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Contents

1 Introduction

1.1 Intended Use

The SNPtower is a thermocycler for amplification of DNA, using polymerase chain reaction (PCR). It has an integrated detector for measurement of sample fluorescence before and after a PCR run. Although the product has been specifically developed for verification of single-point mutation (SNP), it can equally be employed in any PCR-based verification procedure that requires fluorescence measurement prior to or on completion of the PCR reaction. Up to six different dyes can be detected for a given sample position (well) by the SNPtower at a time, with filters selected to match the dyes that are most frequently used for PCR. In Reader mode, the SNPtower is able to measure fluorescence in a PCR plate without requiring a PCR run to be actually triggered.

Fluorescence cannot be measured with the SNPtower after each PCR cycle (real-time-PCR).

ASpect SNP control and evaluation software is provided for graphical and numerical representation of measured values. Available software capabilities:

- Operation control and monitoring
- Definition, importation and exportation of measuring methods
- Comprehensive options for graphical and numerical evaluation and representation of data
- Pre-selectable automated data evaluation
- Data exportation to EXCEL or in ASCII file format
- Definition of standards, blanks, master samples and samples on a plate, including supplements
- Quantitative analysis with 13 linear and non-linear models for calculation of calibration graphs
- Up to twelve mutually independent experiments (groups) on a plate
- Positive/negative analysis
- SNP diagnostics
- Exportation and importation of plate layouts
- Configurable result listing
- User administration with three authorization levels

1.2 Notes Regarding the Use of This Manual

Warning and information symbols used throughout this Manual:



Danger!

Information of this kind must be followed under all circumstances in order to prevent physical injury to people.



Caution!

Notes of this kind must be followed in order to prevent damage to the product.



Dangerous electrical contact voltage!



Note

Useful advice must be observed in order to obtain correct measurement results.

Systematic guidelines used throughout this Manual:

- Chapters and illustrations are numbered consecutively.
- Each picture has its own caption.
- Work steps are numbered.
- Cross-references to other sections are marked with an arrow (e.g. → "Notes Regarding the Use of This Manual" p. 1)

2 Safety Requirements

2.1 General Safety Requirements for Working with SNPtower

For your own safety and to assure failsafe operation, you should carefully read this chapter before you proceed with any kind of SNPtower start-up action.

Comply with all safety requirements contained in this Manual and follow all messages and prompts that are displayed by the control software on the monitor.

Safety requirements relating to included system components from other manufacturers (e.g. PC, printer) must equally be observed.



Intended use!

The SNPtower may not be used for applications other than described in this User Manual. No manufacturer warranty can be assumed in the event of any other type of use, including that of individual assemblies or single parts. This shall equally apply to all kinds of service or repair work that is not performed by authorized service personnel. All claims for warranty/guarantee will be null and void in such cases.



Local requirements!

Local safety provisions and rules which are applicable to product operation should be followed (e.g. industrial labor protection practice, accident prevention rules, industrial safety regulation).

A reference to potential hazards contained in the User Manual must not be regarded as replacing compulsory workforce safety requirements.



Personnel!

The SNPtower may not be operated by anyone other than duly trained and qualified personnel.

Prior knowledge of this Manual is indispensable and assumed to have been acquired before operation.



Shut-down in the event of emergency!

In the event of an emergency, the power plug must be detached from the line socket in order to cut power supply to the system and its components.

Caution! There is danger of loss of data and damage to the operating system on the PC side!



Electric shock!

The power plug may only be inserted into a line socket with PE contact. This is necessary to comply with safety class I (PE-connection) state. You are prohibited from bypassing this safety state by installing an extension cable without PE conductor.

Safety Requirements

Turn power off and detach the power plug before you open the SNPtower or remove protective shielding!

Use only fuses of specified type for replacement.



Refrain from operation in rooms with an explosive atmosphere!



Hot sample block!

Where a running temperature program is aborted in the phase of heating up, the sample block is likely to still be hot at the time the lid is opened.

There is danger of burns to the skin!



Danger of injury by the motorized lid.

Do not touch the sample block while the lid of the device is closing. There is danger of squeezing your fingers!



Heat build-up

Thermal build-up may cause overheating and malfunction of the SNPtower. Ensure that its ventilation slots are unobstructed at all times! You should also check for unhindered air intake through the slots in the system underside. These must not be covered by objects, for example, a loose sheet of paper.



Water

Take care to prevent penetration of liquid into the inner system space. Otherwise, the system may suffer damage.



Danger of corrosion

Do not operate the SNPtower in the direct vicinity of aggressive vapors, for example, strongly etching acidic or alkali fumes! Such fumes might corrode its terminals, mechanical and optical parts.

2.2 Standards & Directives

Protection class and degree of internal protection

The SNPtower qualifies for protection class A.
Its casing is designed to comply with internal protection standard IP 20.

Operating safety

The SNPtower meets the following two safety standards:

- DIN EN 61010-1 (VDE 0411T.1; IEC 61010-1)
- DIN EN 61010-2-061 (IEC 61010-2-061)

EMC compatibility

The SNPtower has been tested for radio interference suppression and noise immunity and found to fulfil the requirements according to:

- DIN EN 61326

Environmental compatibility

The SNPtower has been tested for environmental compatibility and found to meet the requirements according to:

- DIN ISO 9022-3:2000
- DIN ISO 9022-32-03-0
- DIN ISO 9022-2:2003/01

EC directives

The SNPtower was built and tested to comply with the requirements of EC directives 2006/95/EC and 2004/108/EC. It is factory-shipped in a faultless and absolutely safe technical condition. To preserve this condition and ensure reliable operation, the user must observe all safety notes and instructions provided in this Manual. Integrated accessory or system components from other manufacturers should be treated in accordance with the appropriate user manuals.

Safety Requirements

3 Technical Data

Thermocycler

Heat source	High-power long-life Peltier devices
Lid	Contacted pressure (with 60 kg/plate) heated (to 120 °C) with lens array for fluorescence measurement
Sample volume	2 µL – 17 µL
Sample block temperature	4 °C – 105 °C
Control accuracy	± 0.2 °C
Block homogeneity	± 0.2 °C
Heating rate	12 °C/s max. (0.1 – 10 °C/s controlled mode)
Cooling rate	8 °C/s max (0.1 – 6 °C/s controlled mode)

Fluorescence photometer

Principle	Patented 8-channel epi-fluorescence photometer with fiber multiplexer and mechanical scanning unit
Light source	3 power LEDs (red, white, blue)
Detector	Channel photo multiplier
Excitation wavelength	Color 1: 475 nm Color 2: 530 nm Color 3: 565 nm Color 4: 625 nm
Detection wavelength	Color 1: 515 - 530 nm Color 2: 565 - 580 nm Color 3: 615 - 645 nm. Color 4: 685 - 730 nm
Limit of detection	1 nM FAM in PCR buffer
Dynamic range of detector	17 bit (0 – 131072)
Reproducibility	< 5 % CV in well (single measurement)
Measuring rate	4 s for entire plate (96 wells) and 4 colors
Plate formats	96-well SpeedCycler PCR plate

Technical Data

Other technical data

Energy supply	
Line voltage	110 – 240 V \pm 15%
Line frequency	50 – 60 Hz
(Max.) Power consumption	450 W
Built-in fusing	3.15 AH, 250 V, inert
Phys. dimensions (WxDxH)	240 mm x 260 mm x 450 mm
Weight	About 8 kg
Data terminal	USB
Software-driven PC requirements	Not below Pentium III, 900 MHz level
Operating system	Windows 2000 / XP (SP2) / VISTA

4 System Description & Operating Principle

4.1 System Setup & Components

The SNPtower is a rapidPCR- thermocycler that combines with a patented fluorescence spectrometer.



- 1 Upper part of fluorescence spectrometer
- 2 Lower part with thermocycler

Fig. 1 SNPtower

Thermocycler

For SNPtower operation, a rapidPCR thermocycler has been selected. With a special microplate, it is optimized for small sample quantities and rapid changes in temperature.

High-power Peltier devices are included for thermal stabilization of a sample block of gold-coated solid silver. This helps achieve very high heating and cooling rates.

The sample block lid is heated to a temperature that can be selected. Built into the sample block lid is a lens array for fluorescence measurement.

Fluorescence photometer

A patented 8-channel epi-fluorescence photometer with fiber multiplexer and mechanical scanning unit is used as the detector.

4.2 Function

4.2.1 Lid Heating/PCR Start

A specific temperature can be set for the heatable lid to apply to a given PCR cycle. It will be kept during the entire temperature program sequence. Three different modes are available for lid heating and PCR start:

- SPS
- SPS with manual start
- simple start

SPS

Sample Protection System

After a starting command, the block will be thermally adjusted to the standby temperature, whereas the lid is heated to the specified lid temperature. Once the specified lid temperature is reached, the lid will be automatically pressed onto the samples and the temperature program will be triggered.

Because the lid is not pressed on before its preset temperature level is actually reached, early heating of the sample with potentially early or undesired chemical reactions are prevented.

SPS with manual start

In this starting mode, the program will start with some delay. Once triggered, the program will initially heat the lid to its specified temperature level and adjust the thermo block to the standby temperature as in the case of **SPS**. Upon reaching the preset lid temperature, the software reports that temperatures were adjusted and a sample can be inserted. The temperature program will not start, unless it has received another manual start acknowledgement.

Accordingly, this mode allows the thermo block and the lid to be adjusted to their respective starting temperatures before a sample is installed in the block. This option should be used for temperature-sensitive samples, in order to achieve maximum uninterrupted cooling prior to PCR.

Simple start

On receipt of a starting command, the temperature program sequence will begin without delay and without activation of SPS. The lid is pressed onto the sample block at room temperature and heated to nominal temperature at the beginning of a temperature program cycle.

4.2.2 Temperature Control

Temperature control can work in any of these modes:

- Block Control
- Simulated Tube Control
- Manual Control

Block Control

Temperature control relies on the temperature level that was measured at the sample block.

This option can be used as a basis for adaptation of long standard log-sheets. Compared to simTubeControl, this mode requires more control time to reach a given in-sample temperature.

Simulated Tube Control

This temperature control mode uses a calibration model that calculates the temperature inside a sample. This facilitates express adjustment of the temperature inside a sample while reducing the time to reach the specified temperature inside a sample.

Manual Control

By defining a factor, you are able to set a temperature control mode for **Simulated Tube Control** that is similar or close to **Block Control**. A factor of **0** corresponds to **Block Control**, a factor of **10** corresponds to **Simulated Tube Control** (fastest temperature control mode).

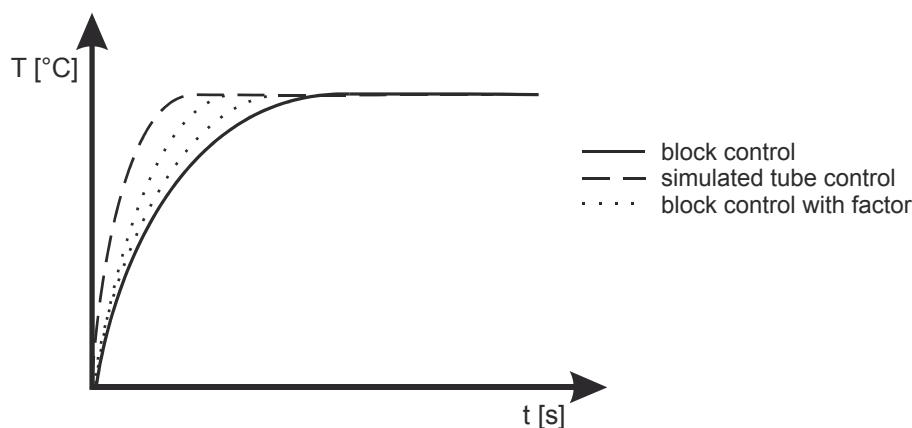


Fig. 2 Schematic diagram showing ramp-up graphs to sample end temperature for the various temperature control modes

4.2.3 Low-Profile Rapid Block & Microplate From Analytik Jena

The Low-Profile Rapid-Block (LPR-Block) is a special offering from Analytik Jena. It consists of a combined system of a high-performance thermo block and a 96-well microplate.

The microplate is specifically adapted to the shape of the sample block and optimized for low consumption of reagents. It is made from polypropylene. This plastic material provides a number of benefits when used for PCR:

- Polypropylene is chemically inert.
- There will be no unspecified bonds on the surface of reaction cavities as occurs when using glass capillaries.
- Blocking reagents such as BSA are not required.

System Description & Operating Principle

Propylene has thermo-elastic properties that prove convenient in SAC technology applications (**S**elf **A**dapting **C**ontainer). The wells of a microplate extend while a PCR is in process as a result of heat and pressure, thus closely adhering to the depressions of the sample block like skin. This facilitates perfect contact with the block during the process and guarantees a very strong transfer of energy from the block to the sample.

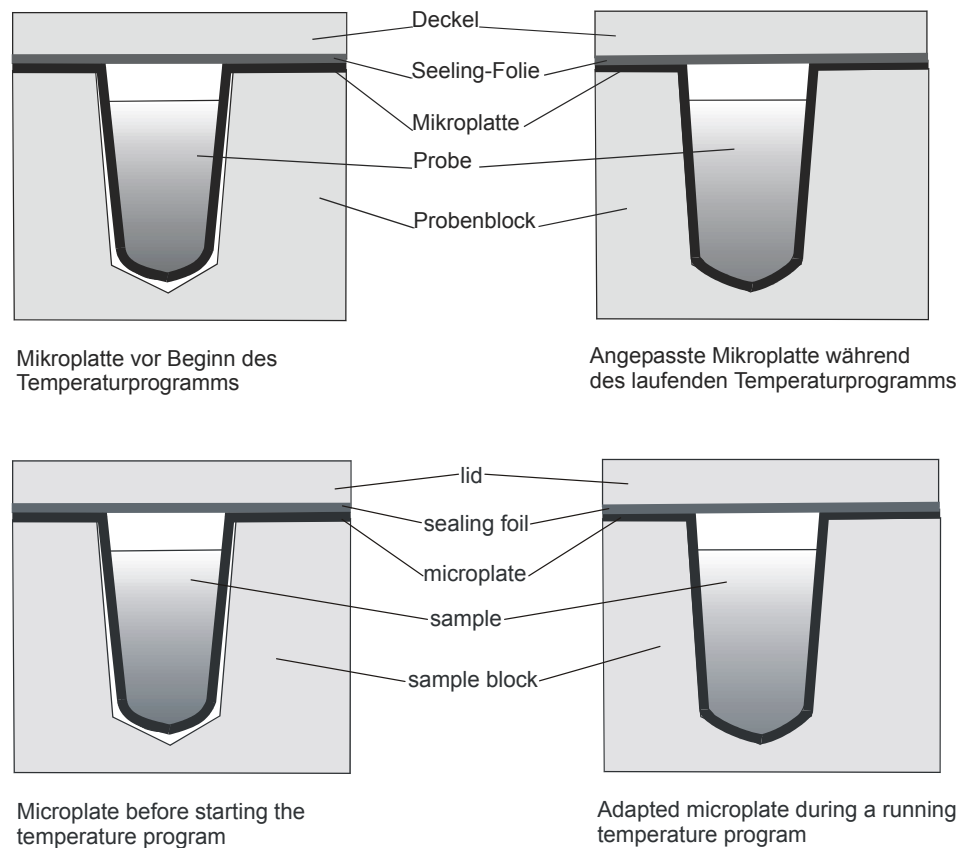


Fig. 3 Adjustment of microplate to sample block

5 Transportation & Installation Requirements

5.1 Transportation & Storage

For transportation and storage, the following ambient conditions must be maintained:

Temperature range	-40 °C – +70 °C
Rel. air humidity	10% to 30%

Use drying agent!

5.2 Installation Requirements



Caution! The following compulsory rules must be observed during operation!

Keep ventilation slots unobstructed!

Do not place objects onto the SNPtower!

Prevent operation in rooms with an explosive atmosphere!

There must be no aggressive vapors, for example, strongly etching acidic or alkali fumes in the immediate surroundings of the system.

The installation site must meet the following requirements:

- Absence of draught effects, dust, etching vapors and mechanical vibration.
- No electromagnetic fields (e.g. motors) located nearby.
- No dripping, gushing or splashing water near the SNPtower.
- No exposure to incident solar radiation or radiation emitted by heaters.

Temperature range	+10 °C - +40 °C
Max. rel. air humidity	93% at +40 °C

Footprint requirements

With physical dimensions as quoted above and approximately 100 mm of clearance on all sides, the SNPtower requires a minimum footprint area of 500 mm x 580 mm (W x D).

Transportation & Installation Requirements

6 Installation & Start-Up

6.1 Connecting the SNPtower



Ensure correct position!

Transport the SNPtower only in upright position (use marker on transport case for guidance).

Prevent overturning as you perform unpacking.

1. Retrieve the SNPtower, supply cabling and user manual with installation CD from the transport package. Wait until the SNPtower has reached room temperature level.
2. Store the transport package for future transportation requirements.
3. Connect the USB cable to the SNPtower and the PC (Fig. 4/6).
4. Connect the power supply cable (Fig. 4/3).

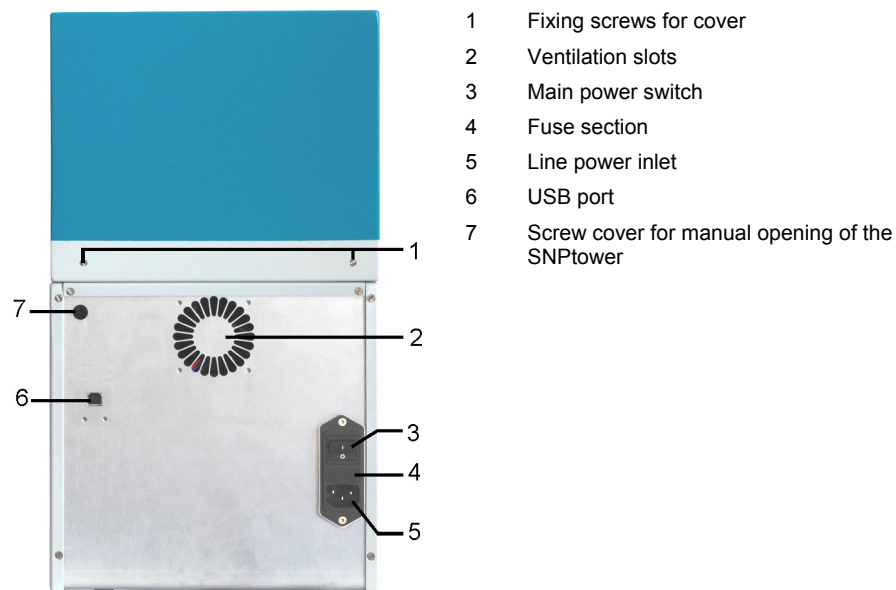


Fig. 4 Rearside terminals of SNPtower

6.2 Starting Up

1. Install ASpect SNP software on your PC. Follow instructions in the software manual.
2. Turn the SNPtower on at the main power switch (Fig. 4/5).

On completion of the automated driver installation routine, you can work with the SNPtower. Should the drivers fail to install automatically, you can use the Windows routine for installation. The drivers are contained in directory: C:\Programs\ASpectSNP\DriverUSB or on the installation CD.

3. Launch ASpect SNP software session.
4. Trigger system initialization to establish connection between the SNPtower and the PC.

Click  in ASpect SNP or select **Measurement / Initialize device** menu command.

The SNPtower is operational now. Equipment operation is controlled via software under ASpect SNP. For further information about settings for measurement or temperature program, please consult the software part of this User Manual.

6.3 Turning the SNPtower Off

Do not turn the SNPtower off before a PCR run has finished!

1. Use the main power switch at the back to turn off power to the SNPtower.
2. Keep the lid closed as long as the SNPtower is in power-off state, in order to prevent soiling of the sample block.
Dust penetrating into the wells or other types of contamination may falsify the results of fluorescence measurement (→ section "Cleaning the Sample Block").


7 Insertion of Samples

The SNPtower has been adapted to 96-well capacity SpeedCycler PCR plates. It is also possible to use stripes of this plate material. Once the PCR samples have been pipetted into the plates, they must be sealed with transparent tape (sealing foil). The optical transparency of a selected foil has an essential influence on the fluorescence signal. For this reason, you are advised to exclusively use clear sealing foil of the type offered for real-time PCR tasks.

1. Place a PCR plate onto the thermo block with well A1 located on the left-hand side (white arrow in Fig. 5).

In this position, the wells can uniformly submerge into the sample block. The lid cannot be closed, unless a sample plate is correctly inserted and not too badly warped!

2. Close the lid:

Motorized lid: Trigger a **Measurement / Start Measurement** menu command or click the  icon.

Manual lid: Pull the upper system part to the front-end mechanical stop.



Note

The motorized lid cannot be opened or closed other than by push motion of the upper system part. Opening or closing motion can only be accomplished via software-control commands in an ASpect SNP program session!



Fig. 5 SNPtower with lid open

Insertion of Samples

8 Maintenance & Care

The SNPtower is largely maintenance-free.

User maintenance and care actions are restricted to:

- Cleaning of the enclosure
- Cleaning of the sample block if necessary
- Cleaning of the lens array if necessary

To maintain your laboratory in a certified state with product validation, we offer you a maintenance contract.

In the event of malfunction, system failure or defects, you should contact our Technical Customer Service.

8.1 Cleaning of Enclosure

Use only a clean soft piece of cloth to wipe down the enclosure surfaces of the SNPtower. It can be slightly moistened with standard available neutral cleaning agent as may be appropriate from case to case.

**Caution!**

The use of solvents may cause damage to the paint coating.

8.2 Cleaning of Sample Block

After longer periods of operation or also idle periods of the SNPtower with the lid open, dirt may penetrate into the depressions (dust or reagent residue) and result in an increased background signal.

- Blow depressions of sample block out, using compressed air.
- To remove reagent residue from affected wells, fill a maximum of 20 μL of distilled water or ethanol into these wells. Aspirate this volume after a residence time of one minute approximately. Repeat this process until the background signal is found to be restored to within standard limits.

8.3 Cleaning of Lens Array

The lens array may have to be cleaned if:

- a strong background signal is still measured for some wells despite completed cleaning of a sample block
- sample liquid emerges from the sealing foil.

**Note**

Work of this kind requires the system to be opened. We recommend that cleaning be performed by our Customer Service.

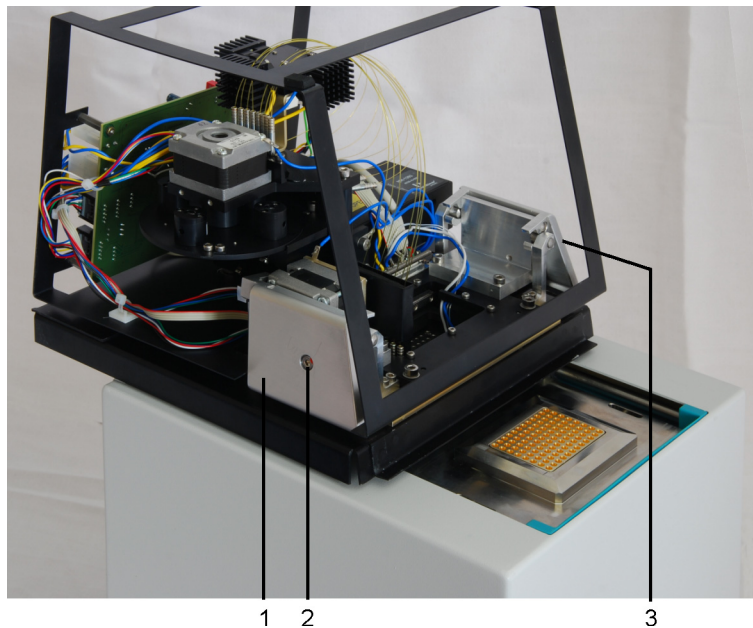
1. Remove the screws for mechanical attachment of the system cover at the back-end side of the SNPtower (Fig. 4 / 1).

2. Take the system cover off.

Raise the enclosure shell by approximately 2 mm at the back end, then push it towards the front. Take the cover off from the top.

Caution: The sensitive light conductors will be exposed now. Proceed with utmost care for cleaning!

3. Remove the locking screws from the handle grips (Fig. 6).



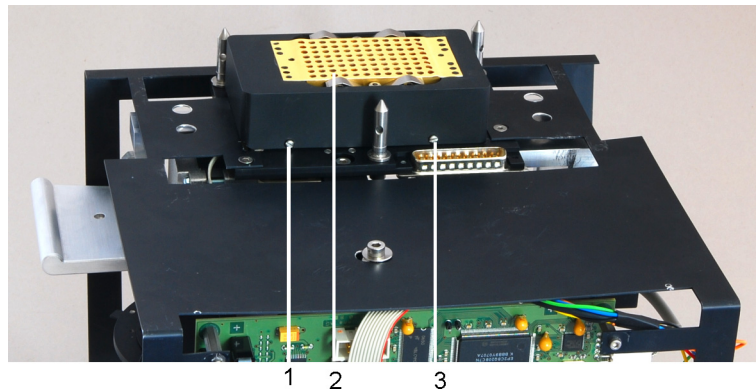
- 1 Handle grip
- 2 Locking screw
- 3 Handle grip with locking screw (covered up)

Fig. 6 Handle grips with locking screw

4. Tilt both handle grips up.

The entire measuring head will be released and somewhat raised as you do this.

5. Seize the handle grips, take the measuring head off from the top and place it down on its lateral face so the lens array faces to the top.

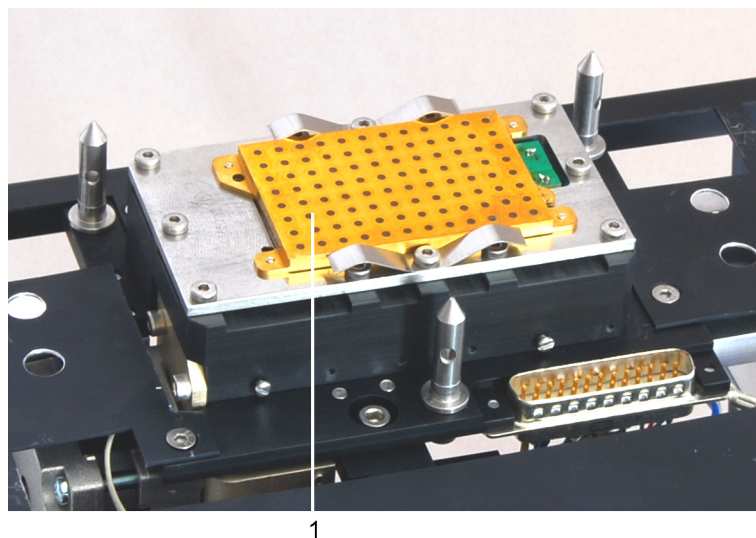


- 1, 3 Locking screws
- 2 Protective cap with silicon mat

Fig. 7 Protective cap over lens array

6. Remove the locking screws in the protective cap and carefully pull the cap off from the top.

The silicon sealing mat will come off slowly and the smooth lens array surface be exposed as you take the cap off.



- 1 Lens array

Fig. 8 Lens array, exposed

7. Use a piece of cloth moderately moistened with ethanol for cleaning until the lens array surface shows a uniformly smooth appearance. Use a dry piece of cloth to remove striae-like patterns that may be forming on the surface.
8. Put the protective cap on again and press it firmly into position. Make sure that the silicon mat is replaced onto the lens array in such a position that each of the 96 lenses is roughly center-aligned to its mating silicon mat hole. Tighten the locking screws in the protective cap.
9. Hold the measuring head by its handle grips, then place it onto the basic system unit with the three guide pins fitted into the mating sprocket holes.

10. Press both handle grips down at the same time. This will firmly clamp the measuring head to the basic system unit.
11. Screw the locking screws into the handle grips.
12. Put the system cover on again.
Hold system cover below the sheet-metal rim at the front end, insert it and push it backward until the cover can be properly pressed own at the back end of motion.
13. Turn the fixing screws in.

8.4 Replacement of Fuses

Current supply v is protected by fusibles on the system's inlet side.

1. Remove the electric power cable.
2. Remove fuse holder from power inlet module (4 in Fig. 4 p.17).
3. Replace fuses. Use only fuses of this type for replacement:
 - 2 x 3,15 AH, inert
4. Mount fuse holder again.
5. Reconnect electric power cable.
6. Turn power to the SNPtower on again.

9 Trouble Shooting

Manual lid opening

Should motorized lid opening fail, the lid can be opened using manual force.

Required auxiliary tooling: screwdriver (about 5 mm blade width)

1. Remove the black screw cover in top left position at the system's back wall (7 in Fig. 4 p.17).
2. Insert screwdriver into the groove of the screw that will be exposed after cap removal.
3. Turn the screw slowly in anticlockwise direction.

The lid will slowly tilt open.

Manual down-motion of sample block

If the sample block gets stuck in upper position, you should at first trigger a system initialization routine, in order to try to restore the sample block to its correct position. If this fails to remove the error, you can move the sample block down with mechanical force.

Required auxiliary tooling: screwdriver (about 5 mm blade width)

1. Place the SNPtower carefully onto one of its lateral sides.
2. Remove the protective cap at the bottom side of the system and introduce the screwdriver until mechanical stop position.
3. Rotate the screwdriver in anticlockwise direction.

The block will move down.

Retrieval of a jammed microplate

The lid cannot be opened due to a jammed microplate if:

- the microplate was inaccurately inserted into the block
- there is adhesive residue at the edges of the sealing foil.

1. Try to use the slots in the front panel to restore the microplate to proper position in the block.
2. Open the lid with manual force, as described in section "Manual lid opening".

If this fails to remove the error, the measuring head must be taken off. For a description of the procedure for head removal, refer to section "Cleaning of Lens Array" p.21.

Reinstallation of system software

In some cases, Windows may require you to provide driver software for communication with the SNPtower.

1. Insert the installation CD and follow instructions of Windows. If no installation CD is at hand, you can also find the required drivers in this directory: C:\Programs\ASpectSNP\Driver USB.

10 Disposal

It is the owner's/operator's responsibility to dispose waste materials (sample matter) resulting from measurement with the SNPtower in accordance with statutory rules and local practices.

Dispose the system, including its electronic components, on expiry of its lifetime as electronic waste under currently binding provisions of law.

Disposal

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