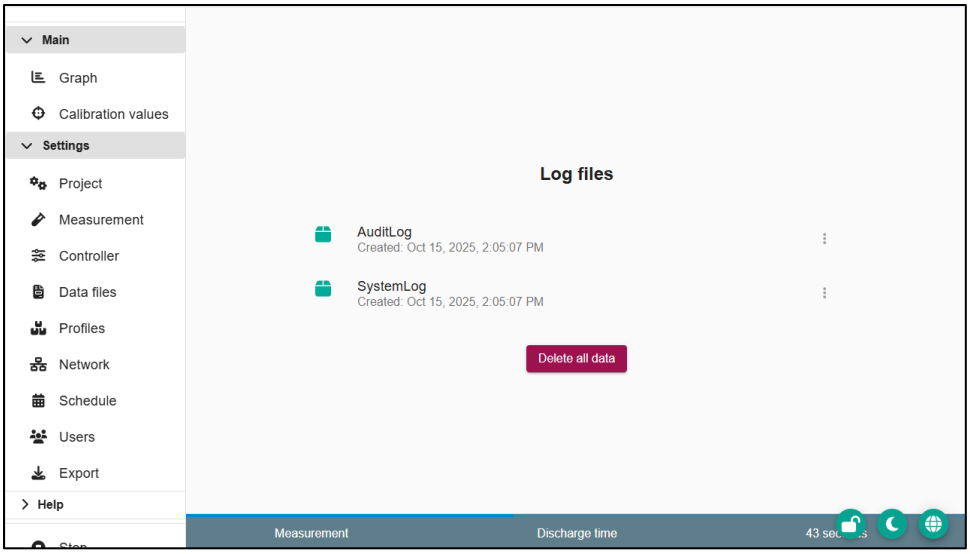
- **Non-Admin** users are permitted to operate all analytical functions on the MAVEN system, including calibration, starting measurements, and viewing the resulting data.
- **Admin** users are permitted to perform all the functions above, plus system administration tasks such as user account creation, changing network configuration and performing maintenance/support tasks.



Export

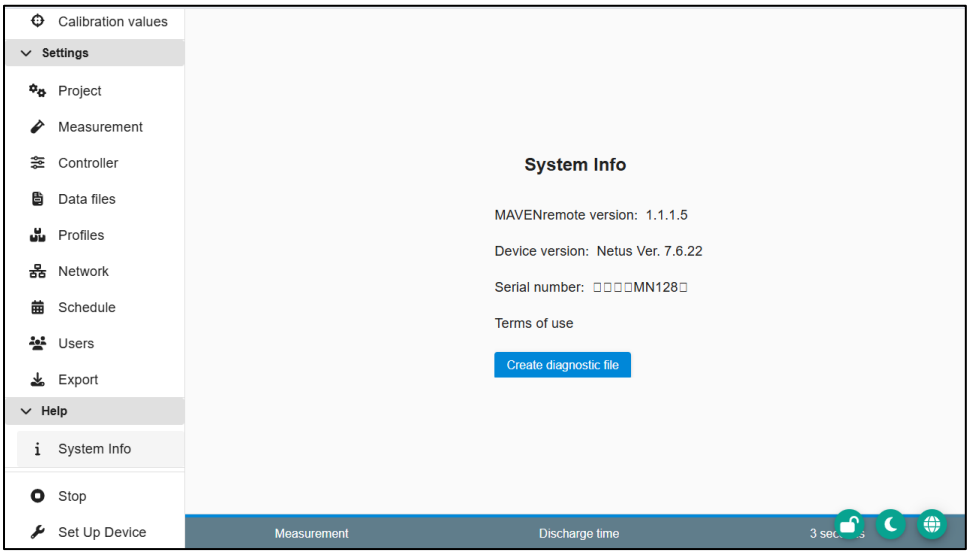
Audit logs and system logs can be exported here. System logs are only available when Network Storage is enabled (see above).

NOTE: *When "Delete all data" is pressed, all data is cleared from the system.* ***This data cannot be restored.*** *Please ensure all necessary data is saved before using this button.*



8.5 System Info

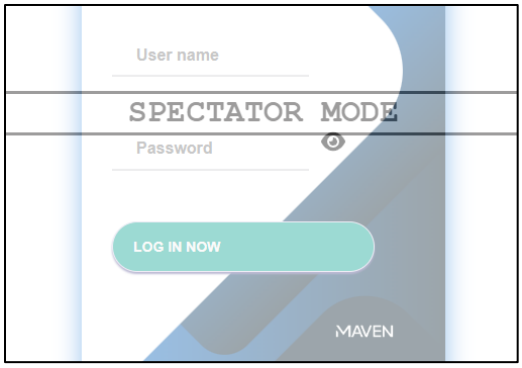
The System Info screen displays version numbers of MAVEN Remote and the internal device software, along with serial number of your device and the terms of use to review. It is also possible to create a diagnostic file containing technical system information; this is intended exclusively for Repligen service personnel.



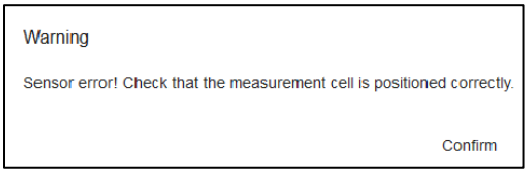
8.6 Error Messages

Spectator Mode

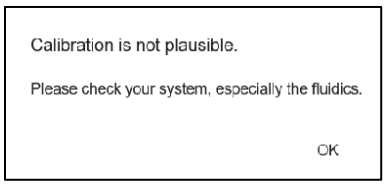
If you are already connected to your MAVEN System as the primary user on a different computer, other connection attempts will appear in Spectator Mode to prevent competing commands. Close MAVEN Remote on all other computers before trying to connect again.

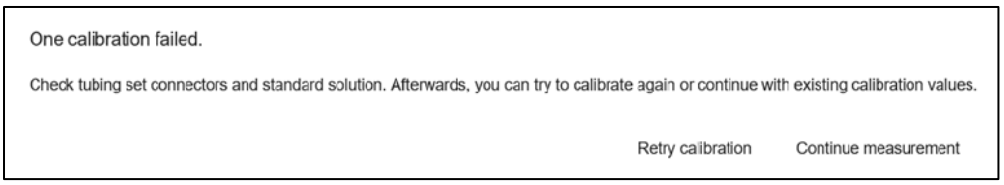


Sensor Error
Ensure that the biosensor is correctly mounted. See section 4.4 Mount Tubing Set.

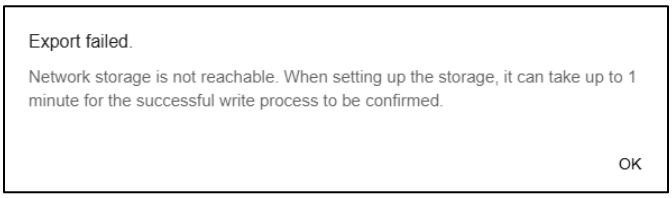


Calibration Error
There are two calibration errors. In either case, check the device and ensure that all fluidic connections are tight and that there is enough calibration standard solution in the bag.

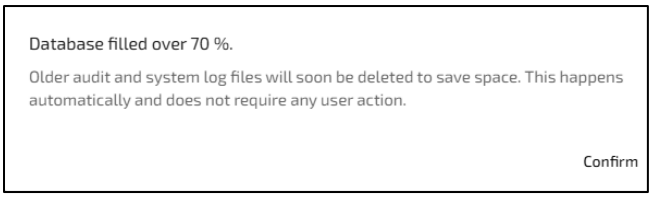




Export Failed
Make sure that the device and the network storage are connected to the same network. When setting up the storage, it can take up to 1 minute for the process to be confirmed as successful.



Database filled over 70%
Older audit and system log files will soon be deleted to save space. This happens automatically and does not require any user action. This does not affect data files or any log files exported to the network storage.



9. Feed Pump Connectivity

9.1 Analog and Serial Outputs

The MAVEN System can control a feed pump. The signal at the analog output is changed each time a new measurement is acquired and remains unchanged until the device is rebooted or a new tubing set is activated. Under Parameters (Settings > Parameters), the output format can be switched between 0–10 V and 2–10 V or 0–20 mA and 4–20 mA, respectively.

Table 5. Serial Output Specifications

Output	Description	Color
Analog	Glucose conc. output: 0/4–20 mA	White
	Glucose/Lactate conc. output: Ground	Brown
	Lactate conc. output: 0/4–20 mA	Green
	External feed pump: Ground	Yellow
	Glucose conc. output: 0–10 V	Gray
	Lactate conc. output: 0–10 V	Pink
	External feed pump: 0–10 V	Red
Serial	+5 V	Brown
	GND	Blue
	RX4	Pink
	TX4	Black

Measured values are available as analog signals for glucose (○ White) and lactate (● Green). An additional voltage output (● Red) is intended for connecting an analog-controlled external feeding pump and can be configured via the Parameter settings.

The serial output of the MAVEN System can be used to output measured values or to control a digital feeding pump. For connection to the analog and digital outputs, ready-made cables are available as accessories. Cables that are not used should be removed.

9.2 Open Platform Communications Unified Architecture (OPC UA)—Data Transfer Via TCP/IP

OPC UA is an open standard communication protocol for industrial automation developed by the OPC Foundation. It is manufacturer-independent and can be used for different kinds of data exchange.

The MAVEN System can act as an OPC UA server to send data to external clients, such as a process control system or a feed pump. This function is disabled at the factory but can be enabled in the MAVEN Remote web app. For more information, see KB25002 *MAVEN System OPC UA Integration* or contact technical support.

9.3 Data Transfer via Modbus – TCP/IP

Modbus TCP/IP is a standard communication protocol used in industrial automation for data exchange over Ethernet networks. It is a manufacturer-independent, open protocol, enabling easy integration between different devices and systems. The MAVEN System can operate as a Modbus TCP/IP server, allowing external Modbus clients such as process control systems, SCADA software, and feed pumps to connect and retrieve data over a network. For more information, please contact technical support.

10. Technical Information

10.1 Specifications

Table 6. System Specifications

Specification	Value
Measuring principle	Selective flow-diffusion with enzyme-based amperometric biosensor
Measuring range (glucose)	0.01–40 g/L
Measuring range (lactate)	0.05–10 g/L
Measuring frequency	Up to 30 per hour (every 2 minutes). User configurable.
Measurement precision (glucose)	<1.5% at 2.0 g/L
Measurement precision (lactate)	<1.5% at 1.0 g/L
pH range of bioreactor medium	4.8–9.2
Biosensor service Life	30 days or 5,000 analyses
Ambient operating temperature	15–35°C (59–95°F)
Ambient operating humidity	10–90% RH (non-condensing)
Communication interfaces	RS 232, Ethernet
Data exchange modes	OPC UA, Modbus TCP
Software requirements	PC operating system Windows XP, 7, 8, 10; Windows Server 2012 R2
Analog output options	0–10 V; 0–20 mA; 4–20 mA
Power requirements	100–120, 220–240 VAC ; 50–60 Hz
Device battery	Lithium (0.07 g, UN test 38.3) Type CR2032 (3 V)
Dimensions (W x H x D)	280 x 140 x 140 mm
Weight	3 kg
Device ingress protection rating	IP54

10.2 Front Panel LED Status

The front LED panel of the MAVEN System shows the device's operating status, separate from the operating software on your PC. The unmarked LED on top changes color based on the current state of the device.

Table 7. Front Panel Descriptions

LED Color	Status
⊗ Off	Boot process
Cyan, steady	Stopped
Cyan, flashing	Filling
Green & cyan, alternating	Premeasurement
Magenta & cyan, alternating	Cleaning
Green, steady	Measuring mode—loaded
Green, flashing	Measuring mode—unloaded
Yellow, steady	Standby—ready
Yellow, flashing	Interval—rest
Magenta, steady	Media change
Magenta, flashing	Rinse probe
Blue, steady	Sensor control / Reference—loaded
Blue, flashing	Sensor control / Reference—unloaded
Red	No network connection

11. Disposal

Packaging

If the packaging is no longer needed, it can be discarded according to local waste disposal and recycling guidelines.

Device

The device and accessories should not be discarded in regular household waste. European Directive 2012/96/EC on Waste Electrical and Electronic Equipment (WEEE) requires that electrical and electronic equipment be collected and disposed of separately from other unsorted municipal waste, with the aim of recycling it.

11.1 Hazardous Materials

The device does not contain any hazardous materials that would necessitate special disposal measures.

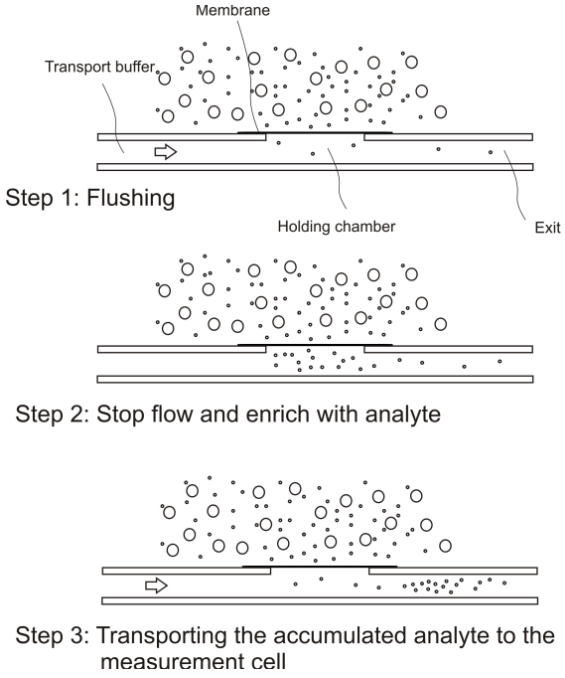
The cultures and solutions used during fermentation processes are potentially hazardous materials that could cause biological or chemical hazards.

Appendix 1: MAVEN System Referencing Guide

Theoretical Background

The sampling technique used by the MAVEN System is based on the principle of diffusion. By stopping the buffer flow behind the membrane, glucose and lactate molecules can migrate through the membrane and accumulate to a representative sample. The enriched buffer flow is then transported and measured at the sensor. The diffusion is described via Ficks's first law and is dependent on various parameters, including membrane dimensions (e.g. area, thickness), media characteristics (e.g. analyte concentration, viscosity) and process parameters (e.g. temperature). Many parameters are kept (nearly) constant, such as time, and analyte properties, while others depend highly on individual process parameters.

Without a reference measurement, the MAVEN System will qualitatively detect relative changes in glucose and lactate concentration and display a profile proportional to the absolute concentration profile. To obtain accurate, quantitative results, the reference measurement is necessary. The reference measurement captures the individual characteristics of the given process by comparing the measured signal with the current concentration of the process (obtained from the offline analyzer of your choice). The resulting reference factor is applied from that moment on to every new measurement and ensures precise and accurate monitoring of the process. In theory, as long as critical process parameters are constant, the reference value should remain constant throughout the process. However, changes in media composition, fouling of the membrane, etc. can make it necessary to reference again during the process. For more information, see the Best Practices section below.



Fick's first law:

$$dq = -D \cdot A \cdot \frac{dc}{dx} dt$$

Sutherland-Einstein equation:

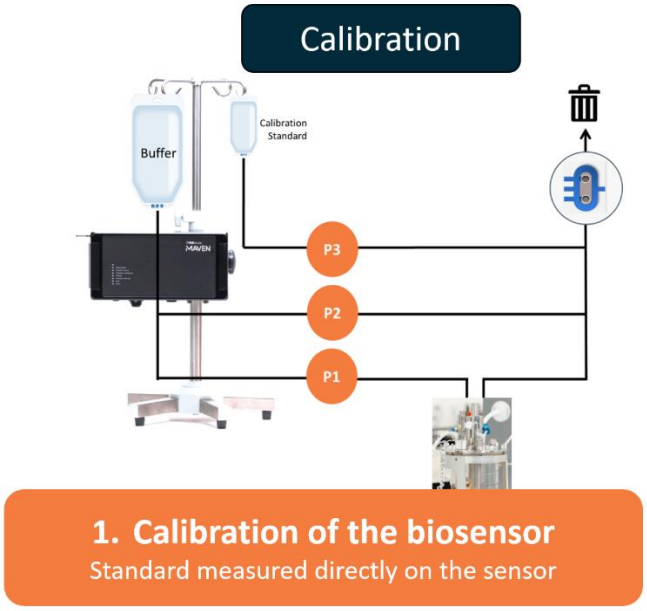
$$D = \frac{R \cdot T}{6\pi\eta r N}$$

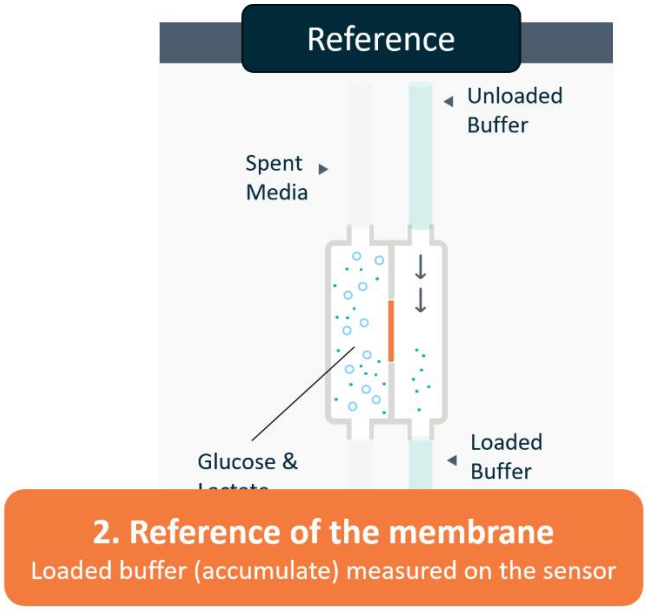
dq	Amount of substance diffusing
dt	Time
A	Membrane area
dc/dx	Concentration gradient
D	Diffusion coefficient
R	Molar gas constant
T	Temperature of media
η	Viscosity
r	Radius of particle
N	Lochschmidt number

Differences between Calibration and Reference

The purpose of performing a calibration is to quantify the activity of the enzymatic sensor. A calibration standard with a defined concentration is measured directly at the sensor and the calibration parameters are calculated. Since the enzymatic activity can decrease over time, we recommend a daily calibration to take this into account. You can easily set up a daily, automated calibration on the Schedule page in MAVEN Remote software.

The purpose of reference measurement is to determine the diffusion characteristics at the membrane. The reference measurement should only be performed once the process parameters are stable (especially process temperature) and a representative amount of glucose/lactate is present. More on best practices can be found below.





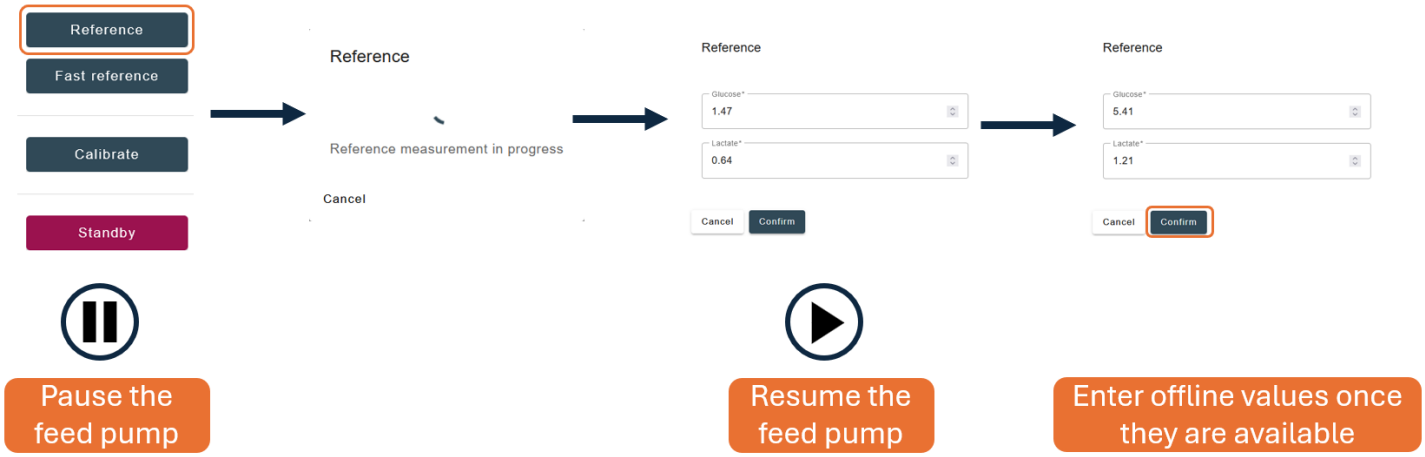
Differences between Reference and Fast Reference

In the MAVEN Remote software, there are two different buttons to perform a reference measurement: Reference and Fast Reference. Both buttons determine the diffusion characteristics by comparing the unreferenced reading to the actual concentration measured by the offline analyser, but they are designed for different conditions.

The Reference button starts a reference measurement, captures the signal at the time it is triggered, and saves it until the reference concentration is inserted and confirmed. This function is more accurate than Fast Reference, since it saves the signal at the moment when the offline sample is taken. It is highly recommended to use this function when there is a significant delay between the sampling and inserting the concentration, especially if the process is fast (e.g. microbial process) or there is active addition of glucose or lactate (feedback control) enabled during that time, since the deviation in concentration during that delay can cause a significant offset.

Important: Reference button should be triggered immediately before the offline sample is taken. Make sure you overwrite the default values with the values you obtained via your offline analyser.

If feedback control is enabled, accuracy can be improved by pausing the feed pump until the reference measurement is completed and the entry window (see screenshot below) appears. This is especially important if there is significant overshooting of the setpoint, which can cause concentration differences between offline sample and reference readings. If the process is tightly controlled, this step might not be necessary. Delays can be minimized if the MAVEN System continuously operates at high frequency when the reference measurement is triggered.



The **Fast Reference** button provides a faster option to enter the offline concentration measured. It eliminates the step of triggering the reference button prior to take an offline sample. In this case, the button would be triggered once the offline results are obtained and can be entered directly. This function should be only used if the offline result is obtained fast and the analyte concentration does not change significantly during that time (e.g. cell culture processes with low consumption rates) or the initial media concentration is known. If a significant change in concentration is expected in that time, the Reference function should be used.

Important: Do not use Fast Reference if you are actively feeding glucose or lactate!

Referencing using Flow Cells

The main principle of reference measurements apply equally to a flow cell setup as a diffusion probe setup. However, there are some considerations to keep in mind:

- The conditions at the flow cell are not as defined and stable as they are at the diffusion probe. Fluctuation of ambient temperature is higher than in a temperature-controlled bioreactor, which can cause deviations in measurements.
    - Even in rooms with air conditioning, fast temperature oscillations of ±1°C commonly occur.
- Mass transfer between media and the MAVEN side of the flow cell depends on pump speed of the bypass. For optimal performance, flow rate should be constant. If there is a change in flow rate, a new reference measurement might be needed to account of the change in properties.

Best Practices

Do	Don't
• Ensure process parameters are stable before the reference measurement is taken. • Prior to reference, let the MAVEN System operate at high frequency until the readings are stable (no air bubbles present in the system). • If sampling normally takes place at a fixed time of day, set up daily calibration about 1 hour beforehand. This can be done using the Schedule function. • Check deviations from offline samples after 24 hours and perform an additional reference measurement if needed. • Take a new reference if critical process parameters change (e.g. temperature) or if the deviation from the offline value is too high.	• Do not reference below 0.5 g/L (below 0.1 g/L in "method low") to ensure the reference measurement is representative. ○ If e.g. lactate is referenced below 0.5 g/L in the standard application, be aware that an additional reference might be needed to be accurate at higher concentrations. • Do not use Fast Reference when there is a significant time delay and/or fast-changing concentrations (e.g. feedback control). • Do not type "0" in the pop-up window; leave the field blank. • Small deviations between on- and offline measurements are normal due to variations in sample positions and measurement principles. There is no need to reference if there is no significant difference.

Appendix 2: Trace_mon Application

If the MAVEN Remote user interface is unsuitable for your lab environment, you may download and install Trace_mon, which provides the same functionality but in a local executable program.

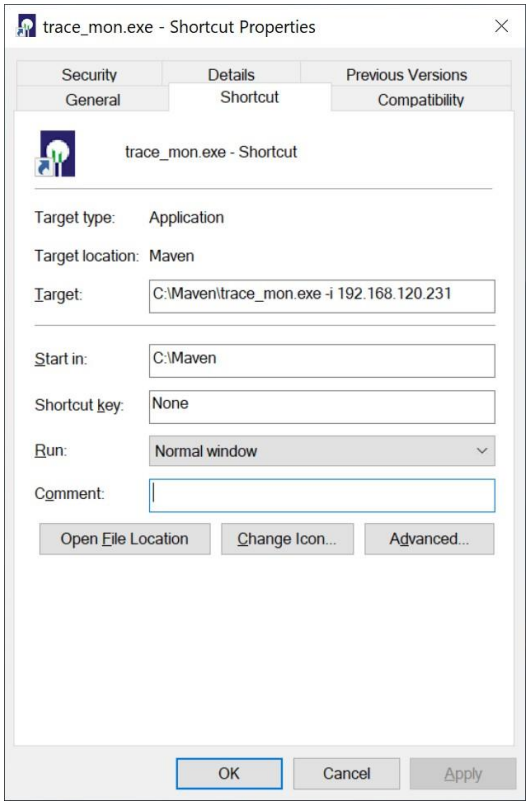
Table 8. Operational Checklist for Trace_mon

Item	Action	Section Reference	Page	☑
0	Initial Setup		40	
	Download and install the MAVEN System control software onto PC	Trace_mon—Installing the Operating Software	40	
	Ensure PC is set to “always on” and automatic sleep mode is disabled	Trace_mon—Installing the Operating Software	40	
1–4	Hardware setup	See main Table 1. Operational Checklist	43	
5	Switch on the device	Trace_mon—Start Up	45	
6	Launch PC software	Trace_mon—Start Up	45	
	Connect device	Trace_mon—Start Up	45	
	Initialize new tubing set	Trace_mon—Start Up	45	
7	Set operating parameters	Trace_mon—Setting Measurement Parameters	49	
	Review basic settings	Trace_mon—Start Up	45	
	Select measurement method and parameters	Trace_mon—Setting Measurement Parameters	49	
	Create log file to save measured values	Trace_mon—Start Up	49	
8	Start measurements	Trace_mon—Home Screen Commands	48	
	Click the “Fill" button and wait for the sensor control to initiate	Trace_mon—Start Up	49	
	Alternative: Activate the "automatic start" option	Trace_mon—Start Up	49	
9	Check the biosensor for air bubbles	4.5. Connect Supply and Discharge Lines to Diffusion Probe	18	
10	Perform reference measurement/calibration	Trace_mon—Calibration	46	
	Reference with an external sample or a known measured value	Trace_mon—Calibration	46	
11	Optional: connect analog outputs to process control system	Feed Pump Connectivity • 8.1 Analog and Serial Outputs • 8.2 Open Platform Communications Unified Architecture (OPC UA)—Data Transfer Via TCP/IP	50 36	
		Trace_mon—Feed Pump Control • Proportional Integral Derivative (PID) Control • Min-Max Two-point Controller	50 51	
		Trace_mon—Scheduling Actions • Events • Workflow	51 52	

Trace_mon—Installing the Operating Software

Prior to installing the operating software, please make sure the MAVEN System is connected to your network via either option A (Direct Connect) or B (Gateway PC) as described above in “Network Setup.” Contact technical support to download the installation and setup files.

To install the operating software on your computer, run setup_tracemon.exe. You will be prompted to enter a new IP address, overwriting the factory preset IP address (Option A). If you have not changed the IP address (Option B), click Next. If you change the IP address, follow these steps to update the start settings in the program shortcut to ensure that the device connects automatically:



1. Go to your desktop.
2. Right-click the trace_mon.exe shortcut icon.
3. Select Properties.
4. In the Target field, after ".exe", type " -i " (include spaces before and after), followed by your new IP address.
5. Confirm the change by clicking Apply.
6. Click "OK."

The software will start the device at the specified IP address and connect to the device automatically.

During installation, you will also be prompted to specify data storage locations.

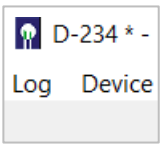
Make sure that the PC remains permanently active and does not switch to energy-saving/stand-by mode, which may result in incorrect measurements or lost data.

Trace_mon—Start Up

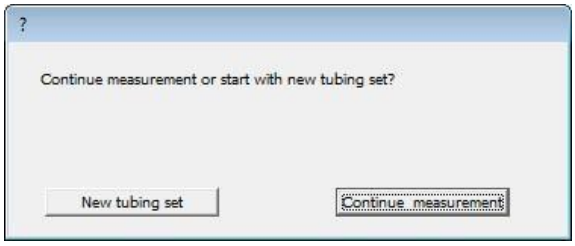
1. Activate the power switch at the bottom of the device.

2. Double-click the Trace_mon icon on your desktop to start the application.

3. Wait for automatic connection between PC and the MAVEN System.

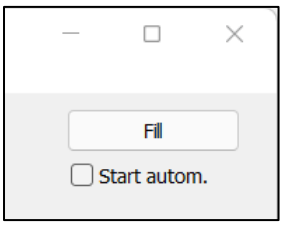


4. A dialog box will appear.
   - Choose “New tubing set” if you have changed the tubing set or if a longer interruption has occurred. In this case, it is recommended to perform a sensor check before continuing with further measurements. (See section 7.3 Calibration)
   - Choose “Continue Measuring” to use the same calibration values as before. No flushing processes or sensor checks will be performed.



Tip: *If the MAVEN System is taken out of service for less than two days, it may be left standing, filled with buffer. If the system is not used for a longer period, the tubing set must be changed before restarting.*

5. Navigate the menu to **Log > New** to create a new *.bpd file to store your data. The MAVEN System will not store your data unless a file is created first.
6. Navigate the menu to **Settings > Basic Settings** and check the box for “Adjust time” to ensure that the MAVEN System clock matches the PC clock.
7. Click OK.
8. Click the Fill button and wait for sensor calibration to initiate.



Notes: *This process will flush buffer through the tubing and run pre-measurements to ensure that the sensor system is in a stable state. This initial process takes 40–60 minutes. Review the section on Calibration in this guide for more information. After priming, the instrument enters the standby state, ready to take measurements.*

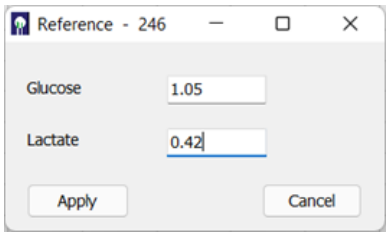
You may also activate the "Start autom." checkbox to automatically begin measurement immediately after the priming process, however, this will skip the calibration/referencing step. If you choose to automatically start the system, make sure all tubing is properly connected to the bioreactor.

Trace_mon—Calibration

Calibration of the MAVEN System is a two-step process:

1. The sensor is calibrated using the MAVEN System Calibration Standard Solution. It is recommended to calibrate the MAVEN System once per day. There are several ways to start this process:
    - Click the "**Sensor control**" button on the home screen
    - Auto sensor control, after a set number of measurements (see section 7.1.2 Measurement Parameters)
    - Automatically via the scheduler (see section on Scheduling Actions in this guide)
    - Automatically via the workflow (see section on Scheduling Actions in this guide)

2. The **probe membrane** diffusion factor must be calibrated to account for the environmental conditions inside the bioreactor. This process is accomplished through the "**Reference**" or "**Fast Reference**" buttons on the home screen.
    - **Reference:** should be used when the user plans to take samples to confirm measurements from the MAVEN System with off-line analysis. After clicking the Reference button, a dialog box pops up, displaying current measurements. After you enter confirmed measurements from off-line analysis and click "Apply," the MAVEN System will calculate a new reference factor based on the two values.
    - **Fast Reference:** allows the user to enter known concentration values of the medium before the reference measurement is made.



Tips

After starting your process, it is recommended run another sensor calibration and reference factor after 12 hours and 36 hours. Afterwards, continue to calibrate daily.

(0h): Calibration + Reference → Start
(12h): Calibration + Reference
(36h): Calibration + Reference
(After, daily): Calibration

Do not overwrite low lactate reference measurements at the start of your culture.

At the start of cultivation, the culture typically has abundant glucose and no lactate. When performing a reference, the device suggests a value after the reference measurement, which is usually overwritten by entering a known value. If the existing lactate concentration is still very low, do not overwrite this value at first (the reference factor for lactate then remains at 1.0). As cultivation continues, increase in lactate concentration can be better observed and a normal referencing, in which both values are overwritten, can be carried out at the appropriate time.

Trace_mon—Home Screen Commands

After the priming process is complete, the Fill button will be hidden, “standby” will appear in the status bar at the bottom of the window, and commands will appear in the lower right of the window. You are ready to begin measuring with the MAVEN System.

Table 9. Trace_mon: Home Screen Functions

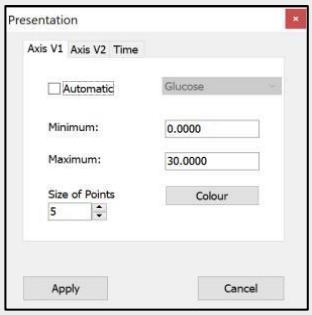
Function	Details
Start	Begins measuring. This command can also be scheduled for a specific date and time using the Schedule menu.
Standby	Ends the current action of the device. This command can also be scheduled for a specific date and time using the Schedule menu.
Sensor Control	Begins a sensor calibration cycle. This command can also run automatically: • Auto sensor control (after a set number of measurements). See section 7.1.2 Measurement Parameters. • Scheduler entry—see Trace_mon—Scheduling Actions (page 51).
Single Sample	Begins a spontaneous, unscheduled single measurement. This function can be useful during long pauses between intervals. The current measurement program is not interrupted, and scheduled intervals are retained. This command can only be triggered if there is sufficient time to perform the measurement.
Reference	See Trace_mon—Calibration (page 46).
Fast Reference	See Trace_mon—Calibration (page 46).
Workflow Active	When checkbox is activated, the schedule list will run. If this box is unchecked, the measuring sequences from the default parameter list are processed instead. See Trace_mon—Scheduling Actions (page 51).
Graph Area	Plot parameters can be adjusted at any time by right-clicking in the graph area, which opens a popup (pictured right) allowing the user to change point sizes, colors, and axis scales. The left y-axis (Y1) corresponds to glucose, and the right y-axis (Y2) corresponds to lactate. Units are g/L. By default, the values for glucose are displayed in blue and lactate in red. **Zoom in**: click-and-drag a box diagonally from left to right. **Pan/move the graph**: Right-click and drag in the desired direction. **Zoom out:** Click-and-drag in the plot area from right to left. 

Table 10. Trace_mon: Menu Functions

Function	Options	Details
Log	New	Creates a new *.bpd file, which records all measured values in a text format (also plotted on the on-screen graph). By default, this is stored in the "Data" subfolder. The MAVEN System will not store your data unless a file is created first.
	Load	Displays measurement data from an existing file
Device	Connect	Connects a new device. Any new device must have its IP address configured before further measurement can take place.
	Setting up operation	Overrides previous sensor activity and reference data after changing the tubing set. Requires a new priming of the tubing system.
	Cleaning	Starts automatic cleaning cycle; recommended if the system will be idle for more than two days. Connect supply and buffer lines to the cleaning solution. Once the cleaning solution container is empty, repeat the process with deionized water to ensure no salt residues remain.
	Stop	Suspends measurements and halts pump activity. You may close the software and switch off the device without affecting the biosensor or calibration data. When restarting, the system will check whether tubing sets
Display	Print Diagram	Sends the graph currently shown on screen to your printer.
	Sensor activity	Opens a pop-up window showing the residual activity of the biosensor module relative to its activity at start-up; 1.00 corresponds to 100%. The slope and reference factor (“Reference fr”) are also displayed. Clicking the "Reset references" option resets the reference factor to 1.0.

	Sensor History	Opens a pop-up window showing recent activity values. Right-click to save the biosensor module history as a *.txt file.
	Status	Shows/hides status bar at the bottom of the window. Field 1 shows the number of pending group measurements (or pre-measurements). Field 2 counts down the time until the end of the current action (in seconds). Field 3 shows the remaining time in the interval of the measurement period (in seconds).
Settings	Parameters	Allows user-specific setting of measurement frequency, frequency of sensor checks, data transmission, etc. See Trace_mon—Setting Measurement Parameters below for more details.
	Basic settings	Changes general information about the device and the project, which will later be used in the data output. This is where you can choose glucose and lactate or glucose-only modes, in addition to synchronizing system clocks between device and PC.
	Language	Choose a different language for menu navigation. Current options include Chinese, English, French, German, Italian, and Spanish.
Schedule	—	See Table 14 Schedule Display Functions.
Controller	—	See Table 13 Trace_mon—Setting Measurement Parameters.
Login	—	Contains options to set up individual user logins and access levels.
Information	—	Displays version numbers of the device firmware, trace_mon control software, and device serial number.

Trace_mon—Setting Measurement Parameters

In the menu, navigate to **Settings > Parameters**. All relevant parameters for the measuring operation can be set in this window.

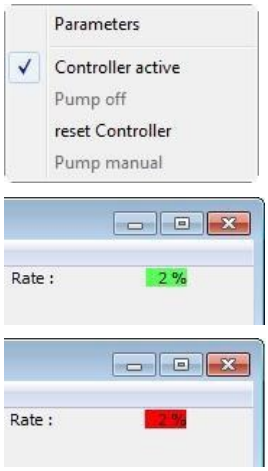
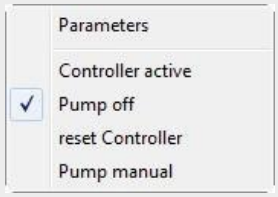
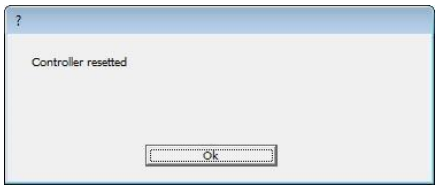
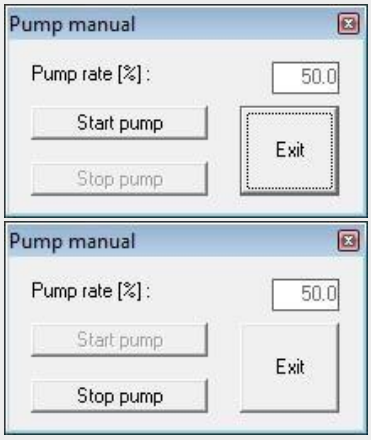
Table 11. Trace_mon—Setting Measurement Parameters

Parameters	Details
Measuring period	Enter the desired measuring interval here. A value of 1 means measurement is performed every minute (this is also the maximum frequency). A value of 60 means once per hour. You can change of the frequency any time and it becomes effective immediately after clicking “OK.”
Auto sensor control	Yes/No. If this option is activated, an automatic sensor calibration takes place every X measurements (see “Measurements between sensor controls” below).
Measurements per group	In the case of larger measurement intervals, it can be useful to run several measurements in quick succession at a desired time, for example, a group of 10 measurements every 6 hours. You can set the number of measured values in the group here. Each value is output directly after measurement, not an average. If the time necessary for processing the group is longer than the measuring period, then the next group starts with the new measuring interval.
Measurements between sensor controls	Set the number of measurements before an automatic sensor calibration occurs. Requires “Auto sensor control” to be enabled. For example, if measuring period is set to every 2 minutes and “measurements between sensor controls” is set to 30, then a sensor calibration will take place every 60 minutes. You can also trigger a sensor calibration at any time by pressing the "Sensor control" button. When changing the auto sensor control setting during operation, the changes will apply with the next control.
Output range glucose / Output range lactate	Set ranges of the analog outputs here. The procedure is as follows: The upper limit of the measuring range is always specified. The lower limit is preset to 0. With a desired measuring range of e.g. 0–10 g/L glucose, Glucose 10 (upper limit) is set for the output range. When selecting the voltage range 0–10 V, 10 volts then correspond to 10 g/L glucose.
TRACE SeMDaP— Data output via serial interface	The TRACE SeMDaP is a protocol to output data via an interface. Standard is the serial interface. The protocol contains telegrams of variable length and variable contents. This function is switched off at the factory and can be activated here. For more details about the protocol, please contact Repligen Customer Service.
OPC UA— Data transfer via TCP/IP	The device can act as an OPC UA server and send data to external clients. This function is switched off at the factory and can be activated by the end-user. Please read the section on OPC UA in this guide for more information.

Trace_mon—Feed Pump Control

Under the **Controller** menu are options to help you set parameters for automating an external feed pump via the serial interface or analog output on the bottom of the device.

Table 12. Trace_mon—Feed Pump Control

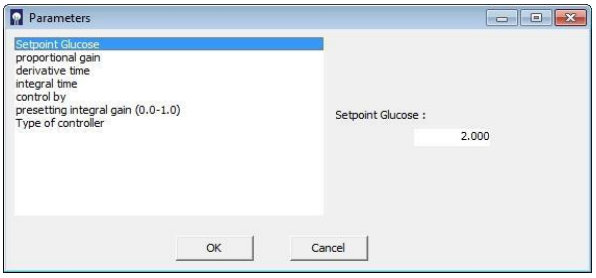
Screen Prompt	Details
	When "**Controller active**" is selected, the controller function is switched on and the feeding pump is activated. • While the controller function is active, the pump cannot be switched off or operated manually. • When the controller function is active, a green field appears in the main window indicating the current delivery rate (0–100%) of the feed pump. If the pump is turned off, the background turns red. Un-check "Controller active" to deactivate the controller. Although the controller is now inactive, the feeding pump will continue to run at the rate last set by the controller.
	With "**Pump off**", the feeding pump is switched off manually. It can then only be switched on again by reactivating the controller.
	In order to avoid a too high influence of the integral gain on the PID- controller at the beginning, the integral gain can be reset to the pre-set value by the "**Reset Controller**" command at any time. Click "OK" to save. ***Note:*** *This function has no effect on the Min-Max controller.*
	The "Pump manual" function can be used to fill the feeding tube. In this operating window, the pump rate can be set and the pump can be started or stopped. ***Note:*** *After clicking "Exit" or closing the window, the pump is stopped automatically—do not close this window if you require the pump to continue operating.*

To choose between PID control or Min-Max control, navigate to Controller > Parameters in the menu.

Proportional Integral Derivative (PID) Control

If you are using the PID control function, click on the individual options within the Parameters window to set the ideal glucose levels, proportional gain, integral time, and derivative time.

Under "Set via" option, you can select whether the control acts on an external pump via the serial interface or the analog output 3.



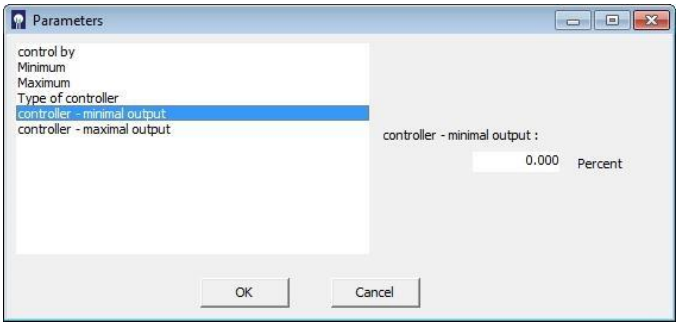
Microbial Culture Recommended PID Settings		Cell Culture Recommended PID Settings	
P	0.1–0.5 %/conc. (depending on the concentration of the feed, maximum delivery rate of the pump, pump tubing diameter, reactor volume, etc.)	P	0.01–0.1 %/conc. (depending on the concentration of the feed, maximum flow rate of the pump, pump tubing diameter, reactor volume, etc.)
I	45 min (reset time)	I	60 min (reset time)
D	2 min (lead time)	D	1 min (lead time)

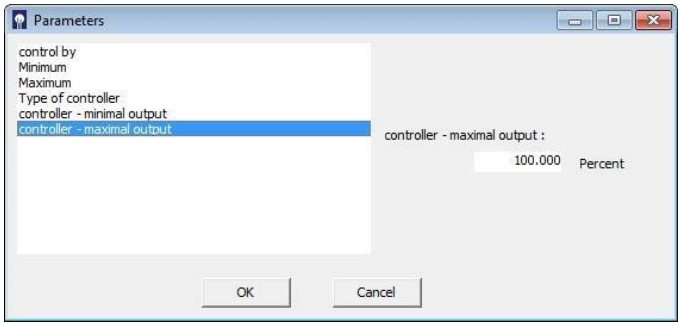
Notes:

- In most cases, adjustment of the P factor is sufficient and the I and D values can be maintained at the recommended value. If the feeding rate is too high, reduce the P-value. If the feeding rate is too low, increase the P-value.
- To avoid a too high integral gain (I-component) of the PID controller at the beginning, the I-component of the controller can be reset to the default I-component at any time with the "Reset controller" command.
- It is recommended to always reset the controller after filling the feeding line or in case of unknown history to avoid overdosing.

Min-Max Two-point Controller

After selecting the Min-Max control, the minimum and maximum values for the control can be entered in Parameters. The min-max controller switches the feeding pump to the minimum delivery rate or maximum delivery rate when the limit values are exceeded or not reached, respectively. "Minimum control value" and "maximum control value" set the minimum and maximum delivery rates of the pump. The default settings here are 0% and 100%.





Trace_mon—Scheduling Actions

The Schedule menu allows you to set actions at specific times (Events tab) or regular intervals (Workflow tab).

Events

Events are actions set to fixed points in time, *e.g.*, “next Tuesday at 9:30”.

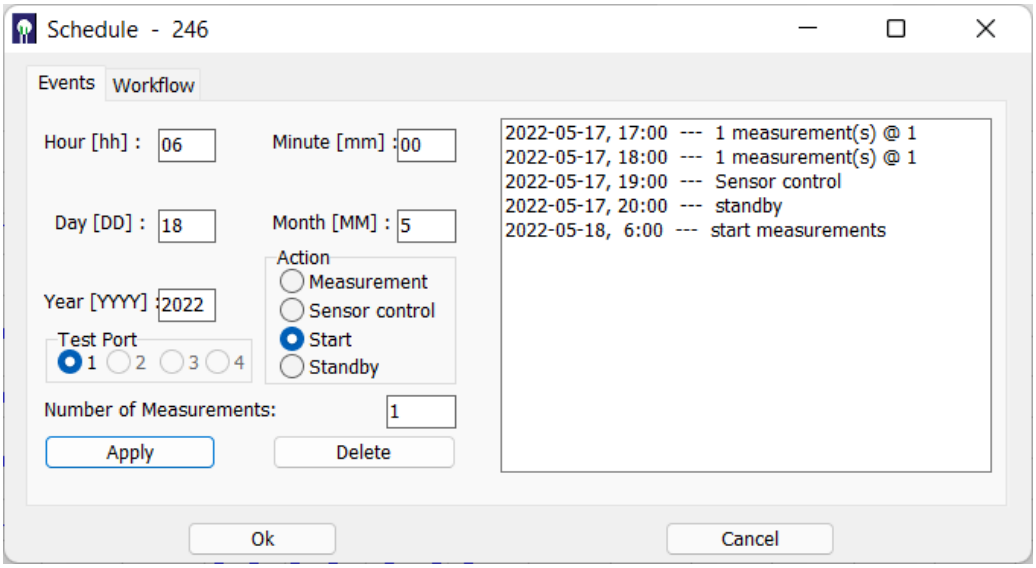


Table 13. Schedule Display Functions

Parameter	Details
Hour [hh], Minute [mm] Day [DD], Month [MM], Year [YYYY]	Sets time and date of event. *Note that 24h format is used, so 1:00 pm should be written as 13:00.*
Action	Choose between Measurement, Sensor control (calibration), Start, or Standby
Number of Measurements	This field corresponds to “Group” in the parameter list. Enter the number of measurements to take place at the specified time.
Apply	Transfer the current settings to the list box on the right. Actions are automatically sorted earliest to latest.
Delete	Removes the highlighted event from the list.
OK	Saves all entries.
Cancel	Discards changes.

Notes:

- Schedule Events are always treated with higher priority than others, e.g., actions from the Workflow tab or the main parameter list. If an action from another source needs to run during a scheduled event, the system waits until the scheduled action is finished. For example, you may schedule the MAVEN System to come online (start) and go back into standby at specific times. While online, the MAVEN System will execute auto-calibrations and measurements according to the main parameter list.
- After a scheduled event has been carried out, the entry is removed from the list and does not reappear when the schedule is reopened later—only the events that are still pending are displayed.
- Duplicate entries are ignored.
- For simultaneous entries, only the command further up is processed.

Workflow

Workflow creates a sequence of actions to happen at specific regular intervals.

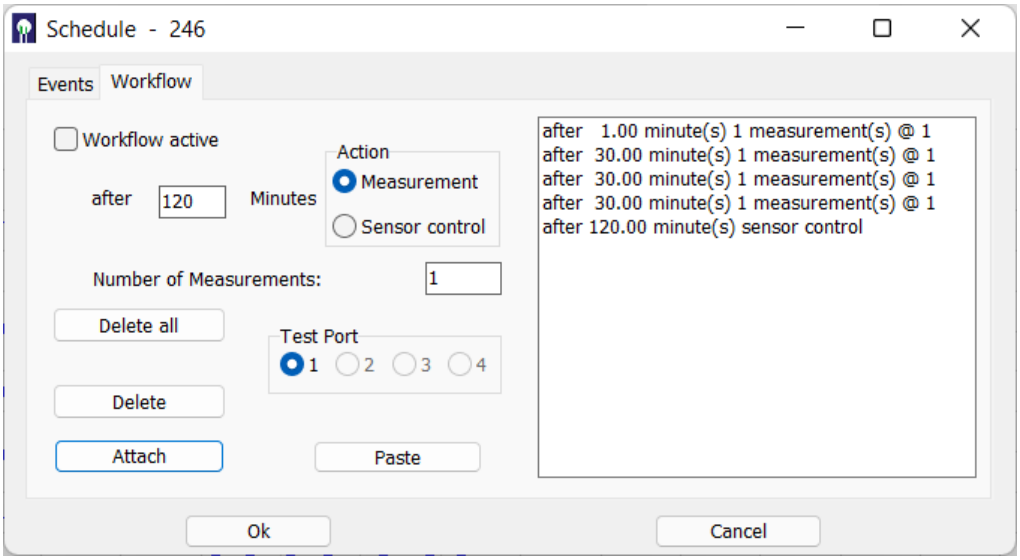


Table 14. Workflow Display Functions

Function	Details
Workflow active	When checkbox is activated, the schedule list will run. If this box is unchecked, the measuring sequences from the default parameter list are processed instead.
after ___ minutes	Enter the desired time interval between individual actions. ***Note:*** *If "1" is entered here, the next action takes place after a probe flush. By selecting larger intervals, the measuring frequency is reduced accordingly.*
Number of Measurements	Enter the number of measurements to take place at the specified interval. *This field corresponds to "Group" in the parameter list.*
Action	Choose between Measurement or Sensor control (calibration)
Attach	Appends the current settings to the workflow list box as the last entry.
Paste	Inserts the current settings above the selected line in the workflow list box.
Delete	Removes a selected line from the workflow list.
Delete All	Removes all entries from the list box.
OK	Saves all entries.
Cancel	Discards changes.

Notes:

- The time interval selected for the first action in line 1 only becomes active during the second run of the list. This ensures that processing of the list is started immediately after the start. During the second run, the selected interval then also applies to the action in line 1.
- The list repeats until stopped or device is placed in standby mode.

Trace_mon—Data Transmission, Storage, and Visualization

The MAVEN System offers several output options for easy, flexible integration into your data recording system.

- The MAVEN System can act as an Open Platform Communications Unified Architecture (OPC UA) server to transfer data to another device (PC, process control system) on your local network.
- Standard analog output for signal ranges from 0 to 20mA, 0 to 10V, or 4 to 20mA.
- Ethernet connects the device to a PC via a network. If the network connection between the device and the PC is interrupted, data will be buffered within the device until a connection is restored. The missing data is then automatically transferred to the trace_mon software.
- The supplied software allows you to configure and control measurements as well as a feeding pump.
- Measurements are plotted directly on screen and stored as text in a user-defined log file. The user must start a new log file PRIOR to data acquisition in order to access the data. This file is saved as a .bpd file in the default subdirectory “Data” and can be exported in a spreadsheet format.
- Data will include date and time of measurements, temperature*, glucose, and lactate levels. If the controller is active, the respective delivery rate (1–100%) is also recorded.

**Note:* *Temperature data comes from bioreactor controller if your equipment supports it. The MAVEN diffusion probe does not provide temperature data.*

Data transfer to Excel via Macro

The easiest way to transfer data from the MAVEN System is through a macro, which is available by contacting technical support. The macro will help transfer the data into a table and plot the points on a graph.

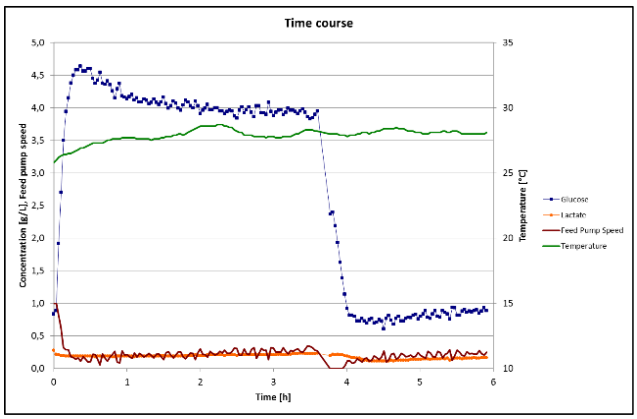
To use the Macro:

- Open “Macro_bpd.xlsm”
- Start the transfer by pressing ctrl + M on your keyboard
- The macro will generate a table and graph in Excel, similar to the examples below:

Figure 7. Macro table example.

Date	Time	Reactor No.	Temperature	Glucose	Lactate	Feed pump sp	Time of Exp.
23.04.2015	09:13:59	0	25,800	0,840	0,280	1,000	0,000
23.04.2015	09:15:59	0	26,000	0,890	0,220	1,000	0,033
23.04.2015	09:17:59	0	26,200	1,920	0,210	0,828	0,067
23.04.2015	09:19:59	0	26,300	2,700	0,200	0,633	0,100
23.04.2015	09:21:59	0	26,400	3,500	0,200	0,322	0,133
23.04.2015	09:23:59	0	26,400	3,940	0,190	0,288	0,167
23.04.2015	09:25:59	0	26,500	4,150	0,190	0,289	0,200
23.04.2015	09:27:59	0	26,500	4,380	0,190	0,185	0,233

Figure 8. Bioreactor Temperature



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