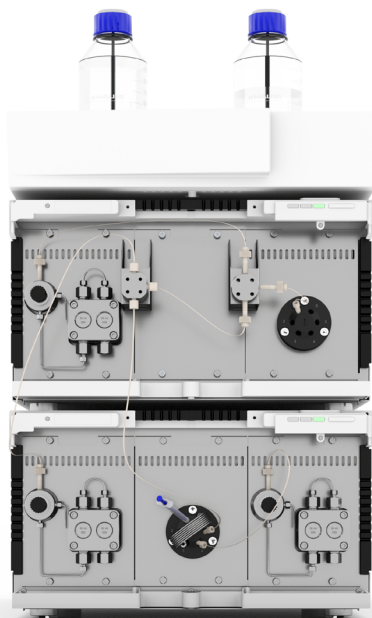


Science with Passion



AURA

IJM NanoScaler System Instructions



Document no. V6776



Note: For your own safety, read the instructions and follow the warnings and safety information on the device and in the instructions. Keep the instructions for future reference.



Note: In case you require this instruction in another language, please submit your request including the corresponding document number via e-mail or fax to KNAUER.

Support: Do you have questions about the installation or the operation of your instrument or software?

International Support:

Contact your local KNAUER partner for support:

www.knauer.net/en/Support/Distributors-worldwide

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These instructions apply to products with the product number A48035/A48035V1 and A48040XYZ. Also valid for variants with A48040XYZ. X, Y, Z = 0-9, or A-Z, or blank.

The information in this document is subject to change without prior notice. For the latest version of the instructions, visit our website: www.knauer.net/library.



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1. General

1.1 About these instructions

These operating instructions enable the safe and efficient operation of the device. The user must have carefully read and understood these operating instructions before starting any work.





The basic prerequisite for safe operation is compliance with all safety instructions (see chapter 2 on page 3). In addition to the safety and warning instructions in these operating instructions, the local accident prevention regulations and the national industrial safety regulations apply.

These operating instructions are an integral part of the device. It must be kept in the immediate vicinity of the device and accessible to the user at all times.

You can download these and other instructions from the KNAUER website: www.knauer.net/library

1.2 Signal words

Possible dangers related to the device are distinguished in personal and material damages.

Symbol	Meaning
	DANGER (red) indicates a highly hazardous situation. If not avoided, it will result in death or serious injury.
	WARNING (orange) indicates a hazardous situation. If not avoided, it could result in death or serious injury.
	CAUTION (yellow) indicates a moderate hazardous situation. If not avoided, it could result in minor or moderate injury.
	NOTICE (blue) is used to address issues which are not related to physical injury.

1.3 Additional typographical conventions

Note: Specific information are prefixed with the word "Note" and an information icon.

 **Note:** This is an example.

1.4 Legal information

1.4.1 Liability limitation

The manufacturer is not liable for the following issues:

- Non-compliance of these instructions
- Non-observance of necessary safety precautions
- Improper use
- Operation of the device by unqualified personnel (see chapter 2.2 on page 3)
- Use of non-approved spare parts
- Technical changes by the user such as opening the device and unauthorized modifications
- Violations of General Terms and Conditions (GTC)

1.4.2 Transport damage

The packaging of our devices provides the best possible protection against transport damage. However, check the packaging for transport damage. In case you notice any damage, inform the Technical Support and the shipping company within three workdays.

1.4.3 Warranty conditions

For information on warranty please refer to our general terms and conditions on the website: www.knauer.net/terms

1.4.4 Warranty seal

A blue or orange warranty seal is affixed to some devices.

- A blue seal is used by KNAUER's Manufacturing or Customer Support for devices to be sold.
- After repair, service technicians attach an orange seal onto the identical position.

If unauthorised persons tamper with the device or if the seal is damaged, the warranty will lapse.



1.4.5 Declaration of conformity

The declaration of conformity is enclosed as a separate document with the product and can be obtained online:

www.knauer.net/en/Support/Declarations-of-conformity

2. Basic safety instructions

The device has been developed and constructed in such a way that hazards arising from its intended use are largely excluded. Nevertheless, the following safety instructions must be observed in order to exclude residual hazards.

2.1 Intended use

Only use the device for applications that fall within the range of the intended use. Otherwise, the protective and safety equipment of the device could fail.

2.1.1 Operating ranges

The device is intended to be used indoors for chromatographic applications.

2.1.2 Foreseeable misuse

Refrain from the use of the device for the following purposes or conditions:

- Medical purposes. The device is not approved as a medical product.
- Operating outdoors. Otherwise, the manufacturer does not guarantee the functionality and safety of the device.
- Operation in potentially explosive areas without special and additional explosion protection. Contact the KNAUER Customer Support for more information.

2.2 User qualification

The users are qualified to handle the device if all of the following points apply:

- They have completed training as pharmaceutical-technical assistants or chemical-technical assistants or comparable vocational training.
- They have fundamental knowledge of the technical equipment for the formulation of lipid nanoparticles.
- They have knowledge about the properties of the used solvents and their health risks.
- They are trained for the special tasks and activities in the laboratory and know the relevant standards and regulations.
- Due to their technical training and experience, they can understand and carry out all the work described in the operating instructions on the instrument and recognize and avoid possible dangers independently.
- Their ability to react is not impaired by the consumption of drugs, alcohol or medication.
- They have participated in the installation of an instrument or training by KNAUER or an authorized company.

If users do not meet these qualifications, they must inform their supervisors.

2.3 Operator responsibility

The operator is any person who operates the device himself or leaves it to a third party for use and who bears the legal product responsibility for the protection of the user or third parties during operation.

The obligations of the operator are listed below:

- Know and follow the applicable work safety regulations
- Identify hazards arising from the working conditions at the place of use in a risk assessment.
- Set up operating instructions for the operation of the device.
- Regularly check whether the operating instructions correspond to the current status of the regulations.
- Clearly regulate and specify responsibilities for installation, operation, troubleshooting, maintenance and cleaning and set clear rules
- Ensure that all personnel who work with the device have read and understood these operating instructions
- Train the personnel who work with the device at regular intervals and inform them about the dangers.
- Provide the necessary safety equipment to the employees working with the unit (see section below).

2.4 Personal safety equipment

The protective measures required in the laboratory must be observed and the following protective clothing worn during all work on the device:

- Safety glasses with side protection
- Protective gloves in accordance with the prevailing ambient conditions and used solvents (e.g. heat, cold, protection against chemicals)
- Lab coat
- Personalised protective safety equipment which is specified in the particular laboratory.

2.5 Safety features on the device

- Power switch: Devices of the AZURA® L series may be switched off using the power switch (toggle switch on the back side of housing) at any time, this causes no damage to the device. To switch off devices of the AZURA® S series, remove the plug from the power socket or use the toggle switch of the power supply unit.
- Front cover: Devices of the AZURA® L series have a front cover as a splash protection for the user
- Leak tray: Devices of the AZURA® L series have a leak tray on the front side. The leak tray collects leaking solvents and protects components from potential damage caused by discharging liquid.
- Lamp: For the detectors AZURA® DAD 2.1L, DAD 6.1L and MWD 2.1L, the lamp switches off automatically when the cover is opened.

2.6 Working with solvents

2.6.1 General requirements

- The user is trained for handling different solvents.
- Note recommended solvents and concentrations in these instructions in order to avoid personal injury or damage to the device. For example, certain chemicals may cause PEEK capillaries to swell or burst (see "14 Chemical compatibility of wetted materials", p. 55).
- Note that organic solvents are toxic above a certain concentration. For handling hazardous solvents see the following section.
- Solvents and samples may contain volatile or combustible/flammable chemicals. Avoid the accumulation of these substances. Ensure good ventilation of the installation site. Avoid open flames and sparks. Do not operate the instrument in the presence of flammable gases or vapors.
- Only use solvents which do not self-ignite under given conditions. This applies especially to the use of a thermostat where liquids could get onto hot surfaces in the interior.
- Degas solvents before use and observe their purity.

2.6.2 Contamination by health-threatening solvents

- Contamination with toxic, infectious or radioactive substances poses a hazard for all persons involved during operation, repair, sale, and disposal of a device.
- All contaminated devices must be properly decontaminated by a specialist company or the operating company before they can be recommissioned, repaired, sold, or disposed (see "11 Disposal", p. 49).

2.6.3 Avoiding leakage

Risk of electrical shock or short circuit if solvents or other liquids leak into the interior of the device. You can avoid a leakage through the following measures:

- Tightness: Visually check the device or system regularly for leaks.
- Solvent tray: The use of a solvent tray prevents liquids get from the bottles into the inside of the device.
- Solvents lines: Install capillaries and hoses in such a way that, in case of a leak, liquids cannot get into the interior of the devices underneath.
- In case of leakage: Switch off the system. Only take the device into operation if the cause of the leak has been resolved (see "9 Maintenance and care", p. 47).

2.7 Specific environments

2.7.1 Earthquake-endangered areas

In earthquake-endangered areas, do not stack more than 3 devices on top of each other. Otherwise there is risk of injury due to falling devices or loose parts.

2.7.2 Explosive environment

Never use the system in potentially explosive atmospheres without appropriate protective equipment. For more information, contact the KNAUER Customer Support.

2.7.3 Cooling room

You may operate the device in a cooling room. To prevent condensation, note the following instructions:

- Allow the device to acclimatize for min. 3 hours before taking it into operation.
- After taking into operation, the device should stay switched on.
- Avoid temperature fluctuations.

2.7.4 Wet room

The device must not be operated in wet rooms.

2.8 Maintenance, care and repair

- Avoiding electric shock: Before performing any maintenance and service work, disconnect the device from the power supply.
- Tools: Use only tools recommended or prescribed by the manufacturer.
- Spare parts and accessories: Only use original parts and accessories made by KNAUER or a company authorized by KNAUER.
- PEEK fittings: Use PEEK fittings only for a single port or brand-new PEEK fittings in order to avoid dead volume or not exactly fitting connections.
- Used capillaries: Do not use any used capillaries elsewhere in the system in order to avoid dead volumes, not exactly fitting connections and spreading contamination.
- Safety features: The device may only be opened by the KNAUER Customer Support or any company authorized by KNAUER (see chapter 1.4.1 on page 2).
- For more information visit the KNAUER website:
www.knauer.net/hplc-troubleshooting

2.9 Service request form and decontamination report

Devices which are shipped without the completed document "Service request form and decontamination report" will not be repaired. If you would like to return a device to KNAUER, make sure to enclose the completed document: www.knauer.net/servicerequest

3. Product information

3.1 Intended use



Note: Only use the system for applications that fall within the range of the intended use. Otherwise, the protective and safety equipment of the system could fail.

KNAUER's benchtop IJM NanoScaler system is designed for lab-scale lipid nanoparticle formulation - allowing scientists to screen for optimal process parameters to formulate API-containing lipid nanoparticles.

The NanoScaler can be used to produce LNPs at a range from 1 ml to hundreds of milliliters meaning the system is perfect for:

- **Proof of concept testing and process optimization** - pure nucleotides are an expensive resource. Carry out proof of concept testing and process optimization at the 1000 µl scale to avoid wastage.
- **Pre-clinical trials** - Pre-clinical testing can be carried out using 100 ml of nucleotides such as, for in vitro studies to determine the tolerability, efficacy and potential toxicity of the mRNA therapy of interest.
- **Small scale production** - Once proof of concept and safety testing have been successfully conducted, production of LNP encapsulated API's can even be carried out at up to 70 ml/min with the IJM NanoScaler or using KNAUER's scaled up IJM NanoProducer Units.

LNP Technology Impingement Jets Mixing Technology (IJM) enables the formulation and production of high-quality lipid nanoparticles carrying API (e.g. for mRNA vaccines). The encapsulation process of active pharmaceutical ingredients with lipids is based on Impingement Jets Mixing Technology, where two streams collide at high velocity in a jet mixing chamber. One of the streams contains the lipids in organic solvents and the other stream the API in buffer. The mixing at high velocity reduces the solubility of the lipids so that homogenous nanoparticles are formed. The quality of nanoparticles depends on the streams' flow stability, the mixer geometry and the fluid velocities. As a final step, the mixture is quenched to stop particle growth.

3.2 Features

The IJM NanoScaler is made for research and development as well as pre-clinical and small-scale production of lipid nanoparticles. Equipped with our lipid nanoparticle producing Impingement Jets Mixing (IJM) technology the NanoScaler allows researchers to optimize encapsulation conditions for their API-based therapy before scaling up the process to run on a larger IJM NanoProducer unit.

The NanoScaler is made for low sample consumption so as not to waste valuable API. Its small footprint means it can comfortably sit on the benchtop of a research and development lab. The system comes with five different KNAUER Impingement Jets Mixers to help researchers determine which conditions result in the optimum level of API encapsulation.

These active pharmaceutical ingredients include complex or delicate API like RNA, mRNA, siRNA, and DNA-based molecules, or products that need specific entry into target cells. In addition, researchers can use their own custom mixing unit and benefit from the flexibility of the system set-up. The formulation process can be remotely controlled by software; ran from a conventional PC or laptop, or even a tablet.

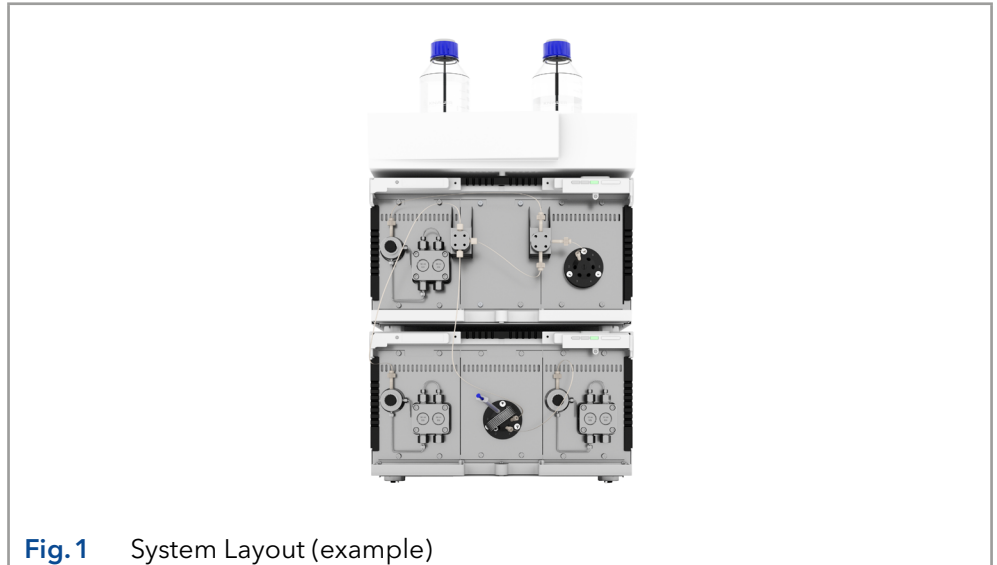


Fig.1 System Layout (example)

3.3 Formulation parameters

The IJM NanoScaler enables the scouting of several key process parameters during the lipid nanoparticle encapsulation stage.

Mixing unit - The five different Impingement Jets Mixer geometries, plus the opportunity to integrate a custom mixing unit, allow determination of the process conditions required to achieve maximum efficiency, optimal particle size and homogeneous size distribution.

Mixing flow rate and ratio - Determine how the specific physicochemical properties of the lipid nanoparticle are impacted by the mixing flow - find out which flow rates and ratio provide optimum lipid nanoparticle encapsulation.

Lipid formulation - Testing of new lipid formulations, for example lipids with embedded antibodies for targeted medicines, is possible using the NanoScaler. Determine the conditions required to ensure lipid nanoparticle encapsulation takes place before producing the therapy at scale for trials.

Dilution protocols - The liquid flow path of the NanoScaler can be configured to either include or bypass the dilution step following lipid nanoparticle formation - allowing scientists to produce formulations at the exact concentration required.

3.4 Scope of delivery

3.4.1 IJM NanoScaler (standard configuration)



Note: Only use original parts and accessories made by KNAUER or a company authorized by KNAUER.

- 1 x AZURA® Assistant ASM 2.2L with 2 x AZURA® Pump P 4.1S (50 ml pump head) and 1 x 6-Port-2-position-valve
- 1 x AZURA® Assistant ASM 2.2L with 1 x AZURA® Pump P 4.1S (50 ml pump head) and 1 x 2-position-valve
- 5 x KNAUER Impingement Jets Mixer
- 1 x quench mixer
- Sample loops for 500 µl*, 1 ml, 2 ml and 5 ml**
- Internal piping
- Eluent tray AZURA® E 2.1L

Valid documents:

- Declarations of conformity for single devices
- VOQ-IJM-NanoScaler

*only for A48040XYZ

** only for A48035/A48035V1

* Also valid for variants with A48040XYZ.

X, Y, Z = 0-9, or A-Z, or blank

3.5 Views

3.5.1 Front view

Legend

- ① Lipid pump
- ② Quench pump
- ③ Impingement Jets Mixer (IJM)
- ④ Fractionation valve
- ⑤ API pump
- ⑥ API loop

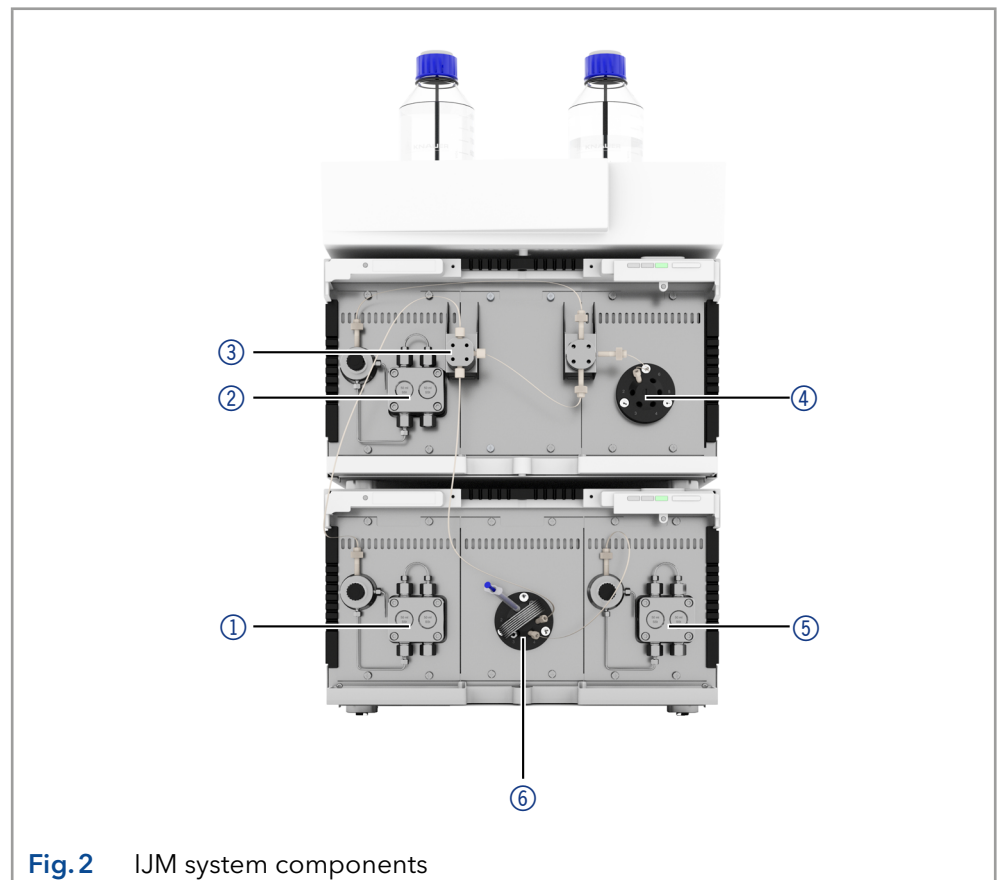


Fig.2 IJM system components

3.5.2 Rear view

Legend

- ① UKCA marking
- ② CE marking
- ③ Label with serial numbers and article numbers
- ④ Warranty seal
- ⑤ On/off switch
- ⑥ Mains connection with mains switch
- ⑦ Warning
- ⑧ Fan
- ⑨ Pin header
- ⑩ LAN-Connection 2
- ⑪ LAN-Connection 1
- ⑫ Service interface
- ⑬ Integrator output

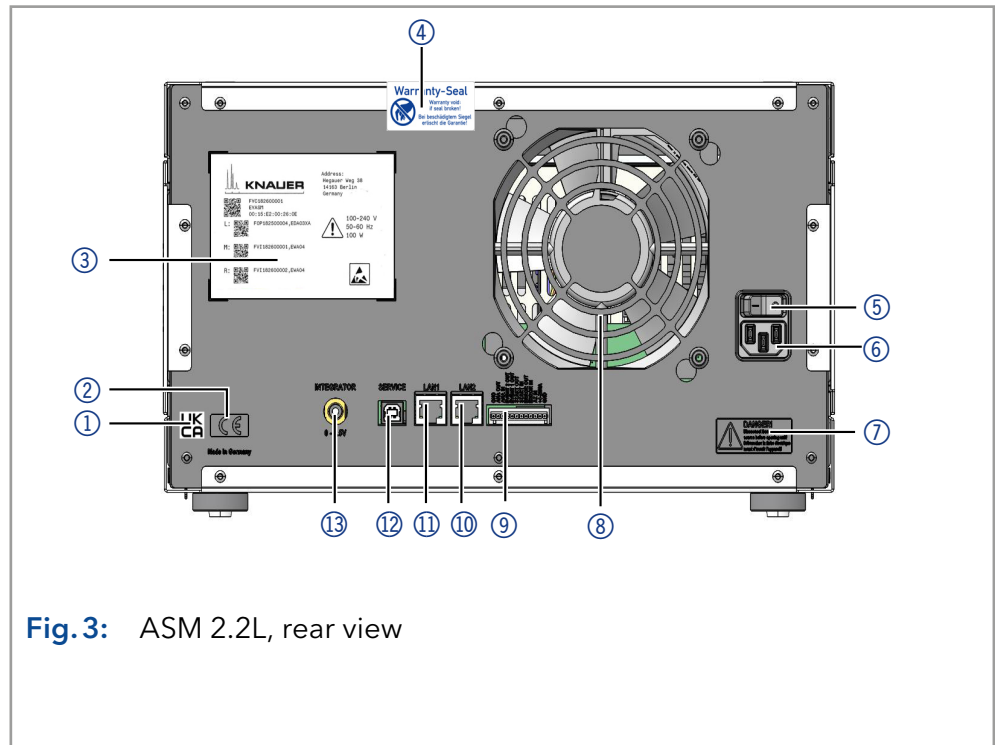


Fig. 3: ASM 2.2L, rear view

3.6 Meaning of the LEDs

There are three LEDs ① and a standby switch ② on the front of the device.

Legend

- ① LEDs
- ② Standby switch

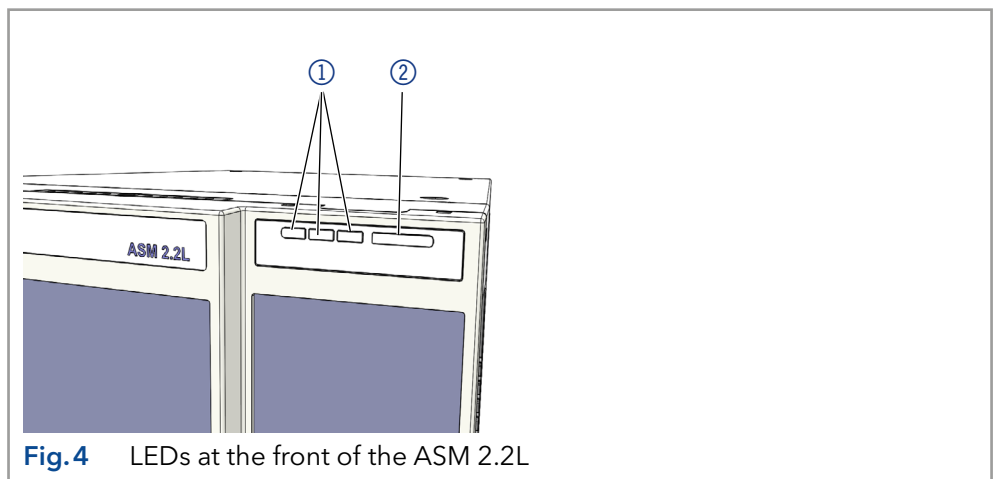


Fig. 4 LEDs at the front of the ASM 2.2L

The LEDs can have different colors depending on the operating conditions.

	Color	Operating condition	Operation
Left LED	flashes red	Error message	Check the system. Shortly press the switch to deactivate the error message.
	red	Serious error	Restart the device. If the operating condition does not change, call the technical support.
	green	Program or sequence is running / has been loaded.	
Center LED	does not light	Not ready for operation	Switch on the device.
	flashes green	Detector is initializing/ calibrating	Wait until the device is ready.
	green	Ready for operation	
Right LED (Operational status)	green	Switched on	
	blue	standby	Exit with the standby switch.









Standby To start the standby, keep the switch pressed for 5 seconds.



Note: Malfunctioning system after repeated standby possible. After repeatedly using the standby, switch off the power switch and back on again, to reset the data storage.

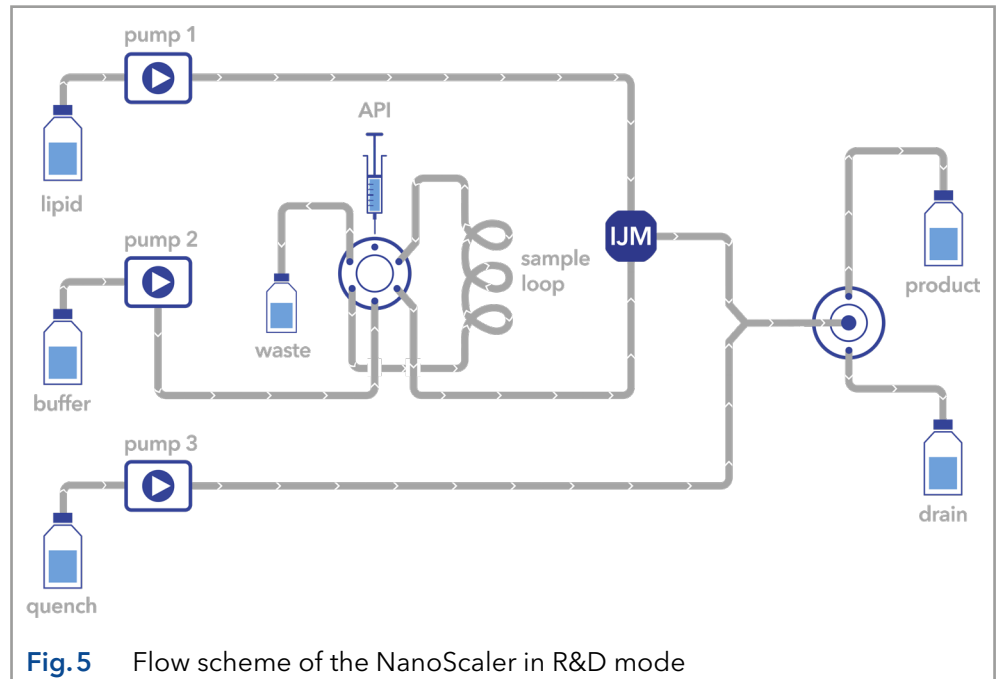
3.7 Symbols and signs

The following symbols and signs can be found on the device:

Symbol	Meaning
	Electric shock hazard. Failure to observe this warning may result in loss of life, serious injury, or damage to or destruction of the device.
	Electrostatic discharge hazard. Damages to system, device, or sensitive electronic components can occur.
	Obay maximum load for leak tray during transportation, installation and operation.
	The device is covered by the Waste Electrical and Electronic Equipment Directive (WEEE Directive). It may not be disposed of as unsorted municipal waste and has to be collected separately.
	A device or system marked with CE fulfills the product specific requirements of European directives. This is confirmed in a Declaration of Conformity.
	The device complies with the product-specific requirements of the United Kingdom.
	Testing seals in Canada and the USA at nationally recognized testing centers (NRTL). The certified device or system has successfully passed the quality and security tests.
	On some devices, a warranty seal is attached. For more information see section "1.4.4 Warranty seal" on p. 2.

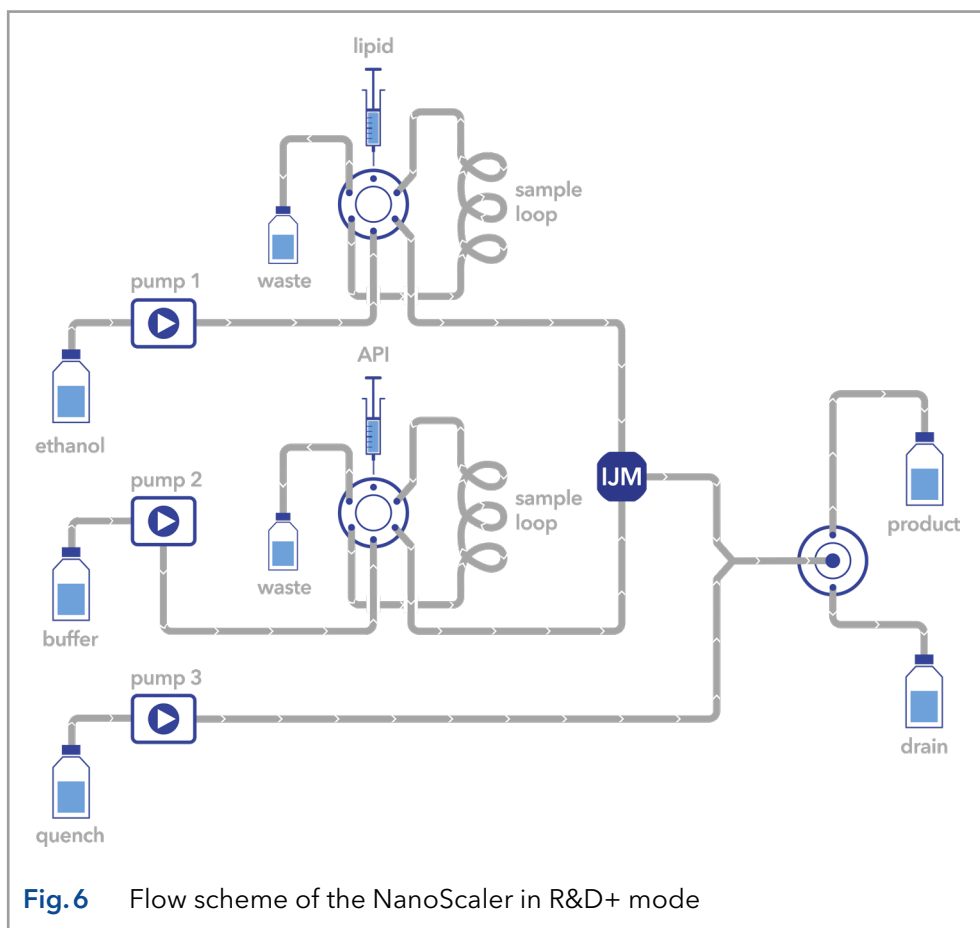
4. Operation modes

In the standard configuration the IJM NanoScaler can be operated in two different modes.

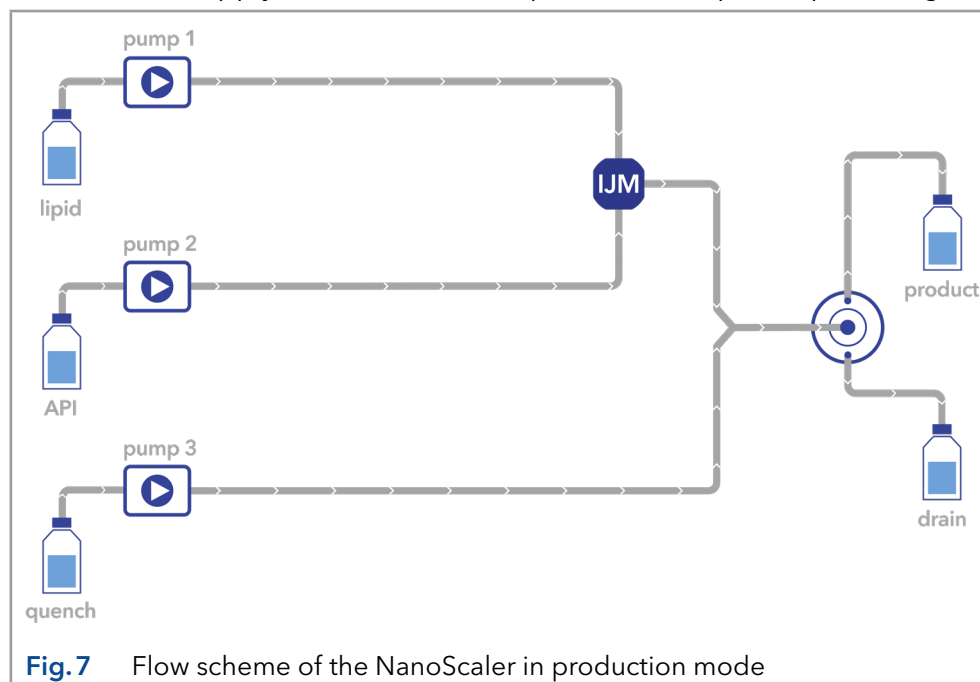


The standard operation mode of the IJM NanoScaler is the R&D mode (see Fig.5). Thereby small API volumes can be encapsulated by the usage of the integrated sample loop. Only the sample loop is filled with API solution by syringe. Pump 2 pumps buffer to push the API solution out of the loop into the system.

This mode is used for API volumes of 500 μl , 1, 2 or up to 5 ml according to the volume of the sample loops.



The R&D mode of the standard IJM NanoScaler can be upgraded to the R&D+ mode (upgrade needs to be ordered separately, see chapter „13. Reorders“ on page 53). The upgrade features a second loop in an additional valve to apply small volumes of lipids via a sample loop (see Fig. 6).



In the second operation mode, the production mode, larger volumes of API (> 5 ml) can be encapsulated by direct transfer of the API solution with pump 2. Therefore, the sample loop and valve 1 are excluded by connecting the pump 2 outlet to the IJM (see Fig. 7).

5. Installation and initial startup



Video: On the KNAUER YouTube channel you will find a short tutorial on how to install an IJM NanoScaler System: [KNAUER NanoScaler Installation](#).

Before you determine the operation site, read the chapter “Technical Data” (see chapter 12 on page 50). There you will find all device-specific information on power supply, ambient conditions and humidity.



Note: The intended use is only ensured if the requirements for ambient conditions of the operating environment are met.

The IJM System will be set up, installed and commissioned by KNAUER or a company authorized and contracted by KNAUER.



Note: KNAUER recommends inviting future users to be present while setting up and commissioning the module so that they can become familiar with the device/IJM NanoScaler and know how to handle it.



Note: To avoid communication problems, do not operate the IJM NanoScaler system with two software packages simultaneously. Operate the system either with Mobile Control or with PurityChrom®.

5.1 Unpacking

Process

Procedure

1. Place the packaging in such a way that the lettering on the label is in the correct position.
2. Check the packaging, the device and the accessories for transport damage.
3. Check the scope of delivery. In the event of incomplete delivery, contact Technical Support immediately.
4. When lifting, carrying or moving the device, grab the unit only from below on the sides. Do not hold onto front cover or leak tray, as these parts are loosely attached to the device.

Next steps

- Keep the included packing list for repeat orders.
- Keep the original packaging for safe storage or transportation.

5.2 Ambient conditions

5.2.1 Operation site

Observe the following requirements for the operation site so that the production results are not influenced:

- Place on a firm, level and straight surface.
- Protect against direct sunlight.
- Do not expose to air drafts such as air conditioning systems.
- Do not set up next to other machines that cause floor vibrations.

- Keep from high frequency sources.
- Ensure adequate ventilation (see 5.2.3 on page 17).
- Avoid temperature fluctuations (see 5.2.2 on page 17).

5.2.2 Ambient temperature

If the ambient temperature of the device is abruptly changed (e.g. when it is installed in a cooling chamber), condensation will form inside the device and may cause damage to the device. Allow the device to acclimate for 3 h, before it is connected to the power supply and taken into operation.

5.2.3 Space requirements

- Make sure that the power plug on the power supply (wall socket or power strip) is always accessible, so that the device can be disconnected from the power supply.
- Ensure adequate ventilation around the device, otherwise it may overheat and malfunction:
 - Min. 5 cm distance if another device is set on one side.
 - Min. 10 cm distance if further devices are set on both sides.
 - At least 15 cm to the cooler fan on the rear.
- The mounting of a small device to an AZURA L device with a mounting bracket does not affect the performance of either device. The space requirements specified in both device instructions do not apply in this case.

5.3 Power supply

NOTICE

Electronic defect

Electronic hazard when using an identically constructed power adapter from another manufacturer.

→ Only use spare parts and accessories from KNAUER or a company authorized by KNAUER.

Power supply requirements

- Failure-free power supply: For failure-free operation, the electrical voltage has to be free of fluctuations, residual currents, voltage peaks and electromagnetic interference. The device must receive sufficient voltage and reserve capacity.
- Check voltage: Only connect devices to a power supply whose voltage corresponds to the permissible voltage of the device.
- Power consumption: The nominal power of the connected devices must not exceed 50 % of the highest connected power capacity, since higher currents can flow briefly when the device is switched on.
- Main connection: The electrical power supply at the operation site has to be connected directly to the nearest main power connection.

- Grounding: The connectors for the voltage have to be grounded accordingly.

Power supply cables and plugs

- Original parts: For power supply, use the supplied power cable and plug to meet the specifications which are described in the chapter "Technical Data" (see chapter 12 on page 50). Detachable power cables are not allowed to be replaced with other cable types.
- Country-specific plugs: Before switching on the device, check whether the supplied plug is approved for your country. Overview of the device- and country-specific plug types from KNAUER: www.knauer.net/plugs
- Power strips: If several devices are connected to one power strip, always consider the maximum power consumption of each device.
- Damaged power supply cables and plugs: For safety reasons, damaged or faulty cables and plugs must not be used to connect the device to the power supply. Replace defective cables and plugs only with KNAUER accessories.

5.4 Connecting the capillaries

Install the capillaries according to the list of piping delivered with the system.

Use one hand to push the capillary into the notch and the other hand to fasten the screw connection (hand tight).

5.5 Connecting the piston backflushing

The pump heads are equipped with connectors for piston backflushing. By backflushing the piston regularly, you increase the service life of the seals and pistons and remove impurities from the area behind the seals.

Functional principle The piston backflushing flushes the rear piston area of the pump head.

- Flush the rear piston area of the pump head for 15 seconds.
- Repeat the piston flushing once a day.

Process

1. Lead a tube from the solvent bottle to the inlet connector for piston backflushing ② on the pump head ③.
2. Lead a tube from the outlet connector for piston backflushing ① on the pump head to the syringe (included in the accessory kit).
3. To flush the backpiston chamber, aspirate the flushing solution using the syringe.
4. After flushing, disconnect the syringe from the tube and dispose of the flushing solution properly.

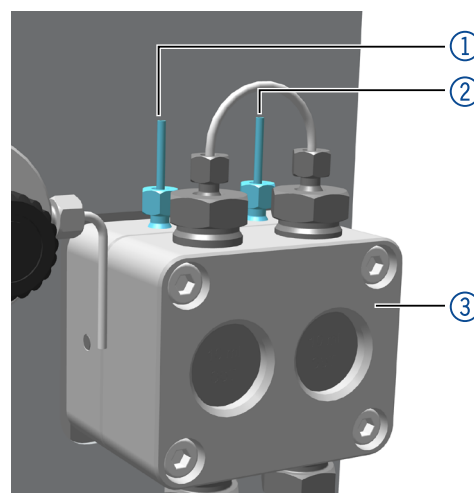
Figure

Fig. 8: Connectors for piston backflushing

For further information see SOP in section „5.9.1 Back piston flushing“ on page 21.

5.6 Initial start-up checklist

Use this checklist to determine if the system is ready for initial start-up:

- Devices are positioned in the correct location.
- The power plugs are connected.
- The network connection is established.
- The software has been installed by KNAUER or a company authorized by KNAUER.
- The capillaries are connected.

5.7 SOP: IJM System power-up and shut-down

5.7.1 Power-up

Procedure**Steps**

1. Power up the switch (if available) and wait until the self-test is performed.
2. Power up all instruments and the PC.
3. If a user management is used on the PC, login with the correct credentials.
4. Start the software with double click on the desktop icon.

5.7.2 Shut down

Procedure

Steps

1. Close the software.
2. Turn off the PC.
3. Turn off all instruments.
4. Turn off the switch (if available).

5.8 SOP: IJM System start-up

Follow this procedure to perform an IJM system start-up.

When delivered the system is filled with 80 % water / 20 % isopropanol.

Procedure

Steps

1. Power-up the system.
2. Connect IJM 3 to perform the SOP.
3. Switch Valve 1 (if available Valve 3) to Load, Valve 2 to Drain.
4. Open the purge valve of pump 1 (Lipid) and connect it to a syringe with a silicon tubing.
5. Set the flow rate at 10 % of the pump heads maximum flow.
6. Purge with deionized water.
7. When no more air bubbles are visible in the inlet tubing, stop the pump and close the purge valve.
8. Repeat steps 3 to 6 with pump 2 (API) and pump 3 (Quench).
9. Flush the system with water for 30 min, using 20 % of the maximum flow rate for every pump.
10. Switch Valve 1 (if available Valve 3) to Inject, Valve 2 to Diluted LNP.
11. Flush the system with water for 30 min, using 20 % of the maximum flow rate for every pump.
12. Continue flushing the system until you reach a stable pressure at all pumps.

Repeat the SOP procedure if you change the operation mode or the IJM.

5.9 SOP - NanoScaler

5.9.1 Back piston flushing

By backflushing the piston regularly, you increase the service life of the seals and piston and remove impurities from the area behind the seals.

Back piston flushing should be performed at least once a day.

Procedure

Steps

1. Prepare 200 ml of a mixture of water (70 %) and isopropanol or ethanol (30 %).
2. Use silicone tubing to connect the back piston flushing. Connect a bottle of flushing solution to the right-hand connection and a syringe to the left-hand connection.



Fig. 9: Arrangement for back piston flushing

3. Pull 10 ml of liquid through the pump head into the syringe.
4. Repeat the procedure with all pumps.

5.9.2 Preparation

Procedure

Steps

1. Choose between the R&D or production mode and the IJM being used. Configure the system according to your selection.
2. Open the purge valve of pump 1 (Lipid) and use a silicone tubing to connect the capillary next to the purge valve with a syringe.
3. Set the flow rate to 10 % of the pump heads max. flow.
4. Purge with your preferred solvent (i.e. ethanol/buffer).
5. When no more air bubbles are visible in the inlet tubing, stop the pump and close the purge valve.
6. Repeat steps 2 to 4 with pump 2 (API) and pump 3 (Quench).
7. Flush the system for 2 min as follows:
Valve 1: Inject,
Valve 2: Drain,
Pump 1: 2.5 ml/min,
Pump 2: 7.5 ml/min,
Pump 3: 5 ml/min
8. After one minute, Valve 1 and Valve 2 are switched to the other position one after another.
9. After 2 min, turn off the pumps.

5.9.3 R&D mode

In R&D mode, tests can be carried out with small volumes of API. The samples are injected with a syringe via Valve 1. In position 1, the syringe is connected to the sample loop. Depending on the sample loop, the injection volume can be modified. The sample is then conveyed to the IJM through the valve at position 2. In the process, Pump 2 delivers the solvent buffer and transports the active ingredient to the IJM.

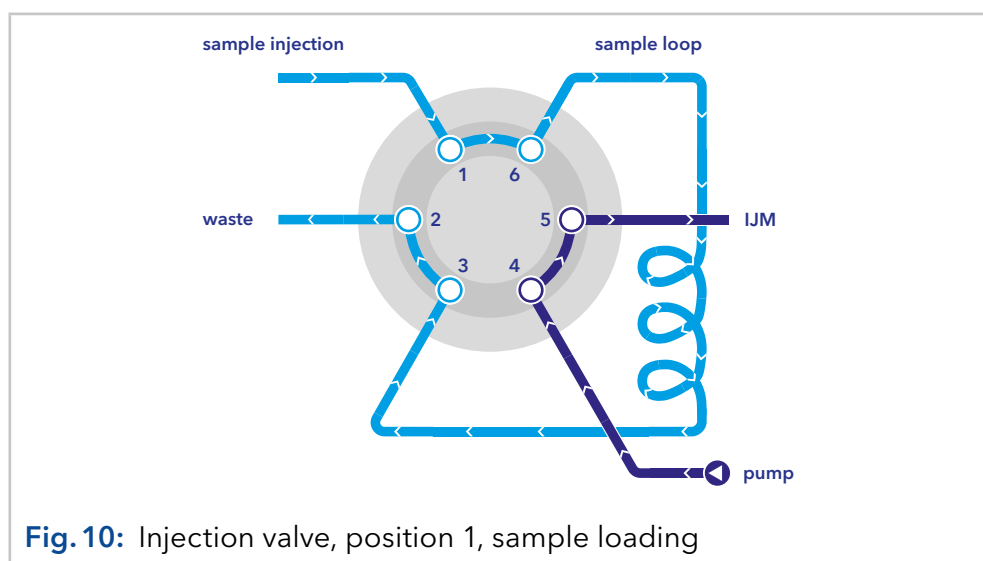


Fig. 10: Injection valve, position 1, sample loading

*Also valid for variants with A48040XYZ.

X, Y, Z = 0-9, or A-Z, or blank

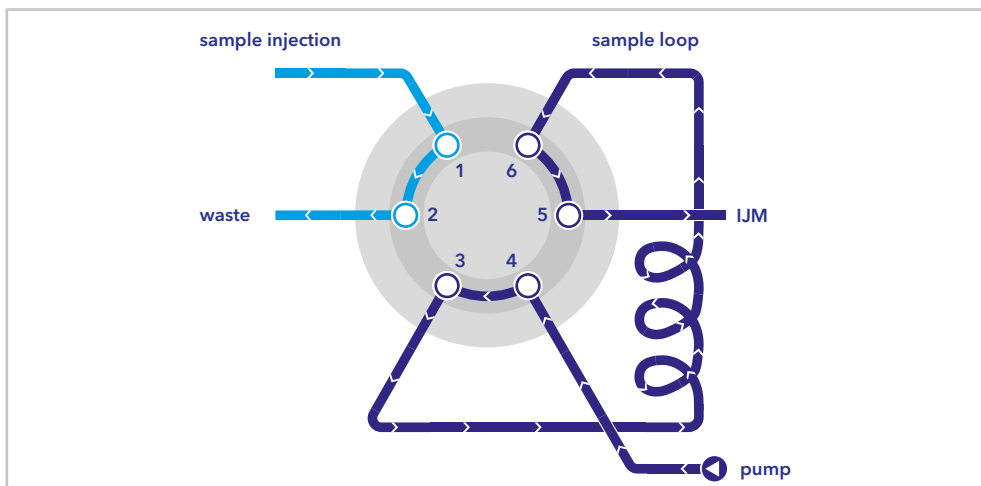


Fig. 11: Injection valve, position 2, sample injection

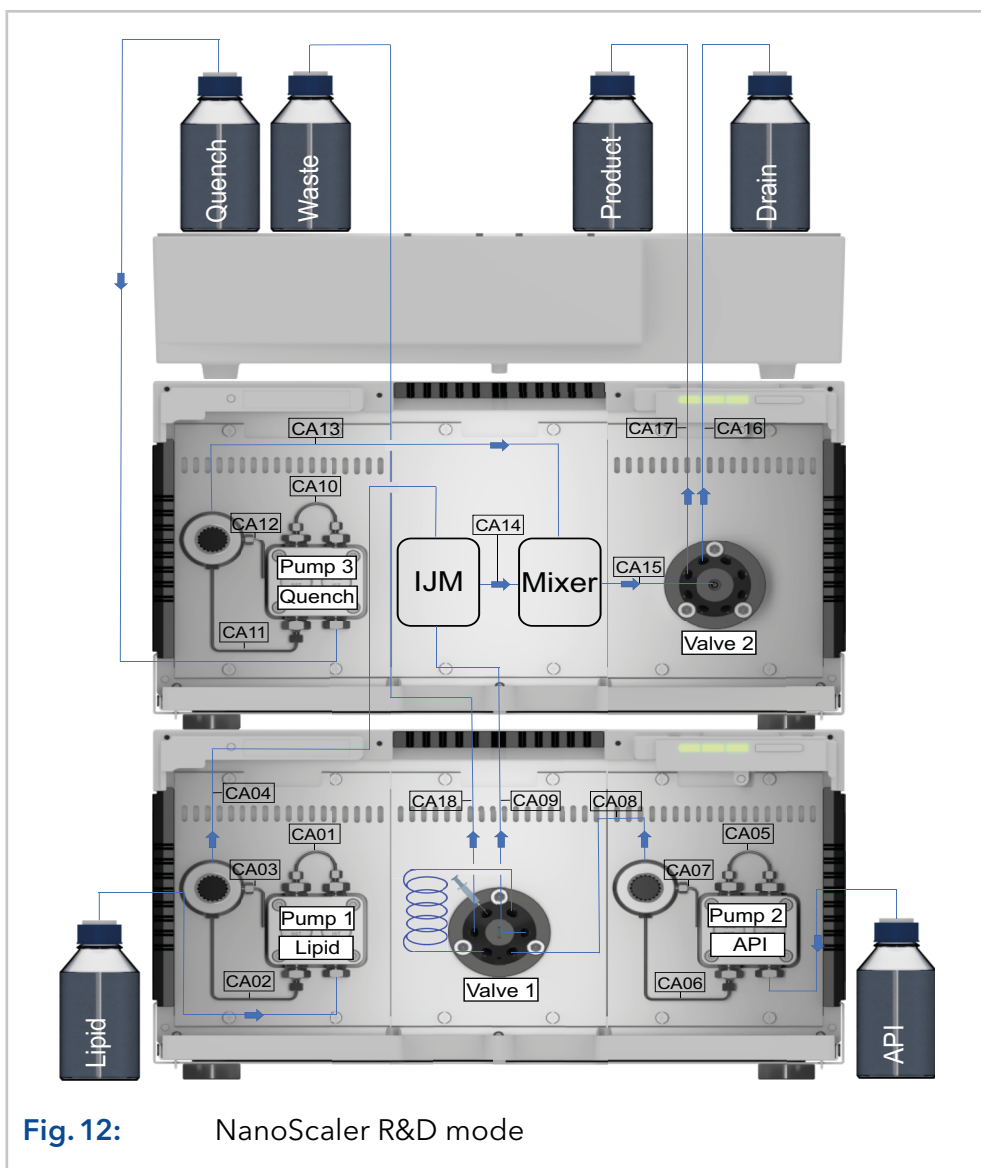


Fig. 12: NanoScaler R&D mode

Procedure Loop filling

Procedure

Steps

1. A syringe is used to fill the sample loop. Fill the syringe with API solution and place it to the injection valve using a luer adapter.

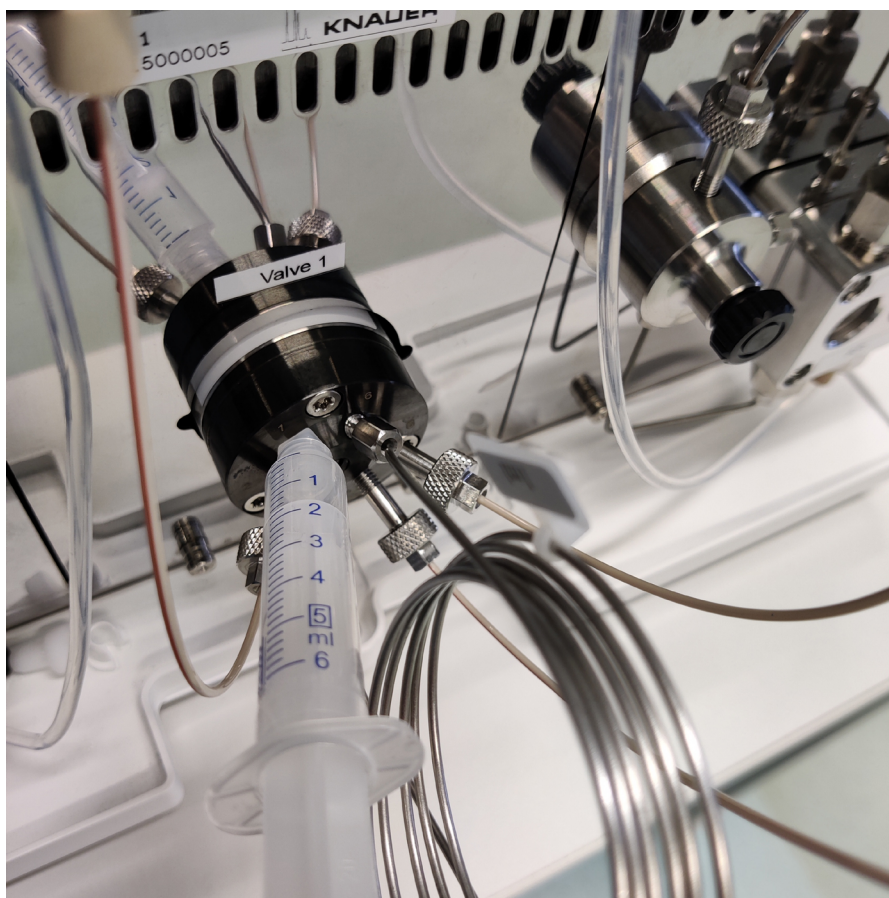


Fig. 13: Loop filling

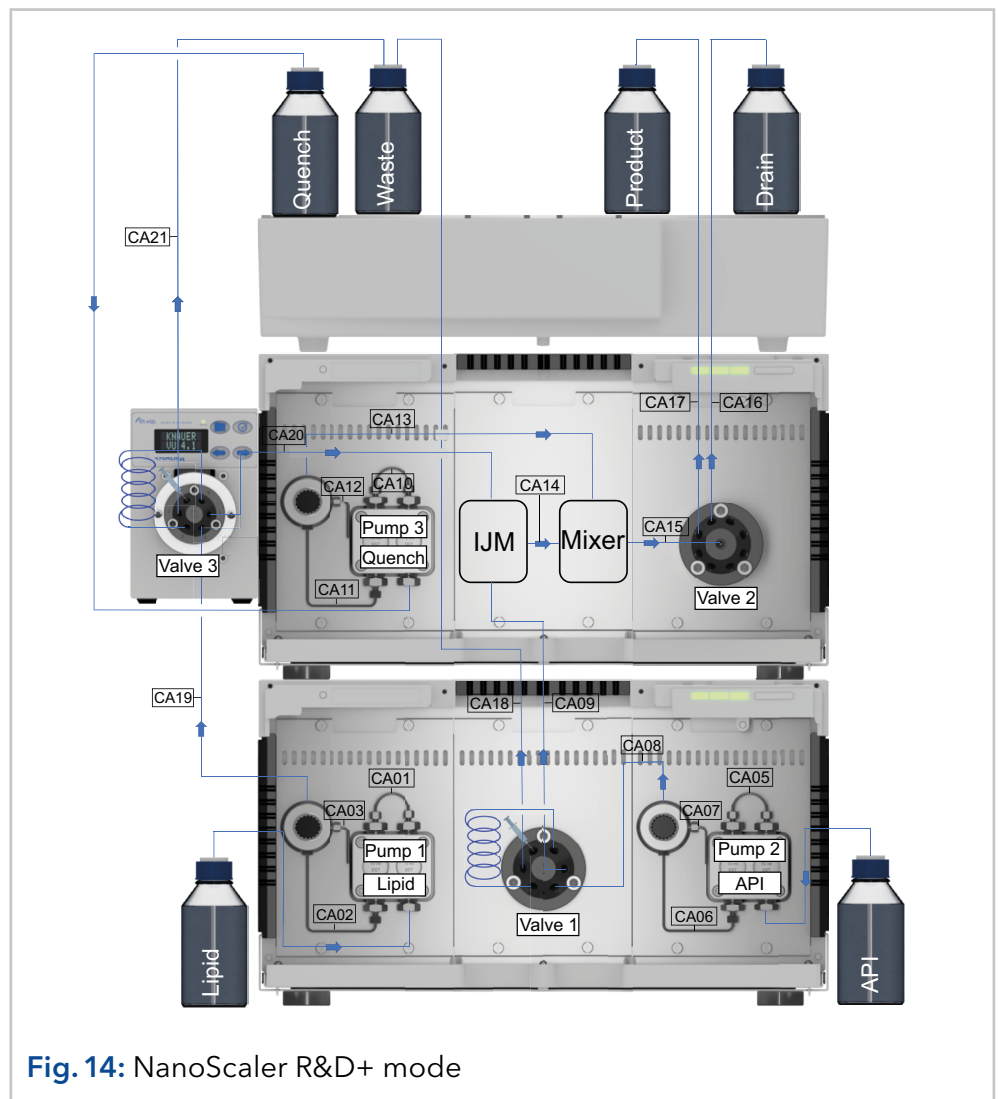
2. To fill the sample loop, switch the injection valve to position 1 = Load.
3. We recommend to overfill the loop with 20 % of its volume. This ensures that impurities are flushed out and the exact volume is injected.

Method

Procedure

Steps

1. Start valve positions: Valve 1 = "Load", Valve 2 = "Drain".
2. Set the desired flow rates of the pumps (i.e. for IJM 2: pump 1 = 2.5 ml/min, pump 2 = 7.5 ml/min, pump 3 = 5 ml/min).
3. Start the pumps and flush the system for 10 to 20 sec.
4. Inject your sample via switching Valve 1 = "Inject".
5. Switch Valve 2 to Product after 1 - 2 seconds (depending on the used flow rates).
6. Stop the pumps (time depends on the used flow rates).



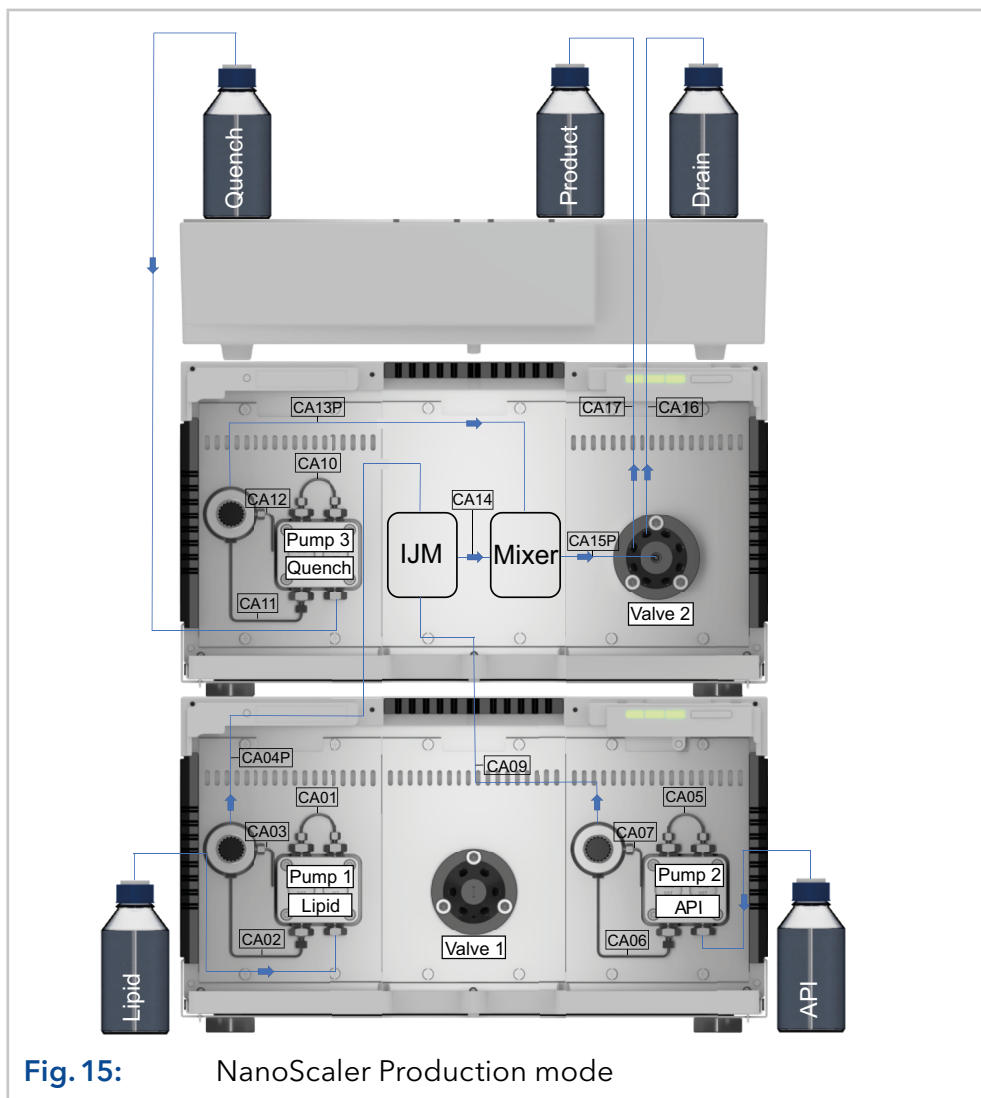
5.9.4 R&D+ mode

In R&D+ mode, tests can be carried out with small volumes of API and lipids. The API samples are injected with a syringe via valve 1 and the lipid samples via valve 3.

The procedure to fill the loops corresponds to section „5.9.3 R&D mode” on page 22.

In the process, Pump 2 delivers the solvent buffer and transports the active ingredient to the IJM and pump 1 delivers ethanol and transports the lipids to the IJM.

5.9.5 Production mode



In production mode, the API can be delivered directly to the IJM by pump 2. For this purpose, the CA09 capillary is connected directly from the pressure sensor of pump 2 to the IJM bottom port. Also change capillary C04 to CA04P, CA13 to CA13P and CA15 to CA15P (see Fig. 15). Pump 2 has to be purged before the first operation.

Method

Procedure

Steps

1. Switch Valve 2 to „Drain“.
2. Start the pumps.
3. Flush the system for 10 to 20 seconds.
4. Stop the pumps.
5. Switch Valve 2 to “Product” and define a run time for your formulation process.

5.9.6 API/Lipid supply by syringe (optional)

The API/Lipid supply by syringe is not part of the scope of delivery. Order article number A71100 separately if needed.

Tool ■ Offset screwdriver, size TX10

Procedure

Steps

1. Screw the clamp to the upper screw connection of the lower assistance module next to the API pump by using the offset screwdriver TX10.



Fig. 16: Mounted clamp on the side of the device housing

2. Clip the syringe into the clamp and connect the supply tubing to the inlet of the API pump.
3. Check all screw connections for leaks, before filling the syringe. To do this, close the stopcock and pour a small amount of water into the syringe. If necessary, tighten any leaking screw connections.
4. To fill the syringe, close the stopcock and pour in the desired liquid.



Fig. 17: Filled syringe

Procedure

Steps

5. Then open the stopcock.



Fig. 18: Syringe after opening the stopcock

6. For the first use of the syringe, the pump must be purged. Otherwise, skip to step 10.
7. Open the purge valve of pump 2 (API) and connect it to a syringe with a silicon tubing.
8. Set the flow rate at 10 % of the pump heads max. flow.
9. Purge with your preferred solvent. (ethanol/buffer)
10. When no more air bubbles are visible in the inlet tubing, stop the pump and close the purge valve.
11. Start your desired pump program.
12. When the first air bubbles appear in the supply tubing stop the run at the latest.
13. Close the stopcock. A new sample mixture can be filled into the syringe, or a new syringe can be connected.

5.10 Cleaning the system

All following cleaning procedures are basic suggestions. Depending on raw materials, formulations and extent of use of the device they may be adapted. Validation by the user as to whether the cleaning is sufficient or needs to be extended is strongly recommended.

- Materials**
- Deionized water
 - 0.1 M NaOH
 - Ethanol
 - Luer adapter
 - Syringe
 - Beaker

5.11 Single IJM cleaning procedure



Note: KNAUER recommends to carry out one of these cleaning procedures under the following circumstances:

- Change of IJMs
- Clogging of IJM

Cleaning the IJM manually is necessary when a blockage occurs. Indications are sudden increases in pressure of the API or lipid pump.

Tool ▪ Double open-end wrench, size 4/5 mm (X0284)

Procedure

Steps

1. Disconnect all the capillaries from the IJM.
2. Connect the luer adapter and the syringe on the lipid/ethanolic port of the IJM and close the API port with a blind plug (Fig. 19). Use a beaker to collect the waste below the open port.

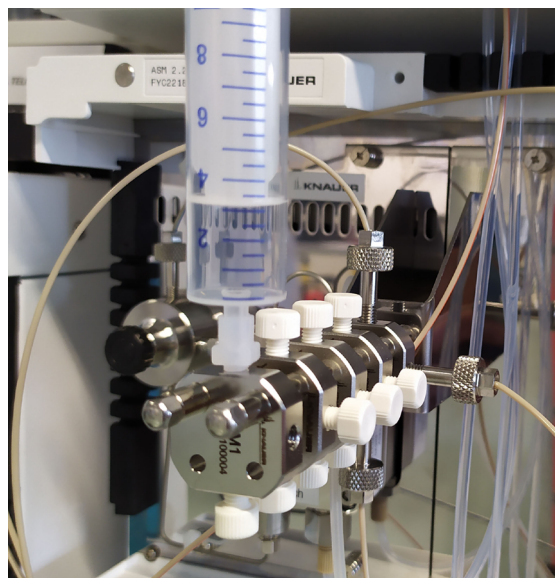


Fig. 19: Manual cleaning the ethanol/lipid pathway

3. Inject, at least, 3 ml of ethanol to remove any lipid residue.
4. Inject 3 ml of NaOH 0.1M.
5. Inject 3 ml of deionized H₂O.
6. Equilibrate with 3 ml of ethanol.
7. Repeat the procedure from steps 4 - 5 by placing the blind plug on the outlet port of the IJM.

Procedure**Steps**

8. Repeat the procedure from steps 4 - 5 (ethanol step is not needed) by placing the luer adapter and the syringe on the API port and the blind plug on the lipid port (Fig. 20). Use a beaker to collect the waste of the open port.



Fig. 20: Manual cleaning the API pathway

9. Repeat the procedure from steps 4 - 5 by placing the blind plug on the outlet port of the IJM. Use a beaker to collect the waste of the open port.
10. If a blockage can not be removed with the above described procedure, remove the IJM from the threaded rods.
 - First remove the two screws by using the open-end wrench and then remove all necessary IJMs.
 - Clean the IJM with isopropanol in an ultrasonic bath for at least 10 min.
 - Reinstall the IJMs and both screws.



Fig. 21: Removing the IJM from the threaded rods

5.12 Intermediate system cleaning

Note: KNAUER recommends to carry out this cleaning procedure under the following circumstances:

- Change of Lipid and/or API composition between different formulation cycles during the same day.
- Change of buffers.

Note: The flow rate for all pumps in all steps is 2 ml/min.

Step 1

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	Ethanol	Deionized H ₂ O	Deionized H ₂ O
Cleaning the loops			
		Load: 2 x loop volume	
		Inject: 2 x loop volume	
Flushing the system			
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 5 min	
Load	Product	Flush system for 5 min	

Step 2

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	Deionized H ₂ O	Deionized H ₂ O	Deionized H ₂ O
Cleaning the loops			
	Load: 2 x loop volume	Load: 2 x loop volume	
	Inject: 2 x loop volume	Inject: 2 x loop volume	
Flushing the system			
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 5 min	
Load	Product	Flush system for 5 min	

Step 3

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	NaOH 0.1 M	NaOH 0.1 M	NaOH 0.1 M
Cleaning the loops			
	Load: 2 x loop volume	Load: 2 x loop volume	
	Inject: 2 x loop volume	Inject: 2 x loop volume	
Flushing the system			
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 5 min	
Load	Product	Flush system for 5 min	

Step 4

Repeat step 2.

Step 5

Repeat step 1.

5.13 Cleaning the full system



Note: KNAUER recommends to carry out this cleaning procedure under the following circumstances:

- Before starting to work with the system.
- At the end of a working day.
- Before short and long time storage.



Note: Before short or long time storage flush the system with isopropanol.

Step 1

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	Ethanol	Deionized H ₂ O	Deionized H ₂ O
Cleaning the loops			
		Load: 2 x loop volume	
		Inject: 2 x loop volume	
Flushing the system			

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 30 min	
Load	Product	Flush system for 30 min	

Step 2

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	Deionized H ₂ O	Deionized H ₂ O	Deionized H ₂ O
Cleaning the loops			
	Load: 2 x loop volume	Load: 2 x loop volume	
	Inject: 2 x loop volume	Inject: 2 x loop volume	
Flushing the system			
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 30 min	
Load	Product	Flush system for 30 min	

Step 3

	Pump 1 (optional Valve 3)	Pump 2 with Valve 1	Pump 3
Solvent	NaOH 0.1 M	NaOH 0.1 M	NaOH 0.1 M
Cleaning the loops			
	Load: 2 x loop volume	Load: 2 x loop volume	
	Inject: 2 x loop volume	Inject: 2 x loop volume	
Flushing the system			
Valve position			
V1&3	V2		
Inject	Drain	Flush system for 30 min	
Load	Product	Flush system for 30 min	

Step 4

Repeat step 2.

Step 5

Repeat step 1.

5.14 Recommended flow rates for different IJMs

The following table contains the recommended flow rates for each IJM.



Note: The maximum operating parameters for flow and pressure depend on the viscosity of the solvents, the customer application, the inner diameter of the capillaries used and the back pressure spike caused by switching the valves.

Higher flow rates are possible if the standard capillaries are replaced by capillaries with a larger inner diameter and without switching the valves.

Recommended flow rates for various IJMs with standard capillary set-up for R&D mode.

IJM No.	Flow rate pump 1 (Lipid) [ml/min]	Flow rate pump 2 (API) [ml/min]	Flow rate pump 3 (Quench) [ml/min]
1	2.0	6.0	4.0
2	2.5	7.5	5.0
3	3.0	9.0	6.0
4	3.5	10.5	7.0
5	4.0	12	8.0

6. Computer control

This chapter describes how to set up a LNP system in a local area network (LAN) and how a network administrator can integrate this LAN into your company network. The description applies to the operating system Windows® and all conventional routers.



Note: LNP devices from KNAUER only work with IP addresses, which have been assigned by IPv4. IPv6 is not supported.



Note: The devices of the IJM NanoScaler are set to fixed IP addresses. We recommend not to change the settings. In the standard configuration no switch or router is needed. The system is directly connected to the network card of the computer. The following chapters describe the options of LAN settings in case you want to change the standard direct connection to the computer.



Note: When using PurityChrom® software, static IP addresses are needed (see chapter 6.7 on page 38).

6.1 Setting up LAN

To set up a LAN, we recommend to use a router. That means the following steps are required:

Process

Procedure

1. On the computer, go to the control panel and check the LAN properties.
2. Hook up the router to the devices and the computer.
3. Set up the router for the computer network.
4. Install the chromatography software.
5. Switch on the device and run the chromatography software.

Next steps

Configure LAN properties (see section 6.2).

6.2 Configuring LAN settings

The LAN uses only one server (which is normally the router) from that the devices automatically receive their IP address.

Prerequisites

- In Windows, power saving, hibernation, standby, and screen saver has to be deactivated.
- In case you use an USB-to-COM box, the option "Allow the computer to turn off this device to save power" in the Device Manager has to be deactivated for all USB hosts.
- Applies to all LAN devices: Disable the setting for the network adapter in Device Manager "Allow the computer to turn off this device to save power".

Process**Procedure**

1. In Windows, open <Network and Sharing Center>.
2. Double-click on <LAN connection>.
3. Click on the button <Properties>.
4. Select <Internet Protocol version 4 (TCP/IPv4)>.
5. Click on the button <Properties>.
6. Check the settings in the tab <General>. The correct settings for the DHCP client are:
 - a) Obtain an IP address automatically
 - b) Obtain DNS server address automatically
7. Click on the button <OK>.

Next steps Connect devices (see section 6.3).

6.3 Connecting devices with LAN

A router ② has several LAN ports ③ and one WAN port ④ that can be used to integrate the LAN into a wide area network (WAN), e.g. a company network or the Internet. In contrast, the LAN ports serve to set up a network from devices ① and a computer ⑤. To avoid interference, we recommend operating the chromatography system separately from the company network.



Note: You will find patch cables for each device and the router in the accessories kit. To connect the router to a LAN, an additional patch cable is required, which is not supplied within the scope of delivery.

Legend

- ① Devices
- ② Router
- ③ LAN ports
- ④ WAN/Internet connection
- ⑤ Computer

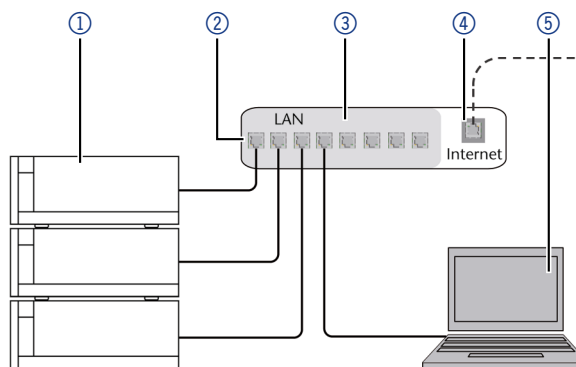


Fig.22: Connecting the devices to the LAN

Prerequisites

- The computer has been switched off.
- There is a patch cable for each device and the computer.

Process**Procedure**

1. Use the patch cable to connect the router and the computer. Repeat this step to connect all devices.
2. With additional patch cables, connect all devices individually with the router.
3. Use the power supply to connect the router to the mains power system.

Next steps Set the router properties (see section 6.4).

6.4 Configuring the router

The router is preset at the factory. Information about address, user name and password is noted in the router manual: www.knauer.net/router.

Process**Procedure**

1. To open the router configuration, start your Internet browser and enter the IP address (does not apply for all routers).
2. Enter user name and password.
3. Configure the router as DHCP server.
4. In the router configuration, check the IP address range and make changes if necessary.



Note: If the IP address range has been changed, it is essential to note this information on the router.

Result

Once the router has assigned IP addresses to all devices, the chromatography software can be used to remotely control the system.

6.5 Integrating LAN into the company network

A network administrator can integrate the LAN into your company network. In this case you use the WAN port of the router.

Prerequisites

- There is a patch cable for the connection.

Process**Procedure**

1. Make sure that there is no overlap between the IP addresses of the router and the corporate network.
2. In case of an overlap, change the IP address range of the router.
3. Use the patch cable to connect the router WAN port to the company network.
4. Restart all devices, including the computer.

Result

The LAN is now integrated into the company network.

6.6 Controlling several systems separately in LAN

Devices connected to a LAN communicate through ports, which are part of the IP address. If more than one chromatography systems are connected to the same LAN and you plan on controlling them separately, you can use different ports to avoid interference. Therefore, the port number for each device must be changed and this same number has to be entered into the device configuration of the chromatography software. We recommend to use the same port number for all devices in the same system.



Note: The port is set to 10001 at the factory. Use the same numbers in the device configuration of the chromatography software as in the device, otherwise the connection fails.

Process

Procedure

1. Find out port number and change it on the device.
2. Enter the port number in the chromatography software.

Result The connection is established.

6.7 Setting IP addresses via software



Note: Check the IT security standards for your lab before intervening in the LAN settings.

PurityChrom®

Static IP addresses are required to run certain chromatography software, e.g. Purity Chrom®. For a comprehensive overview on how to set static IP addresses for PurityChrom®, refer to the document „PurityChrom® Installation Guide“ on the PurityChrom® installation CD.

For Mobile Control and Firmware Wizard, it is possible to set a fixed (static) or dynamic (DHCP) IP address via software.

6.7.1 Mobile Control: Setting a static IP address





Note: The device is preset to a dynamic address (DHCP). To ensure a constant LAN connection between the chromatography software and the instrument, we recommend switching the instrument to a static IP address for certain applications. More information about LAN settings can be found in the [Mobile Control Software Instructions](#) (document no. V6851-2).

Prerequisites

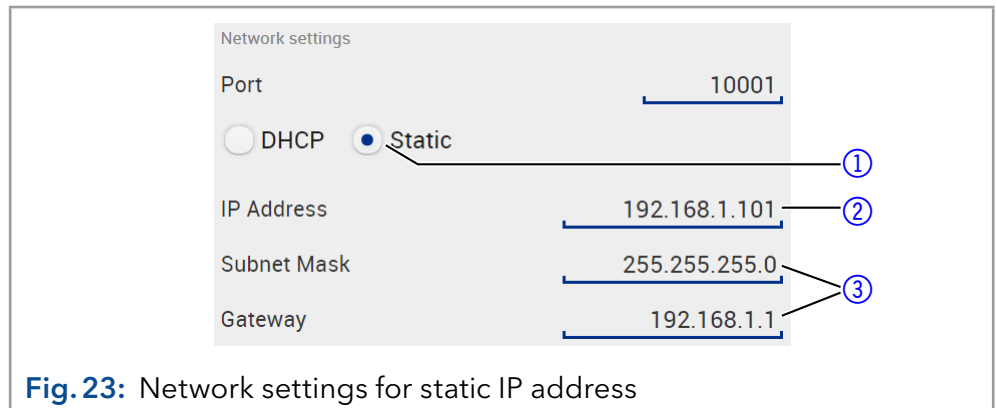
- The device is switched on.
- Mobile Control is installed and running.
- The connection between Mobile Control and the device has been established.

Process**Procedure**

1. In Mobile Control, click  <Settings>.
2. On the <General> tab, choose the device name.
3. In <Network Settings>, choose the setting <Static> ① .
4. Enter the IP address into the text box <IP Address> ② .
5. If necessary, change the subnet mask and the gateway ③ .
6. Click  in the top right corner.
7. Restart the device (recommended).

Legend

- ① IP address mode
- ② Text box for IP address
- ③ Text field for subnet mask/gateway





Result The device is now accessible via the static IP address.

6.7.2 Mobile Control: Setting a dynamic IP address via device name

Prerequisites

- The device is switched on.
- Mobile Control is installed and running.
- The connection between Mobile Control and the device has been established.

Process**Procedure**

1. In Mobile Control, click  <Settings>.
2. On the <General> tab, choose the device.
3. In <Network Settings>, choose the setting <DHCP> ① .
4. Click  in the top right corner.
5. Restart the device (recommended).

Legend

- ① IP address mode

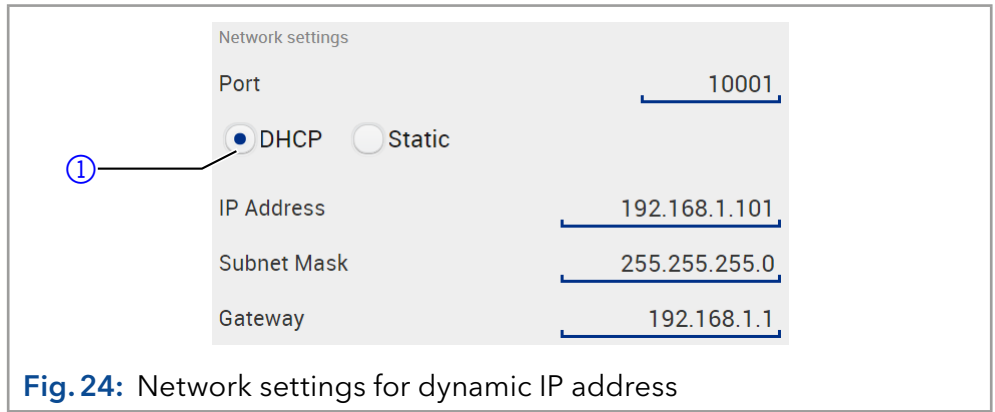


Fig.24: Network settings for dynamic IP address

Result The device is now accessible via a dynamic IP address.

6.7.3 Mobile Control: Setting a dynamic IP address via device serial number

- Prerequisites**
- The device is switched on.
 - Mobile Control is installed and running.
 - The connection between Mobile Control and the device has been established.

Process

- Procedure**
1. In Mobile Control, click <Settings>.
 2. In <Network Settings>, click <Reset>.
The window <Reset communication settings> opens.
 3. Enter the serial number of the device into the text field.
 4. Click <OK>. The device is now reset to default settings.
 5. Restart the device (recommended).

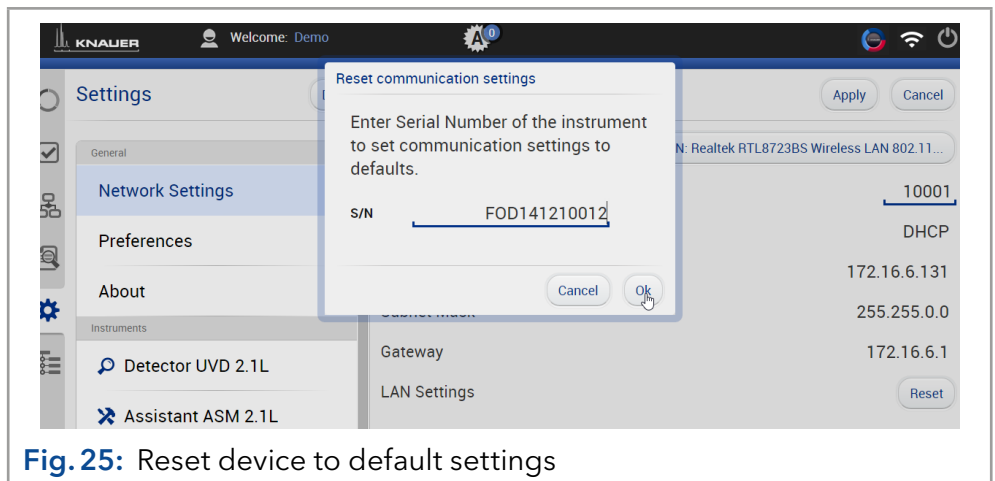


Fig.25: Reset device to default settings

Result The device is now accessible via a dynamic IP address.

6.7.4 Firmware Wizard: Setting a static IP address



Note: More information about LAN settings can be found in the Mobile Control Software Instructions in the chapter "Firmware Wizard" (document no. V6851-2).

Legend

- ① Text box for serial number of the device
- ② Setting IP address manually
- ③ Text box for IP address
- ④ Text boxes for subnet mask & gateway
- ⑤ Confirm changes

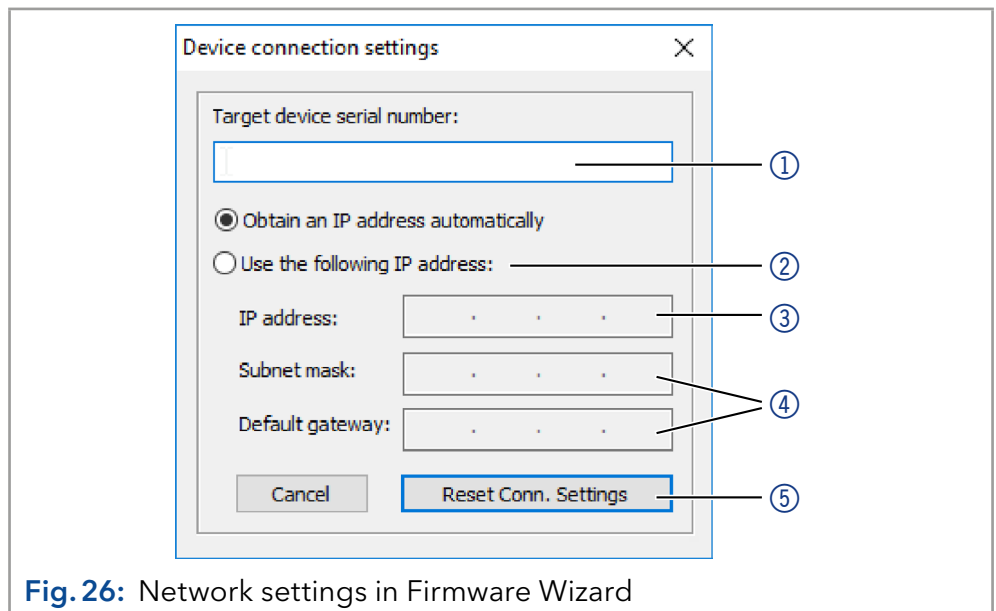


Fig. 26: Network settings in Firmware Wizard

Prerequisites

- The device is switched on.
- Firmware Wizard is installed and running.

Process

Procedure

1. In Firmware Wizard, click <Reset LAN Settings...>.
2. The window <Device connection settings> opens. Enter serial number of the device into the text field <Target device serial number> ①.
3. Select option <Use the following IP address> ②.
4. Enter the IP address into the text field <IP address> ③.
5. Optionally, adjust subnet mask and gateway ④.
6. Click <Reset Conn. Settings> ⑤ to accept changes.
7. Restart the device (recommended).

Result

The device is now accessible via the static IP address.

6.7.5 Firmware Wizard: Setting a dynamic IP address

- Prerequisites**
- The device is switched on.
 - Firmware Wizard is installed and running.

Process

- Procedure**
1. In Firmware Wizard, click <Reset LAN Settings...>.
 2. The window <Device connection settings> opens.
Enter serial number of the device into the text field <Target device serial number> ① .
 3. Select option <Obtain an IP address automatically> ② .
 4. Click <Reset Conn. Settings> ⑤ to accept changes.
 5. Restart the device (recommended).

Result The device is now accessible via a dynamic IP address.

6.7.6 Setting a static IP address via APIPA

To set an IP address for a device, it must be connected to a LAN network. Both LAN ports of the device and be connected as needed with a PC and/or with any other device. Note that the other device can again be connected with a third device and so on, so you may add several devices in a row.

AZURA® Neo Via Mobile Control, you can set the IP address either manually or via DHCP (see previous chapters). In addition, all devices with AZURA® Neo can be set via "routerless" APIPA configuration.

To set an IP address via APIPA configuration, the PC and the LAN control has to be set to DHCP mode. If no DHCP server is detected, the device switches to the APIPA configuration and automatically receives an IP address. This process may take a few minutes.

6.8 Connecting the pin header

To control one device through another, the pin header is used. To use remote control, you have to connect cables to the pin header. The single ports are used to exchange control signals.

- Prerequisites**
- The device is switched off.
 - The power plug is disconnected from the device.
- Tools**
- Depressor tool

NOTICE

Electronic defect

Connecting cables to the multi-pin connector of a switched on device causes a short circuit.

- Turn off the device before connecting cables.
- Pull the power plug.

NOTICE

Electronic defect

Electrostatic discharge can destroy the electronics.

- Wear a protective bracelet against electrostatic discharge and ground.

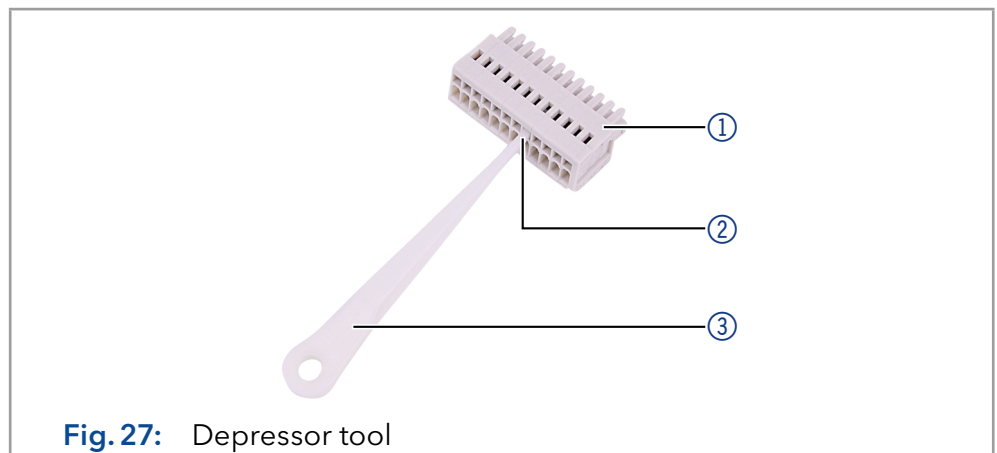


Fig. 27: Depressor tool

Process

1. Insert the depressor tool ③ in an upper small opening at the front of the pin header ①.
2. Insert the cable into the opening ② underneath the inserted depressor tool
3. Pull out the depressor tool.

Next steps Check whether the cables are tightly attached. Press the pin header onto the connector. Finish the installation. Bring the device into operation.

7. Functionality tests



Note: Standard processes regarding IQ and OQ in single devices may be handled differently in individual cases.

7.1 Installation Qualification (IQ)

The customer may request the Installation Qualification, which is free of charge. In case of a request, the technical support of KNAUER or a provider authorized by KNAUER performs this functionality test during the installation.

The Installation Qualification is a standardized document that includes the following:

- Confirmation of flawless condition at delivery
- Check if the delivery is complete
- Certification on the functionality of the device

You can either use the IQ document attached to this instruction manual or download a digital version from our website:



7.2 Operation Qualification (OQ)

The Operation Qualification includes an extensive functionality test according to KNAUER standard OQ documents. The Operation Qualification is a standardized document and free of charge. It is not part of the delivery. Please contact the technical support in case of a request.

The Operation Qualification includes the following:

- Definition of customer requirements and acceptance terms
- Documentation on system specifications
- System functionality check at installation site

- Test intervals** To make sure that the system operates within the specified range, you should test the system regularly. The test intervals depend on the usage of the device.
- Execution** The test can be carried out either by the technical support of KNAUER or by a provider authorized by KNAUER (for a fee). For further information visit our website:



8. Troubleshooting

8.1 First measures

- Check all cables and fittings.
- Check all screw fittings.
- Check whether air has entered the supply lines.
- Check the device for leaks.
- Pay attention to system messages.

Further measures:

- Compare occurring errors with the list of possible errors (see below).
- Contact the Customer Support.

8.2 LAN

Go through the following steps if no connection can be established between the computer and the devices. After each step, check if the problem is solved. If the problem cannot be found, call technical support.

1. Check the status of the LAN connection in the Windows task bar:



If no connection was established, test the following:

- Is the router/switch powered on?
 - Is the patch cable properly connected to the router/switch and the computer?
2. Check the router settings (if router is available):
 - Is the router set to DHCP?
 - Is the IP address range sufficient for all connected devices?
3. Check all connections:
 - Are the patch cables connected to the LAN ports and not the WAN port?
 - Are all cable connections between devices and router/switch correct?
 - Are the cables plugged in tightly?
4. If the router is integrated into a company network, disconnect the patch cable from the WAN port.
 - Can the devices communicate with the computer even though the router is not connected to the company network?
5. Restart the system in the following order:
 - Turn off all devices, the router, and the computer.
 - Turn on the router first and wait for it to successfully complete its self-test.
 - Turn on the devices and the computer.
6. Replace the patch cable to the device which could not be connected.

7. Make sure that the IP port of the device matches the port that is set in the chromatography software.

8.3 Possible problems and solutions



Note: If you have problems with the handling of a single device, please refer to the troubleshooting section of the respective instructions.

Problem	Possible Cause	Solution
Sudden over-pressure on pump 1 and/or pump 2	Clogged IJM port	Cleaning of IJM (see chapter 5.11 on page 29).
	Clogged capillaries from pump pressure sensor to IJM	<ul style="list-style-type: none"> ■ Step by step investigation which capillary from pressure sensor to IJM is clogged. ■ Cleaning or replacement of clogged capillary.
Pressure higher than normal	Partly clogged IJM or capillary	See above.
Pump flow lower than set flow	Clogged check valve	<ul style="list-style-type: none"> ■ Cleaning procedure check valve (see AZURA® Pump P 2.1S / P 4.1S manual on page 33). ■ Replacement of check valve.
Pump flow higher than set flow	Pump works out of calibrated range	Contact Customer Support, possible recalibration of pump.
Pulsation of flow rate	Clogged check valve	<ul style="list-style-type: none"> ■ Cleaning procedure check valve (see AZURA® Pump P 2.1S / P 4.1S p.33). ■ Replacement of check valve.
No flow	Empty eluent	<ul style="list-style-type: none"> ■ Check the eluent reservoir. ■ Check if the purge valve still open. Close purge valve.
	Leakage	Check capillary connection and devices.
Communication error		Perform SOP System power up. If error still exists, contact the Customer Support.

9. Maintenance and care

9.1 Removing a leakage

Prerequisites The device has been switched off.

Material Cloth

Procedure

Process

1. Remove the leakage.
2. Dry the leakage tray with the cloth.
3. Confirm the error message via the chromatography software.

Next step Put the device back into operation.

10. Transport and storage

Regarding the following information, carefully prepare the device for transport or storage.

10.1 Taking the device out of operation

Prerequisites The device is switched off.

Procedure

Process

1. Pull the power plug out of the socket and then out of the device.
2. Pack the power cable together with the device.

Next steps Disconnect all electrical connections. Remove the accessories and pack the device for transport or storage.

10.2 Packing the device

- Original packaging: Ideally you should use the original transport packaging.
- Lifting: Grab the device around the center of both sides and lift it into the packaging. Do not hold onto front cover or leak tray, as these parts are loosely attached to the device.

10.3 Transporting the device

- Documents: If you want to return your device to KNAUER for repairs, enclose the „[Service request form and decontamination report](#)“ which can be downloaded from our website.
- Device data: For a secure transport, note the weight and dimensions of the device in chapter “11. Disposal” on page 49.

10.4 Storing the device

- Flushing solution: Pay attention that all hoses and capillaries have been emptied or filled with flushing solution (e. g. isopropanol) before storage. To prevent algae formation, do not use pure water.
- Seals: Close all inputs and outputs with cap fittings.
- Ambient conditions: The device can be stored under ambient conditions which are listed in chapter “12. Technical data” on page 50.

11. Disposal

Hand in old devices or disassembled old components at a certified waste facility, where they will be disposed of properly.

11.1 AVV-Marking Germany

According to the German "Abfallverzeichnisverordnung" (AVV) (January, 2001), old devices manufactured by KNAUER are marked as waste electrical and electronic equipment: 160214.

11.2 WEEE registration number



KNAUER as a company is registered by the WEEE number DE 34642789 in the German "Elektroaltgeräteregister" (EAR). The number classifies to category 8 and 9, which, among others, comprises laboratory equipment.

All distributors and importers are responsible for the disposal of old devices, as defined by the WEEE directive. End-users can send their old devices manufactured by KNAUER back to the distributor, the importer, or the company free of charge.

11.3 Eluents and other operating materials

All eluents and other operating materials must be collected separately and disposed of properly.

All wetter components of a device, e. g. flow cells of detectors or pump heads and pressure sensors for pumps, have to be flushed with isopropanol first and water afterwards before being maintained, disassembled or disposed.

12. Technical data

12.1 General system parameters

Number of Impingement Jets mixers	5, IJM 1-5 manual selection
Number of pumps	3
Number of valves	2
Process connection inlet ⁽¹⁾	1/8" OD, 2.1 mm, ID FEP tubing (UNF 1/4-28 thread, flat bottom)
Process connection outlet	1/16" OD, 0.5 mm, ID PEEK tubing (UNF 10-32, thread coned)
Volumetric flow rate	up to 50 ml/min ⁽²⁾
Volumetric flow rate	up to 3 l/h ⁽²⁾
Maximum operating pressure ⁽³⁾	140 bar (2030 psi)
Maximum flow rate, single pump	30 ml/min
Liquid temperature range	4 - 60 °C (39.2 - 140 °F)
Hold-up Volume	Pumps to system outlet (valve 2): 4.01 ml ⁽⁴⁾ API and Lipid pumps to IJM: 2.67 ml ⁽⁴⁾
Software	CDS optional available 21 CFR part 11 and Gamp 5 compliant
Interfaces	LAN, pin header connectors

⁽¹⁾ different connections on request

⁽²⁾ depends on IJM, viscosity of solvents and used capillary configuration, in production mode up to 70 ml/min

⁽³⁾ depends on specific pump configuration and application

⁽⁴⁾ inlet tubings of pumps are not considered

12.2 Technical parameters

Ambient conditions	Supported software package	PurityChrom 6, Mobile Control
	Temperature range	4 - 40 °C; 39.2 - 104 °F
	Air humidity	Below 90 % humidity (non-condensing)
	Power supply	Docking station (including pumps and valves): 100-240 V AC single phase, 50/60 Hz; Network switch: 100-240 V AC single phase, 50/60 Hz, 12 V DC Power supply

Power consumption (per device)	Docking station (including pumps and valves): maximum 130 W; network switch: 50 W
Dimensions (Width × Height × Depth)	361 mm x 501 mm x 603 mm
Net weight (approx.)	35 kg

12.3 Wetted materials



Note: For chemical compatibility of wetted materials see chapter “14. Chemical compatibility of wetted materials” on p. 55.

The materials of the wetted parts are subject to change without notice. Detailed information on the materials of the wetted parts are listed in the technical documentation and must be ordered separately.

The components of the LNP system contain the following wetted parts:

Impingement jets mixer

Material	Description
Stainless steel	AISI 316L (1.4404)
Stainless steel	AISI 316L (1.4435)

Pumps

Material	Description
Stainless steel	AISI 316L (1.4404)
Stainless steel	AISI 630 (1.4542/1.4548)
Titanium	Ti6Al4V
Polyetheretherketone	PEEK
Perfluoroelastomere	FFKM
Graphite fiber reinforced polytetrafluoroethylene	GFP 55 HT (PTFE ⁽⁵⁾)
Ethylene tetrafluoroethylene	ETFE ⁽⁷⁾
Polytetrafluoroethylene	PTFE
Fluorinated ethylene propylene	FEP ⁽⁷⁾
Ultra-high molecular weight polyethylen	Filled UHMW Polyethylene ⁽⁶⁾
Aluminum oxide	Al ₂ O ₃
Ruby	Al ₂ O ₃
Sapphire	Al ₂ O ₃
Zirconium oxide	ZrO ₂

⁽⁵⁾ for A48035/A48035V1

⁽⁶⁾ for A48040XYZ* (*also valid for variants with A48040XYZ. X, Y, Z = 0-9, or A-Z, or blank)

⁽⁷⁾ Pump inlet tubing and ferrule

	Material	Description
Valves	Polyetheretherketone (Rotor seal)	PEEK
	Stainless steel DLC* (Stator)	AISI 318LN

* stainless steel, coated with diamond-like carbon

Capillaries & fittings	Material	Description
	Stainless steel	AISI 316L (1.4404)
	Polyetheretherketone	PEEK
	Polyoxymethylene	POM
	Ethylene tetrafluoroethylene	ETFE

	Material	Description
Sample loops	Stainless steel	AISI 316L (1.4404)

13. Reorders

The list of repeat orders is current at the time of publication. Deviations at a later time are possible. Use the enclosed packing list for reordering spare parts. If you have any questions regarding spare parts or accessories, please contact our Customer Support.

Further information

Current information on spare parts and accessories can be found on the Internet at www.knauer.net.

13.1 Device

Name	Order no.
Pump P 4.1S	APG22FA*
Pump P 4.1S	APG22FJ**
VU 4.1	AWA04
2Port MultiPos valve V 4.1, fractionation valve	AVS85AH
6Port 2Pos valve V 4.1, injection valve	AVD26AE

13.2 Accessories and spare parts

	Name	Order no.
Pumps	AZURA® pump head, 50 ml, stainless steel	AHC20*
	AZURA® pump head, 50 ml, stainless steel	AHC20FB**
	Maintenance kit pump head EHC20*	ARH34
	Maintenance kit pump head EHC22FB**	ARH39
	Piston rod	A541511
	Set of gaskets	A0763*
	Set of gaskets	A07631**
	Check valve	A06842*
	Check valve	A06840**
Valves	Stator for 8 Port valve for EVS85AH	A205142
	Maintenance kit rotor seal for EVS85AH	ARV57
	Stator for 6 Port valve for EVD26AE	A205140
	Maintenance kit rotor seal for EVD26AE	ARV33
Mixer	Impingement Jets Mixer No. 1 Certified	A5881
	Impingement Jets Mixer No. 2 Certified	A5882
	Impingement Jets Mixer No. 3 Certified	A5883
	Impingement Jets Mixer No. 4 Certified	A5884
	Impingement Jets Mixer No. 5 Certified	A5885
	Quench mixer	A5831

	Name	Order no.
Capillaries	Reorder PEEK capillary set IJM NanoScaler, without screw connections	A71102
	Reorder set lipid loop, capillaries only	A71103-1
	PEEK capillaries IJM NanoScaler, with screw connections	F48040
API/Lipid supply kits	API/Lipid, starter kit	A71100
	API/Lipid, refill kit	A71101
Tubing	Tubing kit, pump inlet	A9650
	Tubing, pump inlet, 3 m	A9869
	10 ferrules for tubing, pump inlet	A58294
	10 nuts for tubing, pump inlet	A58295
Sample loops	Sample loop, 350 µl	A142615
	Sample loop, 500 µl	A0566
	Sample loop, 700 µl	A142616
	Sample loop, 1 ml	A0567
	Sample loop, 2 ml	A0568
	Sample loop, 5 ml	A0586-2

* A48035/A48035V1

** A48040XYZ

14. Chemical compatibility of wetted materials



Note: The user takes the responsibility for using the fluids and chemicals in an appropriate and safe way. If there is any doubt, contact the Technical Support of the manufacturer.

14.1 General

The device is very resistant against a variety of commonly used eluents. However, make sure that no eluents or water come in contact with the device or enter into the device. Some organic solvents (such as chlorinated hydrocarbons, ether) may cause coating damage or loosen glued components by improper handling. Even small quantities of other substances, such as additives, modifiers, or salts can influence the durability of the materials. Exposure time and concentration have a high impact on the resistance.

The following list contains information about the chemical compatibility of all wetted materials which are used in devices made by KNAUER. The data bases on a literature research on the manufacturer specifications of the materials. The wetted materials of this device are listed in the chapter "Technical data".

All resistances mentioned here are for use at temperatures up to 40 °C, unless stated otherwise. Please note that higher temperatures can significantly affect the stability of different materials.

14.2 Plastics

Polyetheretherketone (PEEK)

PEEK is a durable and resistant plastic and, next to stainless steel, the standard material in HPLC. It can be used at temperatures up to 100 °C and is highly chemical resistant against almost all commonly used solvents in a pH range of 1-12.5. PEEK is potentially moderate resistant against oxidizing and reducing solvents.

Therefore, following solvents should not be used: Concentrated and oxidizing acids (such as nitric acid solution, sulfuric acid), halogenated acids (such as hydrofluoric acid, hydrobromic acid) and gaseous halogens. Hydrochloric acid is approved for most applications.

In addition, following solvents can have a swelling effect and may have an impact on the functionality of the built-in components: Methylene chloride, THF and DMSO in any concentration such as acetonitrile in higher concentrations.

Polyethylene terephthalate (PET, outdated PETP)

PET is a thermoplastic and semi-crystalline material with high wear resistance. It is resistant against diluted acids, aliphatic and aromatic hydrocarbons, oils, fats and alcohols, but not against halogenated hydrocarbons and ketones. Since PET belongs chemically to esters, it is not compatible with inorganic acids, hot water and alkalis. Maximum operating Temperature: up to 120 °C.

Polyimide (Vespel®)

This material is wear-resistant and permanent resilient thermally (up to 200 °C) as well as mechanically. It is chemically broadly inert (pH range 1-10) and is especially resistant against acidic to neutral and organic solvents, but vulnerable to pH strong chemical or oxidizing environments: It is incompatible with concentrated mineral acids (such as sulfuric acid), glacial acetic acid, DMSO and THF. In addition, it will be disintegrated by nucleophilic substances like ammonia (such as ammonium salts under alkaline conditions) or acetate.

Ethylene-tetrafluorethylene copolymer (ETFC, Tefzel®)

This fluorinated polymer is highly resistant against neutral and alkaline solvents. Some chlorinated chemicals in connection with this material should be handled with care. Maximum operating Temperature is 80 °C.

Perfluorethylenpropylen-Copolymer (FEP), Perfluoralkoxy-Polymer (PFA)

These fluorinated polymers hold similar features as PTFE, but with a lower operation temperature (up to 205 °C). PFA is suitable for ultrapure applications, FEP can be used universally. They are resistant against almost all organic and inorganic chemicals, except elemental fluorine under pressure or at high temperatures and fluorine-halogen compounds.

Polyoxymethylene (POM, POM-HTF)

POM is a semi-crystalline, high-molecular thermoplastic material which stands out due to its high stiffness, low friction value and thermic stability. It can even substitute metal in many cases. POM-H-TF is a combination of PTFE fibres and acetal resin and is softer and has better slip properties as POM. The material is resistant against diluted acids (pH > 4) as well as diluted lyes, aliphatic, aromatic and halogenated hydrocarbons, oils and alcohols. It is not compatible with concentrated acids, hydrofluoric acid and oxidizing agent. Maximum operating Temperature is 100 °C.

Polyphenylene sulfide (PPS)

PPS is a soft polymer which is known for its high break resistance and very high chemical compatibility. It can be used with most organic, pH neutral to pH high, and aqueous solvents at room temperature without concerns. However, it is not recommended for using with chlorinated, oxidizing and reducing solvents, inorganic acids or at higher temperatures. Maximum operating temperature: 50 °C.

Polytetrafluorethylene (PTFE, Teflon®)

PTFE is very soft and anti-adhesive. This material is resistant against almost all acids, lyes and solvents, except against fluid sodium and fluoride compounds. In addition, it is temperature-resistant from -200 °C to +260 °C.

Systec AF™

This amorphous perfluorinated copolymer is inert against all commonly used solvents. However, it is soluble in perfluorinated solvents like Fluorinert® FC-75 and FC-40, and Fomblin perfluor-polyether solvents from Ausimont. In addition, it is affected by Freon® solvents.

Polychlorotrifluoroethylene (PCTFE, Kel-F®)

The semi-crystalline thermoplastic material is plasticizer-free and dimensionally stable, even in a wide temperature range (–240 °C to +205 °C). It is moderately resistant against ether, halogenated solvents and toluene. Halogenated solvents over +60 °C and chlorine gas should not be used.

Fluorinated rubber (FKM)

The elastomer consisting of fluorinated hydrocarbon stands out due to a high resistance against mineral oils, synthetic hydraulic fluids, fuels, aromatics, and many organic solvents and chemicals. However, it is not compatible with strong alkaline solvents (pH value > 13) like ammonia, and acidic solvents (pH value < 1), pyrrole and THF. Operating temperature: Between –40 °C and +200 °C.

Perfluorinated rubber (FFKM)

This perfluoro elastomer has a higher fluorine content as fluorinated rubber and is therefore chemically more resistant. It can be employed at higher temperatures (up to 275 °C). It is not compatible with Pyrrole.

14.3 Non-metals

Diamond-like carbon (DLC)

This material is characterized by a high hardness, a low coefficient of friction and thus low wear. In addition, it is highly biocompatible. DLC is inert against all acids, alkalis and solvents commonly used in HPLC.

Ceramic

Ceramic is resistant against corrosion and wear and is fully biocompatible. An incompatibility against acids, alkalis and solvents commonly used in HPLC is not known.

Alumina (Al₂O₃)

Due to their high resistance to wear and corrosion, alumina ceramic is used as a coating for mechanically stressed surfaces. It is a biocompatible material with low thermal conductivity and low thermal expansion.

Zirconium oxide (ZrO₂)

Zirconia ceramics are characterized by their high mechanical resistance, which makes them particularly resistant to wear and corrosion. It is also biocompatible, has low thermal conductivity and is resistant to high pressures.

Sapphire

Synthetic sapphire is virtually pure monocrystalline alumina. It is biocompatible and very resistant to corrosion and wear. The material is characterized by a high hardness and a high thermal conductivity.

Ruby

Synthetic ruby is monocrystalline alumina and gets its red color by the addition of some chromium oxide. It is biocompatible and very resistant to corrosion and wear. The material is characterized by a high hardness and a high thermal conductivity.

Mineral wool

This insulating material consists of glass or stone wool fibres and isolates in high oxidizing conditions and at high temperatures. Mineral wool is valid as commonly inert against organic solvents and acids.

Glass, glass fibre, quartz, quartz glass

These mineral materials are resistant against corrosion and wear and are mostly chemical inert. They are compatible with oils, fats and solvents and show a high resistance against acids and lyes up to pH values of 3-9. Concentrated acids (especially hydrofluoric acid) may embrittle and corrode the minerals. Lyes may ablate the surfaces slowly.

14.4 Metals

Stainless steel

Stainless steel is, apart from PEEK, the standard material in HPLC. Steels with WNr. 1.4404 (316L) are used, or with a mixture of higher compatibility.

They are inert against almost all solvents. Exceptions are biological applications which are metal ion sensible, and applications with extreme corrosive conditions. These steels, in comparison to commonly used steels, are increasingly resistant against hydrochloric acid, cyanides and other halogen acids, chlorides and chlorinated solvents.

The use in ion chromatography is not recommended. In case of electrochemical applications, a passivation must be executed first.

Hastelloy®-C

This nickel-chrome-molybdenum alloy is extremely resistant to corrosion, especially against oxidizing, reducing and mixed solvents, even at high temperatures. This alloy may be used in combination with chlorine, formic acid, acetic acid and saline solutions.

Titanium, titanium alloy (TiAl6V4)

Titanium has a low weight and a high hardness and stability. It stands out due to its very high chemical compatibility and biocompatibility. Titan is applied when neither stainless steel nor PEEK are usable.

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